# The effects of selection at different ages for high and low body weight on the pattern of fat deposition in mice

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## SUMMARY

Two pairs of lines of mice, selected for High and Low weight at 5 weeks of age ($H_5$ and $L_5$) and at 10 weeks of age ($H_{10}$ and $L_{10}$) over 15 generations, were compared with each other and an unselected control line (QC) at three different ages, i.e. at 5, 10 and 21 weeks of age. Differences in percentage fat between High and Low lines were small at 5 weeks, clear-cut at 10 weeks and at 21 weeks the High lines were almost twice as fat as the Low ones. The $H_5$ line was slightly fatter than the $H_{10}$ line at all three ages and the $L_{10}$ line was fatter than the $L_5$ line at two ages. The developmental pattern of fat deposition was unaffected by selection for high or low weight at 5 weeks, i.e. the relationship between fat weight and carcass weight was similar in the $H_5$, $L_5$ and QC lines. Selection at 10 weeks affected the level of fat at low carcass weights and the relative rate at which fat was subsequently deposited. The different correlated responses resulting from selection at 5 and 10 weeks are explained in terms of genetic variation in (1) the rate of food consumption, (2) the efficiency of energy utilization for growth, and (3) the relative amount of fat deposited up to the age at selection.

## 1. INTRODUCTION

Although there have been many studies of the indirect effects of selection for body weight on the degree of fatness in mice (for reviews see Roberts, 1965, and Eisen, 1974) there is no overall interpretation of the recorded correlated responses which have been reported. Perhaps this is not surprising since the results were different in many cases. But the selection lines studied derived from diverse base populations, were selected using various criteria and assessed for fatness at different ages by several methods. Most of the studies involved acomparison of a single a 'large' line selected for increased body weight with an unselected line or a 'low' one. Many involved assessment of fat at a single age – a dubious procedure, as will be seen from the results below, for a trait which changes with age and weight. Only one study, unfortunately unpublished, compared replicate selection lines. It is not proposed to present a detailed and critical review of these experiments in this paper. Where appropriate the more relevant will be discussed as an aid for building up a general interpretation which can be evaluated experimentally in the future. Efforts to explain correlated responses in fatness have been rare. Fowler (1958) suggested

that certain large lines are fatter because selection for rapid growth favours animals with a high degree of fat deposition prior to the age of selection and she implied that changes in the frequency of 'genes causing fat deposition' were involved.

While there have been several studies of the effects of divergent selection, only one explored the possible outcome of selection for body weight at different ages. Hull (1960) reported that selection for high weight at 3 weeks of age resulted in significantly higher levels of fatness at 6 weeks of age than selection for high weight at $4\frac{1}{2}$ or 6 weeks. While the experiment was relatively short-term and the assessment of fat less comprehensive than usual, the result had extremely interesting practical implications. Hull suggested an explanation in somewhat the same terms as Fowler, i.e. that selection for high weight at 3 weeks was more effective at 'picking out those animals which will go on to lay down large amounts of fat'.

This paper deals with lines of mice selected for High and Low weight at 5 and 10 weeks of age. The correlated changes for three different ages in the level of fatness of the resulting lines are presented first in terms of measures of fatness at these particular ages and, secondly, in terms of allometric parameters which describe fat deposition relative to carcass growth. The latter method of presentation of correlated responses in fatness was used extensively by Clarke (1969) but his results were not published in a readily available form.

The results have led us to support and extend a relatively simple model of correlated responses linking body weight, rate of gain, rate of food consumption, efficiency of gain and relative degree of fat deposition which has been mooted in principle but not published by Professor Alan Robertson (Edinburgh).

The model involves a quite different conception of the genetic correlation between body weight and fatness from that suggested previously by Fowler (1958) and Hull (1960).

## 2. MATERIALS AND METHODS

### (i) *Selection scheme*

Two pairs of lines of mice were selected for high and low body weight at 5 and 10 weeks of age for 15 generations. These selection lines were derived from the same base population constituted in 1964 by mating representatives of six replicates of a control stock (Q/Fa) from the Institute of Animal Genetics, Edinburgh (see McCarthy (1967) and Falconer (1973) for details of this stock). This population (QC) was subsequently maintained by mating 16 males and 16 females in a rotational scheme designed to minimize inbreeding and acted as a source of selection lines as well as a control. The two pairs of lines $H_5$, $L_5$ and $H_{10}$, $L_{10}$ are named to indicate the direction of selection, High or Low, and the age in weeks at which selection was practised, denoted by subscript. The lines were originally selected at the same time from litters of the same 14 pairs of Q mice and subsequently bred by rotational mating of 14 selected pairs in each generation. All selection was based on within-litter deviations at a single age and this gave a possible effective population size of over 50 per line. In practice it was nearer 40.

In each generation the weights of progeny were recorded at birth, weaning

(3 weeks of age) and at 5 and 10 weeks of age but on two occasions weights were recorded at additional ages to monitor correlated responses in the growth curve up to 21 weeks of age. At generation 15 selection was relaxed. This has no significance other than that the lines were becoming slightly difficult to maintain; preweaning mortality, in the Low lines in particular, was becoming a problem. It was decided, therefore, to postpone selection indefinitely and breed by random mating in all selection lines after generation 15.

### (ii) *Fat analysis*

A random sample of mice from each line was killed at 5, 10 and 21 weeks of age three generations after relaxation of selection. The samples consisted of roughly equal numbers of males and females and, except for a few cases, all litters in a line were represented. The distribution of the mice according to line and sex at each slaughter age is shown in Table 1.

Table 1. *Numbers of male and female mice sacrificed in selected and control lines at three ages*

| Sex | Age at slaughter (weeks) | Numbers of mice from Line | | | | |
|-----|------|-------|-------|----------|----------|-------|
| | | $H_5$ | $L_5$ | $H_{10}$ | $L_{10}$ | Q |
| Male | 5 | 9 | 8 | 8 | 8 | 11 |
| | 10 | 8 | 5 | 7 | 3 | 10 |
| | 21 | 15 | 12 | 15 | 14 | 14 |
| Female | 5 | 7 | 12 | 7 | 7 | 12 |
| | 10 | 8 | 8 | 6 | 5 | 9 |
| | 21 | 13 | 11 | 13 | 14 | 14 |

Animals were killed by etherization and immediately weighed. The head, feet and tail were removed in a standardized way and the body was skinned and eviscerated. The carcass was then weighed. Carcasses were stored in individual plastic containers which were identified by code number and stored at $-10\,^{\circ}\text{C}$ to await chemical analysis. Carcasses from randomly chosen containers were analysed whole. First, each carcass was chopped repeatedly to roughly 3 mm pieces. The chopped carcass was then dried over silica gel in a vacuum box for 24 h. The fat was extracted from the whole dried carcass in a Soxhlet extractor using petroleum spirit. The petroleum spirit was distilled for 6 h at $41\,^{\circ}\text{C}$ and the fat was collected in a preweighed receiver flask. The flask was then placed in an oven at $100\,^{\circ}\text{C}$ for 3 h to remove any petroleum spirit from the fat, after which it was cooled and weighed. The weight of the fat was estimated by subtracting the weight of the flask from the weight of the flask and fat. For each mouse fat percentage (denoted % fat) was computed as:

$$\frac{\text{weight of fat}}{\text{weight of carcass}} \times 100.$$

### (iii) *Statistical analyses*

Data relating to the fat analysis were analysed in two basically different ways. First, the least-squares means of the different traits and estimates of their variances were obtained by a general least-squares procedure (Harvey, 1960) for each line at each age. Linear contrasts among pairs of line means for percentage fat at 5, 10 and 21 weeks of age were tested for statistical significance. The analysis was based on a model which included line effects, sex effects and sex-by-line interaction as fixed effects and litters-within-line and error as random effects as follows:

$$Y_{ijkl} = \mu + S_i + L_j + (SL)_{ij} + F_{jk} + E_{ijkl},$$

$Y_{jikl}$ = % fat for the $l$th mouse in the $ijk$th subclass,

$\mu$ = mean % fat for the population,

$S_i$ = fixed effect of the $i$th sex,

$Lj$ = fixed effect of the $j$th line,

$(SL)_{ij}$ = interaction of the $i$th sex with the $j$th line,

$F_{jk}$ = random effect of the $k$th litter in the $j$th line,

$E_{ijkl}$ = random error assumed $N(0, \sigma^2)$.

Secondly, the relationship between fat weight and carcass weight in each line was computed to allow comparisons of lines at fixed weights. Arithmetic plots of fat weight against carcass weight revealed a non-linear trend. Regression models that included linear and higher order terms were fitted to the data in an attempt to determine the relationship between fat weight and carcass weight within line-age subclasses. The data were transformed to logarithms and the linear regression of log fat weight on log carcass weight was computed. The value of the regression coefficient estimates the exponent $b$ in the allometric equation $Y = AX^b$, where $Y$ and $X$ are fat weight and carcass weight respectively. Differences among the within-age regression coefficients for a particular line were tested using the following statistical model (Duncan, 1974):

$$Y_{ij} = \mu + A_i + B_c(\bar{X}_{i.} - \bar{X}_{..}) + B_w(X_{ij} - \bar{X}_{i.}) + B_i(X_{ij} - \bar{X}_{i.}) + E_{ij}$$

$Y_{ij}, X_{ij}$ = the $j$th observation for fat weight and carcass weight respectively at age $i$,

$\mu$ = grand mean,

$A_i$ = the effect of the $i$th age class independent of variation in carcass weight,

$B_c$ = the slope of the regression of $\bar{Y}_{i.}$ on $\bar{X}_{i.}$,

$B_w$ = the slope of the regression of $Y_{ij}$ on $X_{ij}$ within classes that is common to all classes,

$B_i$ = the slope effect peculiar to the $i$th age class, and

$E_{ij}$ = random error assumed $N(0, \sigma^2)$.

Using the above model one can also compare the within-age regression coefficient, $B_w$, with the between-age regression coefficient, $B_c$, and differences in fat among the adjusted age means can be evaluated. Differences among lines in regression coefficients and adjusted means were evaluated using the above model with 'age' replaced by 'line' in the definition of the terms in the model.

## 3. RESULTS

### (i) *Body weight*

The long term effects of selection on the rate of growth of mice in the various lines are seen from the interpolated average growth curves of lines selected at 5 and at 10 weeks of age (Fig. 1). Since we propose to present more elaborate analyses of
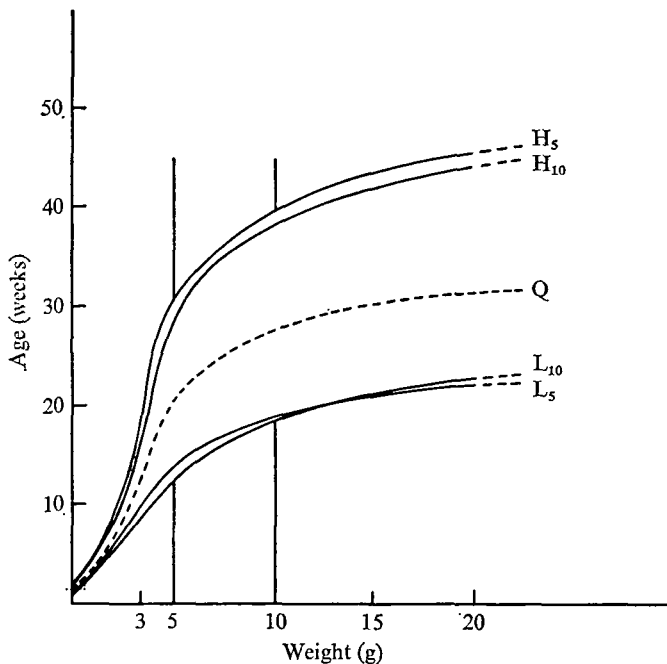


Fig. 1. Growth curves of lines selected for High and Low weight at 5 weeks ($H_5$ and $L_5$), at 10 weeks ($H_{10}$ and $L_{10}$) and of the unselected control population.

the basic data summarized above in future papers on the effects of different methods of selection on the form of the growth curve, it suffices here to summarize these results thus:

(1) The trajectories of the growth curves for the High lines were very similar, both reaching a weight of about 45 g at 21 weeks of age.

(2) The trajectories of the growth curves for the Low lines were also similar, reaching about half the average body weight of the High lines at 21 weeks of age.

## (ii) *Fatness relative to age*

Least-squares estimates of means for body weight, carcass weight and fat weight for each of the samples of mice analysed from the selected and control lines are presented in Table 2 for each of the three ages at which animals were analysed. The weight of fat at any particular age was increased by selection for high weight and decreased by selection for low weight.

Table 2. *Least-squares estimates of means for body weight, carcass weight and fat weight in selected and control mice sacrificed at three ages*

| | Mean weight (g) at week: ($+$ S.E.) | | |
|---|---|---|---|
| Line | 5 | 10 | 21 |
| $H_5$ | $31 \cdot 1 \pm 0 \cdot 53$ | $40 \cdot 1 \pm 0 \cdot 50$ | $46 \cdot 5 \pm 0 \cdot 63$ |
| $L_5$ | $12 \cdot 8 \pm 0 \cdot 54$ | $19 \cdot 2 \pm 0 \cdot 61$ | $23 \cdot 7 \pm 0 \cdot 91$ |
| $H_{10}$ | $27 \cdot 4 \pm 0 \cdot 80$ | $38 \cdot 2 \pm 0 \cdot 90$ | $44 \cdot 8 \pm 1 \cdot 15$ |
| $L_{10}$ | $14 \cdot 8 \pm 0 \cdot 36$ | $18 \cdot 6 \pm 0 \cdot 45$ | $22 \cdot 7 \pm 0 \cdot 42$ |
| QC | $19 \cdot 8 \pm 06 \cdot 1$ | $27 \cdot 2 \pm 0 \cdot 65$ | $31 \cdot 7 \pm 0 \cdot 80$ |

| | Carcass weight at week: | | |
|---|---|---|---|
| | 5 | 10 | 21 |
| $H_5$ | $9 \cdot 9 \pm 0 \cdot 55$ | $18 \cdot 6 \pm 0 \cdot 83$ | $23 \cdot 5 \pm 0 \cdot 56$ |
| $L_5$ | $5 \cdot 1 \pm 0 \cdot 36$ | $8 \cdot 3 \pm 0 \cdot 44$ | $11 \cdot 5 \pm 0 \cdot 56$ |
| $H_{10}$ | $8 \cdot 8 \pm 0 \cdot 41$ | $17 \cdot 4 \pm 0 \cdot 67$ | $22 \cdot 3 \pm 0 \cdot 60$ |
| $L_{10}$ | $5 \cdot 8 \pm 0 \cdot 30$ | $7 \cdot 8 \pm 0 \cdot 53$ | $10 \cdot 0 \pm 0 \cdot 31$ |
| QC | $6 \cdot 8 \pm 0 \cdot 30$ | $11 \cdot 0 \pm 0 \cdot 41$ | $15 \cdot 4 \pm 0 \cdot 50$ |

| | Fat weight at week: | | |
|---|---|---|---|
| | 5 | 10 | 21 |
| $H_5$ | $1 \cdot 2 \pm 0 \cdot 09$ | $3 \cdot 1 \pm 0 \cdot 21$ | $4 \cdot 9 \pm 0 \cdot 33$ |
| $L_5$ | $0 \cdot 5 \pm 0 \cdot 05$ | $1 \cdot 0 \pm 0 \cdot 43$ | $1 \cdot 5 \pm 0 \cdot 12$ |
| $H_{10}$ | $0 \cdot 9 \pm 0 \cdot 12$ | $2 \cdot 8 \pm 0 \cdot 24$ | $4 \cdot 2 \pm 0 \cdot 34$ |
| $L_{10}$ | $0 \cdot 7 \pm 0 \cdot 06$ | $1 \cdot 1 \pm 0 \cdot 11$ | $1 \cdot 2 \pm 0 \cdot 10$ |
| QC | $0 \cdot 8 \pm 0 \cdot 07$ | $1 \cdot 5 \pm 0 \cdot 17$ | $2 \cdot 3 \pm 0 \cdot 20$ |

Equally important in later argument will be estimates of variability for the traits at different ages. Hence the coefficients of variation for body weight and fat percentage, at each age for each line are presented in Table 3.

Estimates of the mean percentage fat at the three different ages in the samples of mice analysed from the selected and control lines are shown in Fig. 2. The deviations of individual means from appropriate control values are presented in Table 4. Without making specific comparisons, it is clear that the age at which lines are compared is critical in comparisons involving fat percentage. For example, at five weeks of age differences between lines were small in magnitude (and, in some cases, of opposite sign) in comparison to differences between the same lines at later ages. An important generalization of practical interest can also be made without further analysis: that the High lines, at 21 weeks of age were much fatter than the Low ones.

The statistical significance of differences between means of primary interest in

Table 3. *Coefficients of variation for body weight and percentage fat in selected and control lines at three ages*

| | Coefficient of variation in: | | | | | |
| | Body weight at week: | | | % fat at week: | | |
| Line | 5 (%) | 10 (%) | 21 (%) | 5 (%) | 10 (%) | 21 (%) |
| --- | --- | --- | --- | --- | --- | --- |
| $H_5$ | 5·9 | 4·3 | 4·7 | 18·4 | 21·1 | 23·6 |
| $L_5$ | 12·0 | 9·0 | 10·8 | 22·4 | 29·3 | 38·1 |
| $H_{10}$ | 10·1 | 8·2 | 8·9 | 21·1 | 22·6 | 26·6 |
| $L_{10}$ | 7·6 | 7·5 | 5·8 | 17·8 | 24·6 | 39·4 |
| Q | 11·9 | 9·3 | 9·7 | 18·1 | 28·0 | 31·4 |
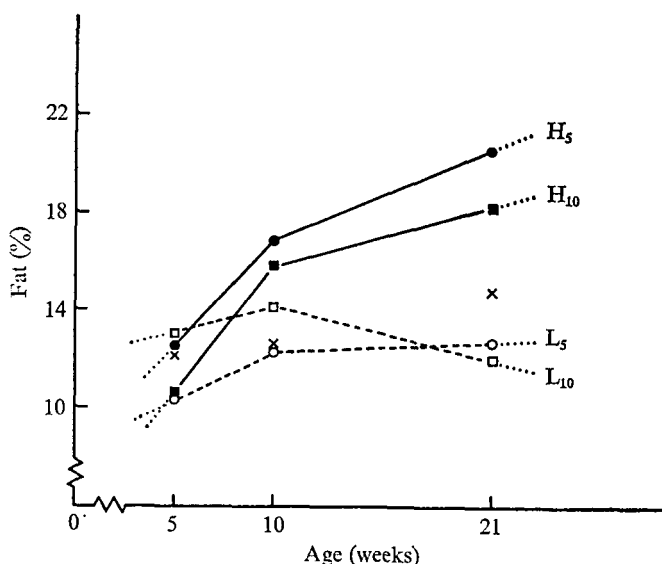


Fig. 2. Trends in percentage fat in High lines and Low lines selected at 5 ($H_5$ and $L_5$) and at 10 weeks ($H_{10}$ and $L_{10}$). (The Control (Q) means at three ages are marked by × ).

Table 4. *Least-squares estimates of the deviations in percentage fat of selected lines from the means of control line shown for three different ages*

| | Deviations from the control at week: ( ± S.E.) | | |
| Line | 5 | 10 | 21 |
| --- | --- | --- | --- |
| $H_5$ | 0·3 ± 0·72 | 4·2 ± 1·21** | 6·0 ± 1·28** |
| $L_5$ | − 1·8 ± 0·69* | − 0·2 ± 1·23 | − 2·1 ± 1·32 |
| $H_{10}$ | − 1·6 ± 0·73** | 3·0 ± 1·26* | 3·5 ± 1·26** |
| $L_{10}$ | 0·7 ± 0·76 | 1·5 ± 1·46 | − 2·6 ± 1·24* |
| QC (mean) | 12·1 ± 0·46 | 12·6 ± 0·77 | 14·7 ± 0·87 |

*, ** Indicate significant at 5 % and 1 % levels in this and following tables.

describing the effects of selection on fat percentage are shown in Tables 4 and 5. In summary, the statistically significant effects of selection were:

(1) Two-way selection for weight at 5 weeks of age produced lines which exhibited divergent positive correlated responses in fat percentage at each age.

(2) Two-way selection for weight at 10 weeks of age produced lines which ranked differently in fat percentage at 5 and 21 weeks of age.

(3) The $H_5$ line had a significantly higher percentage of fat at 5 and at 21 weeks of age than the $H_{10}$ line.

(4) The $L_5$ line had a significantly lower percentage of fat than the $L_{10}$ line at 5 weeks of age.

Table 5. *Least-squares estimates of differences in fat percentage between High and Low lines selected at the same age*

| Lines compared | Difference in fat percentage ( ± s.e.) | | |
| --- | --- | --- | --- |
| | Week 5 | Week 10 | Week 21 |
| $H_5$–$L_5$ | $2 \cdot 1 \pm 0 \cdot 76$** | $4 \cdot 5 \pm 1 \cdot 30$** | $8 \cdot 1 \pm 1 \cdot 37$** |
| $H_{10}$–$L_{10}$ | $-2 \cdot 3 \pm 0 \cdot 83$** | $1 \cdot 6 \pm 1 \cdot 57$ | $6 \cdot 1 \pm 1 \cdot 27$** |
| $H_5$–$H_{10}$ | $2 \cdot 0 \pm 0 \cdot 79$* | $1 \cdot 6 \pm 1 \cdot 34$ | $2 \cdot 6 \pm 1 \cdot 31$* |
| $L_5$–$L_{10}$ | $-2 \cdot 6 \pm 0 \cdot 80$** | $-1 \cdot 7 \pm 1 \cdot 5$ | $0 \cdot 5 \pm 1 \cdot 33$ |

The above significance tests are with respect to a conditional type of sampling that requires each sample of similarly selected lines always to be like the ones in the present study. Because of the variation among several similarly selected lines which may arise due to drift the above condition may not be fulfilled and the conclusion stated regarding the effects of selection may be rather liberal. Formulae for the sampling variances of direct and correlated responses to selection have been derived by Hill (1971). In the case of selection lines produced by divergent selection the sampling variance of the difference between High and Low lines at generation t for a correlated trait is

$$V(C_y) = \left(\frac{2\sigma_y^2}{N_e}\right) \{th_y^2[1 - h_x^2 r^2(1-p)] + (1 - \tfrac{3}{2}h_x^2 h_y^2 r^2)p\},$$

where $y$ is the correlated trait and $x$ is the trait under selection. No estimates of the heritability of percentage fat and its genetic correlation with body weight ($r$) were available for the present population. When values from the literature that seemed reasonable for these two paramenters were used the results shown in Table 6 were obtained. The same conclusions with regard to significance would have been reached using a wide range of values for these two parameters. Only three of the line differences were significant as compared with eight previously. This may indicate that caution is needed when interpreting the above results. The findings are, however, in general agreement with others in the literature, as will be pointed out in the 'Discussion'.

### (iii) *Fatness relative to weight*

When regression models that included linear and higher order terms were fitted to the line-age subclasses there were significant quadratic and cubic terms in most cases. After logarithmic transformation of the data none of the non-linear terms

were significant, except in one line-age subclass. However, the contribution of the non-linear term in this case was small and it was subsequently ignored.

The next step was to test whether the regression slopes of log fat weight on log carcass weight were the same at all three ages for a particular line and to compare the within-age slopes with that between ages. The results are summarized in Table 7. There were no significant differences (1) among the within-age regressions for any line (and so only the pooled values are shown) and (2) between the average within-age regression ($B_w$) and the between-age regression ($B_c$). Also, differences in log fat weight among the age means adjusted to a common carcass weight were not significant. The data from all three ages were thus pooled and one overall regression coefficient was estimated for each line. The estimates of these within-line regressions are presented in Table 8.

Table 6. *Differences in fat percentage at three ages between High and Low lines selected at the same age (and associated standard errors when drift is taken into account)*

| | Difference in fat percentage ($\pm$ s.e.) | | |
| --- | --- | --- | --- |
| | Week 5 | Week 10 | Week 21 |
| $H_5$–$L_5$ | $2 \cdot 1 \pm 1 \cdot 3$ | $4 \cdot 5 \pm 2 \cdot 1$* | $8 \cdot 1 \pm 3 \cdot 0$** |
| $H_{10}$–$L_{10}$ | $-2 \cdot 3 \pm 1 \cdot 3$ | $1 \cdot 6 \pm 2 \cdot 0$ | $6 \cdot 1 \pm 3 \cdot 0$* |

Table 7. *Pooled within-age ($B_w$) and between-age ($B_c$) regression coefficients for the Selection and Control lines and tests of significance of differences among them*

(Log fat weight = dependent variable, log carcass weight = independent variable.)

| Line | $B_w$ | $B_c$ | $B_w\ v\ B_c$ |
| --- | --- | --- | --- |
| $H_5$ | $1 \cdot 2 \pm 0 \cdot 19$ | $1 \cdot 6 \pm 0 \cdot 14$ | $F_{1.56} = 2 \cdot 7$ |
| $L_5$ | $1 \cdot 4 \pm 0 \cdot 14$ | $1 \cdot 2 \pm 0 \cdot 14$ | $F_{1.50} = 1 \cdot 0$ |
| $H_{10}$ | $1 \cdot 9 \pm 0 \cdot 23$ | $1 \cdot 6 \pm 0 \cdot 09$ | $F_{1.50} = 1 \cdot 5$ |
| $L_{10}$ | $1 \cdot 0 \pm 0 \cdot 27$ | $0 \cdot 9 \pm 0 \cdot 17$ | $F_{1.45} = 0 \cdot 1$ |
| Q | $1 \cdot 6 \pm 0 \cdot 21$ | $0 \cdot 7 \pm 0 \cdot 49$ | $F_{1.64} = 3 \cdot 0$ |

The two sets of lines, those selected at 5 weeks and those selected at 10 weeks of age, were analysed in two separate covariance analyses based on the regression of log fat on log carcass weight (see details in Materials and Methods). Two types of difference between lines were assessed:

(1) differences in the value of the regression coefficients of log fat weight on log carcass weight,

(2) differences in the elevation of regression lines of log fat weight on log carcass weight, deemed not significantly different in slope.

The first test allows statements regarding the 'relative rate of fat deposition, (Clarke, 1969), i.e. the percentage change in fat weight per unit percentage change in carcass weight. The second test allows general statements regarding the relative ranking in fatness of lines at similar carcass weights.

The regression lines and the values of the regression coefficients for each of the

selection lines and the relevant statistics in the two covariance analyses are presented in Fig. 3(a) and (b) and in Table 8 respectively. There were no statistically significant differences among lines selected at 5 weeks and the Control line, in the slope or in the elevation of the regression lines. When these three lines were pooled there was no significant departure from one overall regression. This suggests that selection at 5 weeks of age did not change the relative rate of growth of fat in the

Table 8. *Overall regression coefficients ($B_1$) for the Selected and Control lines and tests of significance of differences in slope aud elevation of regression lines among groups of lines selected at a single age and the Control*

(Log fat weight = dependent variable, log carcass weight = independent variable.)

| | Covariance Analysis of | | | |
|---|---|---|---|---|
| Lines | $B_1$ | | Lines | $B_1$ |
| $H_5$ | $1.5 \pm 0.09$ | | $H_{10}$ | $1.7 \pm 0.09$ |
| $L_5$ | $1.2 \pm 0.08$ | | $L_{10}$ | $0.9 \pm 0.15$ |
| Q | $1.3 \pm 0.10$ | | Q | $1.3 \pm 0.10$ |

Tests of differences
(1) Among $B_1$ values     $F_{2.180} = 2.1$ (N.S.)            $F_{2.171} = 8.7$**
(2) Between $B_{1w}$ and $B_{1c}$†     $F_{1.180} = 1.2$ (N.S.)
(3) Among line means (adjusted     $F_{1.180} = 0.6$ (N.S.)
      for log/carcass weight)

† $B_{1w}$ = Pooled within-line regression and $B_{1c}$ = between lines regression for the $H_5$, $L_5$ and Q lines.

selected lines or the relative level of fatness at constant carcass weight. In contrast, lines selected at 10 weeks of age and the Control differed significantly in their values of the regression coefficient which estimates the relative rate of growth of fat. It was not possible, therefore, to test the statistical significance of differences in fatness at constant carcass weight among these lines but it is clear from the regression lines in Fig. 3(b) that the pattern of fat deposition relative to carcass growth was different in these lines. In particular, higher levels of fat were recorded at low carcass weights in the $L_{10}$ line (Fig. 3b).

The statistical significance of differences between estimates of the regression coefficient in the $H_5$ and $H_{10}$ lines (1·5 and 1·7 respectively) and between the $L_5$ and $L_{10}$ (1·2 and 0·9 respectively) were subsequently tested by the same procedures. The difference in the case of the two High lines was significant at the 5 % level. The same arguments regarding the possible contribution of genetic drift to line differences in this parameter apply as in the case of percentage fat at a fixed age. Although Clarke (1969) found higher values of the regression coefficient of log fat weight on log carcass weight in replicate High lines than in Low ones he also found significant differences among replicates in this parameter of fat deposition. In theory, therefore, the differences among the lines selected at 10 weeks of age in the allometric exponent described above may be due in part, at least, to random genetic differences in the relative rate of fat deposition.
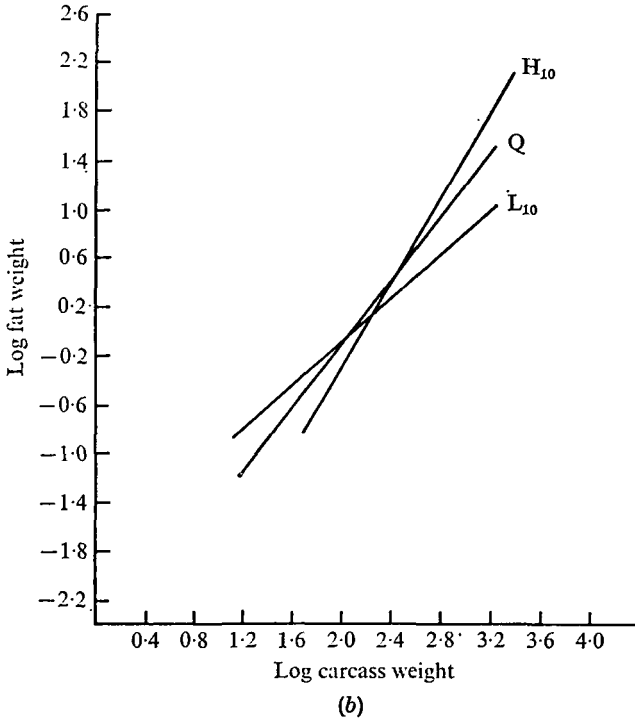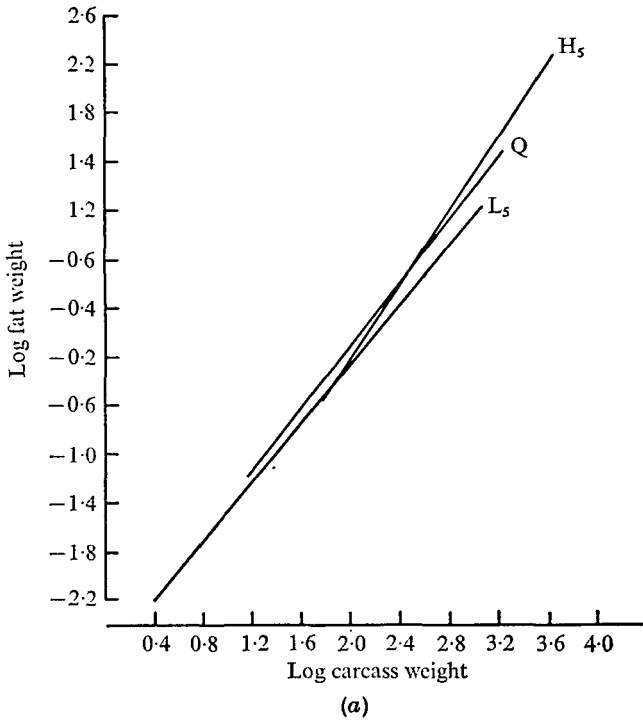
Fig. 3. The regression of log fat weight on log carcass weight in (*a*) lines selected at 5 weeks of age and the control (Q) and (*b*) lines selected at 10 weeks of age and the control (Q).

## 4. DISCUSSION

The first obvious feature of the results is that in every line selection for weight at one age resulted in positive correlated responses in body weight at other ages and in fat weight. High lines grew faster and accumulated fat at a greater rate than Low lines. This is a common finding (Fowler, 1958; Hull, 1960; Biondini, Sutherland & Haverland, 1969; Clarke, 1969) but a vital one for the purpose of interpretation. The correlated responses in percentage fat were complex, however. The results illustrate the danger of relying on estimates of fatness at a single age to monitor changes in carcass composition. The ranking of the $L_{10}$ line in percentage fat, highest at 5 weeks but lowest at 21 weeks illustrates this point aptly. However the correlated changes in percentage fat observed at later ages (i.e. at 10 and 21 weeks) agree with all previously reported results except those of Lang & Legates (1969).

In regard to the effects of selection at different ages, the results agree with those of Hull (1960), in general terms at least. Mice selected at the younger age for high weight were fatter than those selected at the older age. (From the data in Table 2 a rough estimate of the practical significance of the contrast can be computed; at fixed ages the $H_5$ line has at least 10 % more fat than the $H_{10}$ line.) The results for the two Low lines mirror-image the results of the High lines. They show that mice selected for Low weight at the older age were fatter at earlier ages.

The lines selected at 5 weeks of age did not exhibit correlated changes in the weight-related pattern of fat deposition. Taken in isolation, this result might be taken to imply that the deposition of fat in the base population was a wholly weight-determined process, the pattern of which was genetically invariable. Selection would therefore never change the proportion of fat at a constant weight. Further if a perfect genetic correlation existed between the rate of fat deposition and increase in body weight, the correlated responses in fatness at fixed ages would be simple and predictable. High lines would always have the highest proportion of fat at any given age – simply because fat forms an increasing proportion of the carcass as growth proceeds. A Low line, by the same argument, would have the lowest percentage of fat at any age simply because they were lighter. It is, however, obvious that this line of argument does not hold for the lines selected at 10 weeks of age. Nor is it consistent with some other results in the literature. Fowler (1958) and Clarke (1969) have both described Large lines which to quote the latter were 'relatively leaner prior to the age of selection and relatively fatter at older ages'. That is, although their Large lines became fatter at later ages they were *less* fat at equivalent carcass weights at younger ages.

It is obvious from studies of correlated changes in the growth curve, such as those illustrated in Fig. 1 and in several other experiments, particularly that of Roberts (1961), that the gross effect of selection is to reproduce genotypes with accelerated rates of growth in the case of Large or High lines and with decelerated ones in the case of Small or Low lines. We know nothing about the primary physiological action of the divergent genotypes which cause these gross changes. But a well-documented secondary effect of selection is that Large and Small lines differ considerably in

appetite (in terms of food consumed per unit time) (Timon & Eisen, 1970; Roberts, private communication).

In the case of selection for High and Low weight at 5 weeks of age, we suggest that selection operated wholly, or almost so, on variation caused by differences in the rate of food consumption. The effect of such selection, combined with an unchangeable weight-dependent pattern of fat deposition, would be to produce a $H_5$ line heavier and fatter at every age than the $L_5$ line, but having the same pattern of fat deposition relative to growth in body weight. But in the High and Low lines selected at 10 weeks of age in this study, and in the lines described by Fowler and by Clarke, selection for body weight produced different patterns of fat deposition. To explain this, we assume that genetic variation in body weight may also, in some cases, be due to differences in the proportion of fatty tissues which develop before the age at which selection is exercised.
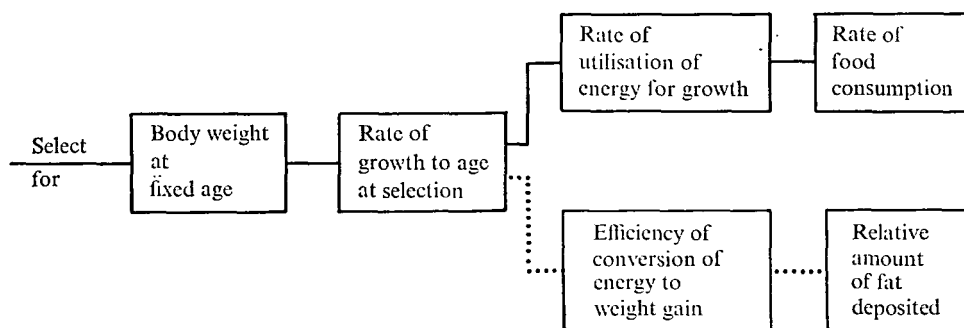


Fig. 4. The causal chain of correlated factors influenced by selection for body weight is shown from left to right. The broken line indicates factors which show correlated responses on selection at *older* ages (in this paper at 10 weeks).

Fig. 4 suggests the causal relationships between sources of genetic variation in body weight. In brief, it shows that differences among animals in body weight at a particular age mainly reflect differences in the rate of growth up to that age; the latter can be caused by genetic differences in

(1) the rate of food consumption,

(2) the conversion of food energy to weight gain.

Gain in weight results from the accumulation of muscle, fat (and bone), but the relative energetic costs of producing and maintaining a given weight of muscle and the same weight of fat are far different for two reasons:

(1) muscle contains upwards of 80% water while fatty tissue usually contains only about 15%,

(2) fat is denser energetically than protein on a dry-weight basis (9·45 $v$ 5·65 cal/g respectively).

The cost of gaining a unit weight as fat relative to a unit as protein is probably about 7 to 1 therefore.

We have some indirect evidence (see Table 3) to support the idea that selection for

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body weight at successive ages might differentially exploit genetic variation in relative fatness. Although the mean percentage fat at 10 weeks was only slightly higher than at 5 weeks in the unselected control, there was a large increase in the coefficient of variation for percentage fat between these ages.

Selection for body weight at young ages (in our case at 5 weeks) seems not to have exploited both sources of genetic variance, whereas selection at 10 weeks apparently did so. Selection in the $H_{10}$ line, according to this interpretation, favoured animals which consumed large amounts of food but which also utilized a relatively low proportion of metabolizable energy for fat deposition during growth up to the age at which selection was exercised. Because of simultaneous selection for these two components of body weight, it follows that animals in the $H_{10}$ line would be expected to have a lower degree of fat deposition at young ages, and a higher-than-average level of food consumption *after* the age of selection, compared with the unselected control. In the $L_{10}$ line selection for a relatively higher degree of fat deposition *before* the age of selection, combined with selection for a lower rate of food intake *after* the age of selection would have occurred. These combinations of correlated changes in our opinion underlie the changes in the allometric equation describing fat development in the $H_{10}$ and $L_{10}$ lines.

The result of most practical interest which agreed with the findings of Hull (1960), i.e. that selection at older ages for high weight produced leaner animals is also explicable in terms of the set of correlated responses postulated above, as follows. Although selection for high weight will favour animals with large appetites no matter when selection is practised, at later ages screening will also occur for relatively lean animals, i.e. ones which grow more efficiently by depositing relatively less fat. It follows that selection for low weight at later ages should produce the fattest mice of all at low weights – as reported for the $L_{10}$ line.

The model introduced above needs further justification on theoretical grounds and testing by experiment. We propose to furnish such justification in review form elsewhere. We are also measuring food consumption and recording fat development in different parts of the body in these lines in an effort to provide more convincing evidence of the postulated genetic relationships between age at selection, the direction of selection and the pattern of fat deposition.

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