A review of the literature on the genetic control of growth and development in the mouse indicated a lack of knowledge of the degree to which variation in the shape of the curve of body weight growth reflects variation in the developmental pattern of fat and non-fat tissue growth and of the precise extent to which these two growth processes are under independent or under common genetic control. The review also indicated the allometric equation to be a useful method of quantifying the developmental changes associated with normal body weight growth.

Preliminary investigations confirmed the utility of the allometric method by its characterisation of fat development in the genetic obese strain of mice relative to their normal litter mates, and showed the fat-free dry matter component of the carcass to be a useful indicator of phenotypic variation in carcass nitrogen content.

The allometric coefficients of linear relationship on a logarithmic scale showed, for normal mice, that fat development occurred at a 2 to 3-fold greater rate in the case of the gonadal fat depot, and at a 10-fold greater rate for total chemical fat, relative to the percentage rate of growth of the carcass as a whole.

In contrast to the positive correlated responses in absolute amounts of fat, relative carcass fat content was altered little at a given age by selection for high or low body weight at that age in the case of total fat, but was decreased in the case of gonadal fat depot. Selection also resulted in a positively correlated response in the rate of development of total fat relative to carcass weight, with the result that the obese strain mice tended to be relatively leaner prior to the age of selection and relatively fatter at older ages. Significant variation was found to exist among replicates in the extent of these responses. Important effects of sex, age and genotype were established for the extent to which variation in the weight of gonadal depot fat reflected variation in total chemical fat weight.

Selection for body weight at six weeks of age was found to have had very little effect upon the shape of the growth curve to 66 weeks of age. Genetic
variation in growth curve parameters was very largely confined to genetic variation in mature body size. Mature body size was positively related to the time which individual mice took to mature, and variation in relative fat content was found to be associated with the joint variation in those two growth curve parameters.

A half-sib analysis demonstrated the presence of genetic variation in relative carcass fat content at 9 weeks of age, - heritability of the order of 0.5 in comparison with an estimate of 0.4 for absolute fat content. Selection for relative fatness - defined in terms of the deviations about the phenotypic regression of fat on carcass weight - was expected to result in a negative correlated response in carcass weight and to sacrifice a little of the progress in absolute fat content relative to that possible from straightforward mass selection for fat weight alone. Selection about the genetic regression line maintained carcass weight constant and made no such sacrifices. Selection for carcass weight at 9 weeks of age was expected to produce animals of lower than average relative fat content at that age.
STUDIES ON THE CHEMICAL CONTROL OF GROWTH IN MICO.

by

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I. INTRODUCTION

The phrase "genetic control" may be used to refer to the way in which genes exert their effects upon the biochemical reactions of the metabolic pathways they control - i.e. to the biochemistry of gene action and effect - or in a more general sense to the degree to which the biological processes are monitored by genetic influences. The first usage relates to the manner of gene action which is the prerogative of the molecular biologist and biochemical geneticist, while the second refers to the degree of genetic determination which is the province of the quantitative geneticist. It is this second usage of the phrase that is relevant to the present thesis.

As has been discussed by Falconer (1960), quantitative genetics is concerned with an analysis of the "genetic architecture" of biological characters in a population of individuals. With the observable properties of such a population being capable of specification in terms of means, variances and covariances for the characters of interest, the broad aim of the population geneticist is to discover the degree to which these parameters are influenced by the properties of the genes concerned, and by the various non-genetic circumstances which may influence the expression of biological characters. For this purpose quantitative geneticists frequently make use of the natural or created subdivision of a population into families for a static analysis of the differing degrees of resemblance between related and unrelated individuals. Their aim is to partition the observed variances and covariances into parameters describing properties of the genes involved and of the environment in which they act. Such an analysis may permit the realisation of his practical objective - that of applying his knowledge to
the task of manipulating the genes in order to change the expression of the character in any desired direction, or to the problem of deciding whether such attempts are likely to be profitable. Although such application involves the manipulation of the available genetic variation and covariation in comparative ignorance of the genes involved, it does permit a further retrospective analysis of a population's genetic properties. As has been emphasized by Robertson (1963), the method is potentially valuable for determining critical points in the biological pathways which determined the observed genetic response, thereby allowing a fuller understanding of the physiological processes which have been altered.

Both these methods have been applied in the present thesis to the genetic analysis of body weight growth. The study has been directed in particular to the separable end-point components of growth in body weight, and especially to the fat and fat-free components of the mouse carcass. Heritable variation in body weight has frequently been utilized in selective breeding to alter body weight growth far beyond the limits found in the original population. The review by Robert's (1965) has discussed the details of this work for the case of the laboratory mouse and has also dealt with changes in genetically related characters which have accompanied the response of body size to selection. Though there now exists a good understanding of the genetic responses to selection for body size at a given age, it is clear from Robert's review that we know less about the precise changes induced in the pattern of body weight growth to maturity. What effect for example, does selection at a given age have upon the shape of the body weight growth curve and is this capable of being clearly specified in any objective way?
Despite the number of reports available the same feature is apparent for work on body composition - an overall picture is apparent, but precise quantitative generalisations have seldom been attempted. Thus while the work has shown that usually all body components contribute to the differences between strains of mice selected for large or small body size, we still know little about the precise contribution that is made by each.

The broad aim of the present study has been to attempt a quantitative description of postnatal body weight growth and in particular of the pattern of association between the fat and fat-free compartments of the body. Attention has been restricted to just these two of the many possible components of body growth because of their immense importance in the field of animal production, and in order that the resources available might be concentrated on obtaining a sufficiently accurate assessment of the degree to which their relative growth is under genetic control. Particular attention has been paid to the following aspects:

(i) Variation in the growth of fat relative to overall body weight growth between strains of mice selected for large and small body size.

(ii) The genetic control of body weight growth patterns and the relationship between growth curve parameters and carcass fat content.

(iii) Genetic parameters of carcass fatness in a random breeding population of mice.

Preliminary investigations have involved a consideration of the extent to which variation in fat-free carcass weight reflects variation in carcass protein content. They have also included a study of the manner in which Ruskey's (1932) allometric equation for representing changes in development
is able to detect gross differences in relative carcass fat proportions by its discrimination between mice containing the obese mutant gene and their normal litter mates.
II. REVIEW OF LITERATURE

A. GENETIC VARIATION AND COVARIATION OF GROWTH AND FATNESS IN THE MICE

The aim of this section of the review is to briefly consider the extent of current knowledge on the genetic control of body weight growth in the laboratory mouse and the genetic relationships between growth and carcass composition particularly in terms of the fat and fat-free components of the carcass.

Because body weight is a convenient biological trait that can be easily measured objectively, it has been extensively used by geneticists concerned with evaluating the theory of quantitative genetics. As a consequence, and because the laboratory mouse has proved to be an extremely useful experimental mammal for genetic research, there has arisen a vast literature which deals with the genetic analysis of body weight growth. However, because much of the information comes from experiments concerned with genetic theory rather than from experiments concerned with analyzing the genetic architecture of the biology of the growth processes, there exists far less knowledge on the genetic variation and covariation in the multiplicity of bodyweight components. This is especially true of the genetic associations between body components and the pattern of age change in growth. Roberto (1965) has thoroughly reviewed the literature on the genetic analysis of body weight growth and only the main conclusions from the earlier work will be highlighted here.

Comparisons of the variation between related and unrelated individuals from random mating populations have provided ample evidence of genetic
variation in the weight of a mouse at a given age. Selection experiments also have established that much of the variation has an additive genetic basis. Estimates of the heritability have ranged from zero to 0.6, depending upon the method of estimation, the population sampled and the particular ages at which body weights have been measured. Selection experiments have elicited responses in mean body weight growth to six weeks of age of as much as 5 - 8 times the original additive genetic standard deviation in the base population (Falconer 1960).

During recent years biologists are beginning to take advantage of the selection experiment as a technique by which large genotypic differences may be produced for the purpose of examining the genetic architecture of biologically interesting characters. Selection for body weight in the mouse has invariably produced concomitant changes in other characters and thus also provides a technique for examining genetic relationships between biological processes. Roberts (1965) has also reviewed correlated responses to body weight selection for the laboratory mouse. Those experiments which are particularly concerned with the correlated changes in growth patterns and carcass constituents will now be examined in greater detail.

1. Genetic Differences in the Pattern of Growth.

The early selection experiments, reviewed by Roberts (1965), established that selection for body weight at a specific age brought about correlated responses in body weights at other ages, both preceding and following the age at which the selection criterion was measured. Fowler (1958) made a detailed study of the patterns in growth for lines of mice (N-strains) which had been selected by Falconer (1953) for large and small body weight at six
weeks of age over a period representing between 20 and 30 generations of selection. She found the differences in body weight between the selected lines and their controls to be apparent at birth and to be maintained up to the oldest age studied of 30 weeks. The patterns of growth appeared to be similar for all 3 lines, although differences in absolute and relative rates of growth reached a maximum between 3 and 5 weeks of age and declined thereafter. The large line grew at a faster rate than the small line with the control line intermediate. The period of maximal line differences in body weight growth thus corresponded to the time at which peak absolute growth rates occurred.

Hull's (1960) experiment which involved the production of lines of mice by within-litter selection for increased body weight at 3, 4, and 6 weeks of age, also demonstrated the high genetic association between body weights at different ages. His direct and correlated responses demonstrated that body weights at these 3 ages were highly genetically correlated with one another, although less so the greater the age interval involved. This appears to be a consistent feature of animal growth, Taylor and Craig (1965) having established for cattle an exponential decline in inter-age genetic correlations between linear body measurements with increasing difference in degree of maturity between the ages correlated. Many workers have concluded from this pattern of high inter-age genetic correlations, that body weight is controlled by a similar set of genes throughout growth (Taylor 1968).

Roberts (1961) in his study of the lifetime growth of strains of mice selected for large and small size found that the line differences in the mean body weights became greater as the animals grew older, although the proportionate difference remained rather constant. Both of two large strains examined
achieved similar maximum body weight. However, one reached its maximum at six months of age and the other not until one year old, thus establishing a genetic difference in the age pattern of growth. Genetic differences in the shape of the Gompertz growth curve have also been found for inbred strains of mice and their crosses by Laird and Howard (1967), this being particularly apparent from Taylor's (1968) extended analyses of their data.

Lang (1967) fitted the von Bertalanffy growth function (Fabens 1965) to the body weight means of mice that were the product of some 30-35 generations of selection for large and small body size at six weeks of age. Unfortunately, the results of Lang's analysis are not particularly informative, even when the analysis was confined to the postweaning growth period in an effort to eliminate an early preweaning sigmoid cycle of growth with an inflexion point around 12 days, and to concentrate on the second growth cycle with its inflexion point around 4 weeks of age. This was perhaps due to the considerable seasonal variation observed for the line differences in comparison with the control animals. Nevertheless, positively associated responses in mature body weight were established, and it seemed that the time of maximum growth rate (inflexion point) was later for the large line (relative to the controls) and a little earlier for the small mice. The sex difference found by Lang (1966) was, however, more marked, males showing higher asymptotic weights and being older at the point of inflexion than females, for all line and season comparisons. Taylor (1968) has established that male mice tend to mature more slowly than females, this still being true when their greater mature size is taken into account.

Timon and Lison (1969) examined the estimated and derived parameters obtained from fitting the generalised sigmoid (Richards 1959) and logistic
functions to mice from the 9th generation of a line selected for high post-weaning growth to 6 weeks of age, along with their contemporaneous random-bred controls. The functions were fitted to 216 individual mice with 14 body weight records between the ages of 5 and 98 days. The results indicated that the 2 functions were not greatly different in their description of the growth patterns of these animals, in that the estimated shape parameter of the Richards' function was not significantly different from the pre-determined shape of the logistic function which specifies an inflexion point at exactly half asymptotic size. In addition, both functions gave similar residual variation about the fitted curve and similar growth trajectories and estimates of asymptotic size. Analysis of line differences showed that selection for post-weaning growth had increased body weight over the entire growth period and had no effect on the relative growth rate or of the shape of the growth curve. There was, however, evidence of sex differences in the shape of the growth curve. Males were also older and heavier at the point of inflexion than females.

Under the assumption that maternal influences are not likely to be of importance, litter differences indicated the presence of considerable genetic variation and some strong genetic correlations among the fitted parameters. The intra-class correlation derived from the between-litter component of variation for the age scaling parameter was very different for each of the 2 functions, being 0.30 and 0.77 for the Richard and logistic functions respectively. This difference and the zero genetic correlation between these 2 parameters suggested that these parameters are biologically very different traits. The high intra-class correlation (0.53) for the Richards shape parameter provides evidence of genetic variation in the shape of the curve of
body weight growth. The authors emphasise the need for growth functions of this type to be evaluated on growth data covering more extended periods of time. This would seem to be important in view of the under-estimation of asymptotic weight by both the functions they evaluated, and particularly in view of the persistent body weight increases that mice have been found to display through to much older ages than they were able to consider (Roberts 1961, Laird 1966).

A genetic analysis of the 3 parameters of the logistic model has also been undertaken by Carion (1965) for 6,000 male mice with weekly body weight records collected over 4 generations and covering the growth period between birth and 8 weeks. The percentage of the total variation, as evidenced by a nested analysis, contributed by generations, sires, dams and error are shown in the following table, along with the within generation heritabilities calculated from these estimates.

Table 1. Percentage Variation in Logistic Growth Parameters
(from Carion 1965)

<table>
<thead>
<tr>
<th>Source</th>
<th>A</th>
<th>B</th>
<th>e^{-k}</th>
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<tbody>
<tr>
<td>Generation</td>
<td>7.6</td>
<td>8.8</td>
<td>3.6</td>
</tr>
<tr>
<td>Sire (S)</td>
<td>3.8</td>
<td>2.1</td>
<td>6.4</td>
</tr>
<tr>
<td>Dam (D)</td>
<td>14.0</td>
<td>26.0</td>
<td>29.6</td>
</tr>
<tr>
<td>Error</td>
<td>74.6</td>
<td>66.5</td>
<td>54.9</td>
</tr>
<tr>
<td>h^2_S</td>
<td>.16</td>
<td>.09</td>
<td>.28</td>
</tr>
<tr>
<td>h^2_{S+D}</td>
<td>.39</td>
<td>.59</td>
<td>.78</td>
</tr>
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The data indicate important dam (i.e., maternal and / or dominance) components of variation, the heritability estimates based on the sire components being quite low. These results thus indicate that the estimation of genetic variation from the between-litter component is likely to be rather misleading for these traits. The importance of the dam component to variation of the time scaling parameter \((k)\) was, however, considerably less for control group animals which were not exposed to irradiation treatment at 70 days of age.

Timon (1968) also found a low heritability for the rate constant \((k)\) of the logistic curve \((0.07 \pm 0.18)\) from his analysis of sire and sex differences in a sample of 246 mice with 6 body weight records between birth and 12 weeks. This analysis did, however, provide a heritability estimate of \(0.51 \pm 0.27\) for age at the inflexion of the logistic body weight curve.

2. Genetic Differences in Carcass Composition

There has been extremely little direct study made of the amounts of genetic variation that exist for components of the mouse carcass. Even for a species such as the sheep where the body components and their relative amounts and distributions are of tremendous importance to the value of the carcass for food, there has been remarkable little in the way of objective investigation of within-breed genetic variation (Bowman 1968). More is known of the genetics of body development for pigs and cattle, but even for these species much of the information lies embedded in a confused mass of literature, largely because of the difficulties of finding biologically suitable quantitative measures of the body components and of deciding what components are of economic interest to the value of the carcass as an agricultural product.
The value of indirect assessments of the relative importance of genetic variation such as can be obtained from the analysis of correlated responses in selection studies has previously been mentioned. It is in this field that most of the present knowledge has been derived for the mouse, a number of studies having been made of the carcass composition of lines of mice produced by selection for body weight growth (Roberts 1965).

Responses to selection for increased body weight at a given age must inevitably lead to genetic differences in the absolute rates of deposition of some or all of the body components. Of particular interest to a developmental study of the genetics of body composition is whether selection for body weight could lead to changes in the relative proportion of the components and whether such genetic changes indicate departures from the normal pattern of differential tissue growth. It will become apparent that this second aspect is one that has barely been considered in the studies that have so far been reported.

A general compositional difference was claimed by Falconer and King (1963) for the positively selected strains of Goodale and MacArthur. MacArthur's strain was described as fat but not particularly large in linear dimensions, while the strain of Goodale was noted to be large-bodied and apparently less plump relative to its body size.

A quantitative study of the comparative carcass composition in mice selected for large and small body weight at six weeks of age was made by Fowler (1958). Working with Falconer's M-strain (Falconer 1953) and C-strain (Falconer 1960) lines, Fowler studied the changes in absolute and percentage carcass components with age. From graphs with the gut, body fat, protein plus mineral, and body water components of the carcass plotted against age, Fowler
concluded for the l-strain mice that protein was deposited at a slower more
even rate over a longer period of time and that there was no sudden increase
in the rate of fat deposition at 5 weeks of age in the small line as compared
to the large line. Both lines showed, a steady increase in the growth of
fat with age and it is difficult to tell from the graphs presented, whether
the shape of the curve of fat growth with age was really very different.
The absolute rates of fat deposition with age were however, clearly different.

In contrast to the l-strain, Podgor (1950) concluded for both the large
and small lines of the C-strain, that protein and water were deposited at a
fairly constant rate up to 12 weeks of age and that the rate of fat deposition
increased only slowly. Her results thus indicate a different pattern of
developmental growth for fat in these two strains of mice.

Following on Podgor's (1950) results, Hull (1960) conducted a study to
test the suggestion that selection before and after 5 weeks of age might
produce different responses in terms of the fat content of mouse carcasses.
He selected for body weight in three separate lines at the ages of 3, 4, and
6 weeks, and examined the changes in the fat content of the carcasses.
Contrary to expectation however, Hull found after five generations of within-
litter selection, that the 3 week line had a greater amount of abdominal fat
at six weeks of age than either of the 4 week or 6 week lines. The following
table presents the heritabilities and average genetic correlations estimated
from his responses to selection and from his half-sib analysis of abdominal
fat weight at 6 weeks of age conducted in an unselected and randomly mated
population.
In contrast to the results of Fowler (1958), Lang (1967) found little change in the chronological pattern of fat (ether extract) percentage between 3 and 6 weeks of age, for mice of large or small strains that had been selected on the basis of their body weights at six weeks of age. A difference was apparent for both sexes between 6 and 8 weeks, small mice exhibiting considerably higher levels of percentage fat at 7 weeks but returning again to the lower level of the large animals by 8 weeks of age.

Variable correlated responses in body components to selection for body weight growth in lines derived from a single base population have been reported by Biondini et al. (1968). They studied whole body components in a random bred control and in 3 replicate lines that had been simultaneously selected for 28 to 77 day body weight gain over a period of 10 generations. Large significant responses in fat content (absolute and percentage levels) were found for 2 of the lines, but were not apparent for the third line despite the fact that body weight gain had been increased significantly (by 58% in comparison with the 84% and 76% increases for the other 2 lines - Sutherland 1966).

<table>
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<tr>
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<th>W3</th>
<th>W6</th>
<th>U6</th>
<th>AF6</th>
</tr>
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<tbody>
<tr>
<td>W3</td>
<td>0.74 ± 0.14</td>
<td>0.94</td>
<td>0.82</td>
<td>1.00</td>
</tr>
<tr>
<td>W6</td>
<td>0.44 ± 0.27</td>
<td>0.94</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td>U6</td>
<td>0.57 ± 0.20</td>
<td>0.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AF6</td>
<td>0.56 ± 0.17</td>
<td></td>
<td></td>
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</tbody>
</table>
One further recent report of Timon et al. (1969) has provided further evidence of large increases in the percentage of fat in the carcass being associated with responses to selection for post-weaning growth to 6 weeks of age. The authors noticed that the line difference for the other extract component was less fully expressed under a restricted feeding regime. They found no line differences in the percentage composition of the fat-free carcass.

3. Relationships Between the Pattern of Growth and Carcass Composition

Very little inquiry has been carried out for any animal species as to whether a knowledge of the way in which an animal has grown to reach a given final body weight provides any insight into the relative proportions of its body components at that weight. Since adipose tissue is energetically more dense than non-fatty tissue - i.e. has a greater calorific content per unit weight - it is to be expected that developmental variation in the partitioning of the energy available for growth between these two components would lead to variation in the pattern of body weight growth.

In the case of the mouse, one such attempt has been made at the phenotypic level by Timon (1968). He failed, however, to demonstrate any really very close relationship between the time scaling parameter of the logistic curve and the percentage ether extract or protein contents of 46 mice which had been slaughtered at 12 weeks of age. The highest correlations found were for percent ether extract and the ratio of protein to ether extract, being 0.3 and -0.4 respectively.

Laird (1966) has made a comparative between-species study of mammalian growth curves by expressing body weight as a fraction of mature size on a time
scale which was transformed to produce a doubling of body weight at the inflexion point of the Gompertz growth curve. Such a presentation suggested that the Gompertz growth function required supplementation by an additional linear growth process, which was far more variable in expression between the species examined than was the underlying sigmoid growth pattern. Although no direct experimental evidence was available, she interpreted this linear process as indicating an accretionary type of growth, suggesting that it may be related to fat deposition. Her reasoning is probably based upon the assumption that the growth of fatty tissue results largely from the inert accumulation of fat in adipose cells, an assumption which is by no means supported by all the available evidence on the physiology and histology of adipose tissue (Kinsall 1962 and Liebelt et al. 1965). It is interesting to note that the laboratory mouse exhibited the largest linear component of all the species examined by Laird (1966).

4. Some Physiological Investigations Relevant to the Genetic Control of Growth and Carcass Fat Content

Amino acid utilisation and protein synthesis, being prerequisites to non-fat increases in body size, induced Gall et al. (1967) to make a study of some genetic parameters of protein metabolism and growth for a randomly mating population of mice. From a nested analysis of variation attributable to sires, dams and litter mates, they demonstrated positive genetic correlations between protein metabolic activity and body weight, carcass weight and the nitrogen contents of the carcass at 28 days, but low negative genetic correlations at 42 days.

This appears to be the only genetic study of continuous variation that
has been made of biochemical traits and their association with gross quantitative growth and carcass characters. For further understanding of the genetics of the physiological aspects of growth and fat development, one must turn to the massive amount of work that has accumulated on the physiology and biochemistry of the discontinuous variation produced in such conditions as the "obese-hyperglycaemic" or "adipose" mutants of the mouse.

Bulfield (1968) reviewed the current state of knowledge in this area, as a part of his study which attempted to find the primary biochemical lesion in these mutant stocks. Although this goal has not yet been fulfilled, the voluminous amount of work that has been carried out has turned up a number of interesting enzymatic associations for these excessively obese conditions and for animals made obese by appetite stimulation through the destruction of the hypothalamic satiety centre.

Animals made obese by hypothalamic interference, frequently called auro-thio-glucose, or ATG. mice because the condition is commonly produced by injection with this chemical, have played an important part in genetic studies of the enzymatic basis to the fatness of obese and adipose mice. The technique provides a phenocopy of the genetic conditions, in that fatness can be elevated to almost the same level at equivalent ages (Bulfield 1968). However, there is evidence which has been discussed by Bulfield (1968) and Mayor (1960), that the ATG. animals represent a completely different syndrome to that of obese animals. Although they are physically similar, there are many important physiological differences between them. These differences have led Mayor (1960) to postulate two quite different mechanisms producing the two conditions. He considers the ATG. animals to be an example of "regulatory obesity", the obesity apparently being entirely due to their
hyperphagia; the obese condition he holds to be an example of "metabolic obesity" in that the cause would appear to be some defect of their metabolism which results in a large proportion of the energy available for their growth being diverted into fat metabolism. Thus, when starvation is employed to bring obese animals back to body weights characteristic of their normal litter mates, it has been observed that ATG. animals also return to similar proportions of their body components. Obese animals on the other hand, remain at higher levels of fatness and appear to carry on laying down fat at the expense of other body tissues. Because of this fundamental difference ATG. obesity has been important in distinguishing between direct and indirect enzymatic differences associated with the obese gene. The levels of activity of the enzymes studied by Bulfield (1968) were found to be comparable for both ATG., obese and adipose animals and for this and other reasons that have been discussed by Bulfield, could not be held to be the enzymes primarily responsible for the genetic conditions.

Yohas et al. (1967) studied the plasma activity levels of four enzymes for 23 inbred strains of mice and found a large amount of between-strain variation and variable amounts of within-strain variation which depended upon the enzyme being examined. They did not, however, consider the levels of enzyme activity in relation to any in vivo biological traits representative of the end-point products of the relevant enzymatic pathways. The pronounced difference in the developmental pattern of fat growth found between the two strains of mice examined by Fenton (1956) would lay emphasis on such an approach for studies of the genetics of fat metabolism.
B. THE ALLOMETRIC APPROACH TO THE ASSESSMENT OF VARIATION IN BODY COMPOSITION.

Seebeck's (1968) detailed reviews on developmental studies of body composition emphasise the advantages to be gained from the analysis of body composition as a developmental study in which the development of an animal is defined as the sum of the changes in overall weight as it approaches its mature size (i.e. growth), plus the associated changes in which the components of an animal alter in their relative proportions (i.e. differentiation).

The developmental approach becomes essential because of the associated changes in the body components that accompany normal body weight growth. These require to be taken into account when assessing differences in body composition between groups of experimental animals which are at different stages of their growth. A great variety of analytical methods have been employed for this purpose, the review articles of Seebeck (1968) and Cock (1966) giving a broad coverage of the literature on this topic.

1. The Assessment of Developmental Changes

The assessment of developmental changes requires that sets of measurements be taken on animals during successive stages of their development and imposes a serious limitation on the type of data that can be collected for body composition studies which often require the destruction of the animal for the measurements to be made. As a result longitudinal studies of development, in which successive measurements are made on the same animals over the growth period, and which are so enthusiastically encouraged by Cock (1966), are frequently not possible using direct measures of body composition. Although the use of indirect methods of estimating body components could make such longitudinal studies possible, Seebeck (1968) doubts whether many of the
proposed existing techniques are sufficiently reliable for this purpose. He also warns of the dangers that would arise from their use should the relationship between the indirect measurements and the body components differ between groups of animals being compared. This is a feature frequently ignored by proponents of indirect estimation.

An alternative to longitudinal studies is to consider measurements made on different animals at the same time or at pre-arranged times or stages of development, and to estimate the mean developmental trend for groups of animals rather than for the individuals. Data of this type have been called cross-sectional data. The classification of data into categories of this type, as has been done by Kavanagh and Richards (1942) and Tanner (1951), has been summarised by Cock (1963). An essential point of difference of cross-sectional data from data of the longitudinal type is that the former fails to yield information on individual variation in body development. However, as both Cock (1963) and Seebeck (1968) point out, the value of cross-sectional data can be enhanced by ensuring there is no bias in the allocation of the animals to the subgroups (i.e. by randomisation), and by minimising the amount of variation within each of the subgroups by restricting the randomisation on the basis of prior knowledge of the animals' growth.

The third class of data, static data, in which the required set of measurements is taken only once on each individual, is unable to contribute information on changes in body development except in the restricted case where patterns of development are known to be relatively consistent from animal to animal and the average developmental trend has previously been established. Despite its limitations static data tends to have been the most frequently used type and have proved useful in the delineation of problems
which need to be investigated using a more precise developmental approach (see, for example Cook 1966).

The great variety of statistical methods which have been used for the analysis of developmental changes may be divided conveniently into two groups; bivariate, which are largely concerned with analysing the relationship between only two measurements at a time, one usually being a criterion of growth and the other a criterion of development; and multivariate methods.

Tulloch (1964a) cites the following bivariate methods that have been commonly used to describe body development:

(a) The weight of a component expressed as a fraction of body weight at various body weights or ages.

(b) The weight of a part expressed as a fraction of body weight at one age (or weight), compared with the fraction calculated at another age (or weight), one of the ages usually being birth.

(c) The measurement of the component expressed as a fraction of its own measurement at an earlier age or weight (usually birth).

(d) The part expressed by a measurement in any one of the above three ways, in relation to a measurement of another part chosen as standard and which shows relatively little change throughout post-natal life.

(e) The measurement of a part is plotted against the measurement of another part, against body weight or against age, using either an arithmetic or a logarithmic grid.

A number of workers, Anderson (1956), Heroux and Gridgeman (1958), Heroux (1961), and Dinkel et al. (1965) have all criticised along with Tulloch (1964a), the indiscriminant use of ratios as in the first of these methods of analyses. They indicate that the prerequisites for using ratios for describing development
(i) that the two measurements can be assumed to be linearly related
(ii) that the regression line intersects the ordinate at the origin and
(iii) that the variance in the numerator is proportional to the denominator.

The ratio is then constant over the range of $X$, the mathematical model relating the two components being:

$$
\frac{Y_i}{X_i} = \frac{\beta X_i}{\epsilon_i} + e_i
$$

where $e_i$ is a random error term which is assumed to be normally distributed with mean zero and variance $\delta_i^2 = N(0, \delta_i^2)$, where $\delta_i = kX_i$ (see Snedecor 1956, p. 153). This is in contrast to the normal linear regression model,

$$
Y_i = \alpha + \beta X_i + \epsilon_i
$$

where $\epsilon_i$ is a random variable drawn from $N(0, \sigma^2)$, i.e. has a variance which is independent of $X$.

The important consequence of using the ratio model when the relationship between $Y$ and $X$ does not pass through the origin (assumption (ii) above), is that the changing value of the ratio $Y/X$ with changes in $X$ is ignored. This becomes apparent if the expected value of $Y_i (\hat{\gamma}_i)$ is expressed as a fraction of $X_i$:

$$
\frac{\hat{Y}_i}{X_i} = \frac{\alpha}{X_i} + \beta_i
$$

The ratio $\hat{Y}_i/X_i$ clearly changes with $X_i$ in a linear way according to the increment, $\alpha/X_i$. Snedecor (1956), Angervall and Carlström (1963) and Tulloh (1964a) give examples of this feature and the way in which it may alter the interpretation of data. Tulloh (1964a) in addition, examined the use of ratios in connexion with the second, third and fourth previously mentioned methods of describing development, and showed that for these cases also their use may often complicate an otherwise simple situation.

The question of non-linearity of the relationship between $Y$ and $X$
(i.e. assumption (i) above) is also discussed by Tulloh (1964a). He refers to cases where non-linear associations have been found between components of the animal body. Under these circumstances, the ratio \( \frac{Y_i}{X_i} \) may change quite dramatically with changing value of \( X_i \), regardless of whether or not the relationship between \( Y \) and \( X \) passes through the origin.

Because of the possible existence of these features, Tulloh (1964a) favours the fifth of the methods previously mentioned as being the simplest way of presenting the data - i.e. simple graphical presentation. He also suggests the allometric equation as a useful method of summarising the data, particularly when the components being examined tend towards being exponentially related.

2. The Allometric Approach to Developmental Studies

The allometric formula or power function, \( Y = ax^b \), has been found to be an extremely convenient method to adequately describe a wide range of growth phenomena, including many cases of developmental changes accompanying the growth of plants and animals. Reeve and Huxley's (1945) review covers a great deal of this work, although these workers were primarily interested in the theoretical problems arising from the use of the method, and accordingly gave considerable emphasis to the theoretical basis of the formula and to recorded deviations from simple allometric growth.

The widespread use of the technique almost certainly rests to a large extent upon the ease with which the formula may be handled statistically, for in its logarithmic form the equation is linear, the slope coefficient (b) representing the ratio of the relative (logarithmic or multiplicative) growth rates in time of \( Y \) and \( X \).
\[ \log y = \log a + b \cdot \log x \]

or

\[ \frac{dy}{dt}/y = b \cdot \frac{dx}{dt}/x \]

since

\[ \int \frac{dy}{y} = \log y \]

where \( \frac{dy}{dt}/y \) is the relative growth rate of \( y \) (Sebebeck 1968). Thus, a percentage increment (\( m \)) in \( x \), is related to percentage increment (\( b \cdot m \)) in \( y \), where \( b \) is the allometric coefficient.

A consequence of these relationships is that the formula has, in practice, generally been applied by plotting the two growth measurements on logarithmic scales. That such plots when made for a wide variety of data have been found to yield linear relationships over a wide range of sizes (Reeve and Huxley 1945) has been held to rest upon the generalisation that growth is essentially a multiplicative process (Bednar 1950).

3. The Estimation and Comparison of Equations Describing Body Development

Their relative ease of interpretation and estimation makes linear relationships particularly attractive for the purpose of statistical analysis, and they have been used more or less exclusively in the past by the workers in the field of body composition. Historically, a great deal of confusion seems to have arisen regarding the use of the different types of linear relationships. Sprent (1968) considers that this stems from a widespread failure to distinguish between a functional relationship where all the variates are on the same footing, and statistical regression, where the dependent variate has a unique role. This is no doubt due to the appearance of much of the past work on functional relationship, often somewhat incidentally, in papers concerned more
specifically with regression topics, and to the dominance in the statistical literature of papers dealing with regression concepts (Healy, 1966).

In general the problem of deciding upon the correct method of estimating a linear relationship reduces to an examination of the assumptions that need to be made concerning the error structure. Thus, the variates may be looked upon as embodying an element that contributes to the departure of a particular observation from a hypothetical and generally unknown value that it would have taken had the linear relationship held exactly. Such departures may be regarded as being composed of random biological variation as well as of errors of measurement. Because of the widespread use of regression techniques in the estimation of allometric relationships the assumptions implicit in this method of analysis will be considered in detail.

The mathematic model of linear regression is specified by the equation:

\[ y_i = \alpha + \beta (x_i - \bar{x}) + \epsilon \]

The assumptions made are that for each value of the dependent variate \( x \), the value of the dependent variate \( y \) is taken at random from a population that has a mean \( \mu \) which lies on the straight line \( \mu = \alpha + \beta (x_i - \bar{x}) \), and that the distribution of \( y \) about its mean has a variance \( \sigma_{y|x}^2 \) which is constant for all values of \( x \). For tests of significance it is also assumed that the random variable \( \epsilon \) is normally distributed.

Since there will normally be errors in the measurement of the independent variable, this model is not entirely satisfactory for evaluating linear relationships in developmental studies. Snedecor and Cochran (1968) have examined the regression model in such situations where the independent variate \( x' \) is also subject to error, i.e., where \( x' \) is made of its true value \( x \) and an error deviation \( \epsilon \). They indicate that if \( \epsilon \), and the true value of the
independent variate \((x)\) are normally and independently distributed, then \(Y\) and \(X'\) will also follow a bivariate normal distribution. In such circumstances, the regression of \(Y\) on \(X'\) is linear, the regression coefficient \((\beta')\) being

\[
\beta' = \beta/(1 + \lambda), \quad \text{where} \quad \lambda = \frac{\delta^2}{\delta_x^2}
\]

Thus, errors in determining \(X\) lead to a downward bias in the estimation of the linear relationship.

It is because of this bias that various workers have searched to develop alternative methods of estimating linear relationships for the case where both variates are subject to error. Sprent (1966) has gathered together the theoretical background to much of this work and has generalised the least squares method of point estimation of the coefficient of relationship to deal with circumstances in which the errors are also correlated, or vary with \(X\).

Hisara and Reeve (1964) have discussed a number of the approaches to this problem that have been made in practice. They illustrate how both the method of minimising the sum of products of horizontal and vertical deviations from the allometry line (Teissier 1948), and the method which assumes that the error variances of \(X\) and \(Y\) form equal fractions of their total variances, give a solution to the coefficient of allometry \((k)\) as,

\[
k = \frac{\delta Y}{\delta x}
\]

This coefficient is therefore related to the coefficient of regression of \(Y\) on \(X\), as,

\[
b_{YX} = k r \quad \text{or} \quad k^2 = \frac{b_{YX}}{b_{X,Y}} \quad \text{where} \quad r \text{ is the coefficient of correlation between } X \text{ and } Y, \text{ and } b_{X,Y} \text{ is the regression of } X \text{ on } Y.
\]

Thus \(k\) describes a line for which the sum of the perpendicular distances of the observed points is at a minimum when \(X\) and \(Y\) are in standard measure.

It is known mathematically as the reduced major axis of the correlation surface of \((X,Y)\). The sampling variance of \(k\) has been shown to be the same
as that for the regression coefficient of $Y$ on $X$ (Tessier 1948).

Other methods which have been suggested are those which group the ranked data into equally represented discrete categories and estimate the relationship from the co-ordinates given by the group means (see for example Bartlett 1949).

Kidwell and Chase (1967) have made a simulation study of ten methods of estimating the parameters of the allometric equation. Their aim was to consider estimation from data of the longitudinal type, although they make the assumption of independent errors and their results are probably therefore, more relevant to a cross-sectional analysis. In addition, for the case of the iterative methods, they failed to consider more than one cycle of iteration. Nevertheless, their interesting result was that Bartlett's (1949) method based on grouping, along with the reduced major axis method applied to logarithmic data (Kermack and Haldane 1950) and the least squares regression method assuming equal error variance for $X$ and $Y$, proved to be the most accurate methods for all the sets of data they examined. Least squares regression, assuming $X$ to be free of error, was only slightly less accurate.

Cock (1963 and 1966) and Hisara and Reeve (1964) show that the effect of the above modifications to the simple regression estimate tend to vanish as the data fit a straight line more and more closely. Seebeck (1966) also indicated that for comparative work, the differences between the slopes for each treatment group will not be altered to any extent unless the variation about the regression line differs markedly between the groups. Such differences can of course, be tested during the analysis of the data in hand.

(a) Methods Based on Least Squares Regression

Snedecor and Cochran (1967) give details of the one-way analysis of
covariance and the way it may be applied to compare regression lines. The method is relevant to the comparison of regression equations estimated to describe body development for groups of animals from data of the cross-sectional type. It is the approach propounded by Reeve (1940) in his study of relative growth in the snout of anteaters.

The comparison involves firstly, an examination of the variation about the regression line for each of the groups. Homogeneity then permits variances to be pooled and compared with the variation obtained about a single regression line estimated from the pooled within-group sums of squares and cross-products. The difference between these two residual mean squares represents a weighted sum of the deviations of the individual group regression coefficients from the pooled within group coefficient,

\[ \sum w_i (b_i - \bar{b})^2 \]

where \( w_i = \sum (x_{ij} - \bar{x}_i) \).

This difference, when compared with the residual mean square for the pooled regression line, affords a test of whether significant differences exist among the group regression coefficients.

The final test described by Snedecor and Cochran is based on the existence of parallel regression lines. It is an F-test of the difference between the adjusted means of the groups and therefore of the elevation of the regression lines. This is made in the usual way from a comparison of the deviations from the pooled within group regression line and with those for a line estimated ignoring the group structure of the data. In circumstances where the group regression lines are significantly different in slope, this test is equivalent to a test of the group differences in the adjusted values of the dependent variate, (i.e. the \( \hat{y}_i \)) for a given value of the independent variate.

The adjustment of the data however, will have usually been based on the common
within-group line, and therefore the adjusted means have little real meaning when there exist significant slope differences between the groups.

This method of least squares analysis can easily be extended to include more than one criterion for grouping the data. Such an extension becomes relevant to the analysis of data of the cross-sectional type where in addition to the treatment classification of the data, interest will be in the cross-classified effect of age or of some other measure of the developmental phase. The appropriate model in this case is given by Harvey (1964) and will be discussed in detail in a later section.

(b) The Developmental Interpretation of Allometric Relationships

If the statistical analysis shows the slope differences to be insignificant, the data may be represented as a series of parallel lines. The question of interest is then whether or not the set of parallel lines exhibit significant positional differences. If so, the interpretation in the case of an analysis on a logarithmic scale, would be that there exist constant percentage individual or group (depending on the type of data being analysed) differences in the developmental relationship, but that these remain steady during the period of growth being studied. They must therefore be attributed to differences in previous development.

In the case of significant slope differences being detected, the developmental interpretation depends upon the relationship between the slopes and elevations of the estimated regression lines. The crucial question is then whether or not the slope differences are acting to increase or decrease the developmental differences between the individuals or groups. That is, whether the differences which have arisen from previous development are being
expanded or contracted during the period of growth under study. This may well depend upon which of the groups or individuals are being compared, although the interpretation may be capable of simplification if, for example, the allometry lines could be regarded as all passing, within the limits of error, through a single point at some stage during the period of growth under investigation.

With data of the cross-sectional type it is, therefore, of some interest to compare the within-age and between-age regression lines for each of the treatment groups. If the regressions appear to estimate the same quantities, they may then be combined to give a better estimate of the treatment regression line (Snedecor and C 1968).

Cock (1966) has given some thought to the relative biological meaning of allometric equations established from static, cross-sectional and longitudinal analyses. He emphasizes the fact that ontogenetic relationships will only be established by between-individual analyses of longitudinal data or between-group analyses of cross-sectional data. For static data, the existence of differences in body components that are related to differences in size at the same fixed age, does not necessarily reflect any pattern of development which might occur through time. Cock (1966) further discussed the relationship between the static and ontogenetic estimates from longitudinal analyses. He concluded that the only general relation between the two is that they are likely to be nearly equal if the static coefficient is estimated towards the end of a long period of growth during which the ontogenetic coefficient has been constant or nearly so.
(c) **Multiple Covariance**

The extension of the least-square analysis of covariance to the case of two or more independent variates can easily be made (Cochran 1968). Seebeck (1968) suggests this extension to allow the square of the independent variate to be included in the model in order to take account of curvilinearity in the allometric relationship. Cock (1966) however, does not feel that this would be a particularly satisfactory method because of the possibilities of needing polynomials of the third or higher degree in order to cope with irregular changes in the coefficient b, and difficulties this would raise to the biological interpretation of the results. The difficulties that Cock refers to would seem, however, to be a function of the data itself rather than of this method of analysis. As an alternative Cock (1966) suggests a method of making the relationship linear by applying a scale transformation to either of the variates.

Seebeck (1968) has also suggested the use of multiple covariance to allow the inclusion in the model of independent variates which would reflect and estimate the effect of possible external factors on body development. He suggests, for example, the inclusion of age (or of growth rate) along with body weight as an additional criterion of body growth. The independent effects of these two criteria may then be investigated.

Yet a further application of this method which is suggested by Seebeck (1968) is the examination of the relationship between two criteria of development. Seebeck and Tulloh (1966) have used this method to study the developmental relationship between the fat content and the yield of sheep carcasses. For this purpose they considered a model which expressed the fat content of the carcass as a function of both carcass weight and body weight. They were thus
able to obtain estimates of the relationship between fat weight and carcass weight at constant body weights, which is in this case synonymous with the relation between fat weight and dressing-out percentage at constant body weight.

(d) The Choice of an Independent Variate

Seebeck (1968) has considered the problem of logically deciding upon an independent variate for use in studies of body development using the allometric equation. This is a question that has frequently been completely ignored by almost all the workers in the field. It is a question however, of some significance to the interpretation of the results.

The problem is one of deciding upon a criterion of growth against which differences in the pattern of development that accompany growth are to be assessed. When framed in these terms it seems intuitively reasonable, as Seebeck suggests, that the weight of the complete growing unit within which the developmental patterns of the components are being studied, should be used as the baseline of growth. Seebeck warns of the possible need to redefine the growing aggregate in cases where it is known that particular components are subject to extraneous sources of random variation. A good example is the weight of the contents of the alimentary tract, the marked variability exhibited by this component of body weight being well appreciated by workers using ruminant animals.

This principle of redefining the criterion of growth in order to more precisely estimate the course of growth would seem to be somewhat different from the principle of excluding a component from the whole on the grounds that the growth of that component is of a completely different nature, or because it is largely independent of the growth of the other components. This has
been suggested for example, for the growth of the fat component of the carcass, fat generally being held to be a product of animal nutrition rather than animal growth. It would seem unreasonable to discard such a component from a developmental study entirely on the basis of such hypothetical grounds; better rather, as Seobeck suggests, to retain the component in order to find out whether or not it is developmentally related to the other components being examined.

(c) Experimental Designs for Studying Body Composition

Seobeck (1968) has given an excellent discussion on designing experiments for the purpose of establishing and comparing developmental relationships for body composition data of the cross-sectional type. He particularly emphasizes the need to kill animals from each treatment group over a range of bodyweights, and suggests a way in which the classical "high-low" change-over designs for nutritional experiments may be modified for greater experimental efficiency.
4. Results from Allometric Studies of Body Composition

The reviews of Seebeck (1968) and Cock (1966) include references to and a discussion of the results from studies in which the allometric equation has been used to study development in terms of composition. The use of the technique in experiments involving the laboratory mouse is noticeably lacking, the only example quoted by Cock referring to the work of MacArthur and Chiasson (1945) who presented data on the relationships involving body length, tail length, ear length and hind foot length.

Fenton (1956) presented for two strains of mice, data which illustrate the relationship between carcass fat content and fat-free wet body weight. His graph showed the two strains to be clearly different in the relative growth of these two components. He did not, however, quantify the relationship for his strains.

Zucker and Zucker (1963) have made a very interesting study of fat development in a number of strains of laboratory rats. The graphs which they present show that the Yale and Wistar strains studied by Harned and Cole (1939) exhibit a strikingly similar allometric relation for the growth of fat relative to empty body weight. Furthermore, the slope of this relationship was essentially the same (approximately 1.8 - 1.9 as judged from the graphs) as that found by Zucker and Zucker (1963) for a similar graph depicting the relationship for young rats of the Sherman and Sprague-Dawley animals. As further evidence of the close relationship between fat weight and body size, irrespective of age, Zucker and Zucker found that their body weight selected strains of Sherman and mixed stock origin, exhibited a very similar logarithmic relationships between the weight of the excised retroperitoneal fat pad and body size (Slope approximately 2.3). This was apparent despite the big age
differences between the large, medium and small strains at a given body weight. Additional published data which illustrates the usefulness of the allometric approach to studies of fat development is also discussed by these workers.

5. Conclusion

Despite a lack of direct experimental evidence on the value of the allometric technique for analysing variation in the developmental pattern of the body components of laboratory animals, the well-founded theoretical backing that regression analysis imparts to the allometric approach, together with the direct evidence that comes from the application of the method in studies of relative development for linear body measurements (Cock 1966), establish the allometric equation as a simple empirical tool of general applicability to a wide range of biological material. Its usefulness to the assessment of variation in the relative proportions of body components is very well illustrated by a recent series of papers published by Scobock (1969) which examine some compositional aspects of developmental growth and body weight loss for beef cattle.
III. METHOD OF CARCASS ANALYSIS

The following method of estimating body components was used in each of the experiments to be described.

The animals were killed and immediately weighed to give an estimate of "slaughter body weight" (SBW). Simple dissection of the abdomen exposed the well defined paired mesenteric fat depots attached to the testes or uterus (Hull 1959, Liebolt et al. 1965). These were removed and placed in a sealed plastic container for weighing. This fat depot has been termed "abdominal fat" throughout the studies reported. The digestive tract was excised from the abdomen, care being taken to avoid removing any mesenteric fat or connective tissue. It was weighed in a covered petri dish to provide an estimate of the weight of the digestive tract and its contents (gut weight). The weight of the "carcass" was determined as slaughter body weight less gut weight. The abdominal fat was returned to the dissected carcasses which were stored in a freezer to await chemical analysis.

Chemical analysis began with the almost complete drying of the carcass for a period of 3 days in a tarred plastic beaker at an oven temperature of 65-75°C. This temperature was selected in preference to the higher one normally adopted in this type of analysis (A.O.A.C., 1955) because of the problem of fat vaporisation. The dried material was transferred to a tarred glass extraction thimble and the fat extracted with 220 ml of petroleum ether (B.P. 40-60°C) for 18 hours in a Soxhlet extraction apparatus. The thimbles were then dried overnight and re-weighed to give the fat-free dry matter (FFDM) content of the carcass. This two stage procedure was found to be a particularly satisfactory way of drying the very fat carcasses of mature mice.
Figure 1. Diagram of Relationships Among Carcass Components

- Slaughter Body Weight
  - Gut plus Contents
    - Carcass including Abdominal Fat
      - Dry Matter
        - Fat-free Dry Matter
        - Ether Extract
      - Water
from the large body weight and mutant strains which otherwise required an extremely long drying time at an oven temperature of 65-75°C. Fat content (ether extract) was estimated from a 25 ml aliquot of the Soxhlet extract.

The water content of the carcass was estimated as carcass weight less the other extract and fat-free dry matter weights, while fat-free carcass weight (FWC) was calculated as carcass weight less the weight of ether extract. The relationships among these carcass components is shown diagrammatically in Figure 1.

Mature animals of the ° strain were used in two small trials aimed at examining some aspects of the accuracy of this extraction technique. In the first of these, which involved 24 animals of each sex distributed over the ° strain selection lines and over a total of 8 extraction 'runs', duplicate aliquots of the fatty extract were taken and the weights of the evaporating flasks recorded after each of two consecutive evaporation periods of 5 or more hours duration. Statistical analysis of the data for the female mice demonstrated that the components of variation between aliquots and between weighings were very small in relation to between-animal within-strain variation (<0.1). It was estimated that these sources of variation would also be small (<1.0) in relation to the relatively low variation in fat weight in the low bodyweight lines at 4½ weeks of age.

A second trial involving only 6 mice showed that a second 18 hour extraction period failed to produce any detectable increase in the estimated fat content of animals which were chosen as being above average in their fat content. Indeed, it was evident that greater than 98% of the chemically extractable fat was removed after only 6 hours extraction using the technique described. The longer 18 hour overnight period was chosen for the convenience of routine daily extraction runs.
IV. COMPARISON OF TWO ESTIMATES OF CARCASS FAT-FREE CONTENT

In order to examine the relationship between the fat-free dried residue and the nitrogen based estimates of protein content, the opportunity was taken to analyse some suitable data which were kindly made available by Dr. D.C. Dalton of Leeds University.

Seabock (1968) has emphasised the importance, when examining a relationship between alternative or indirect estimates of carcass composition with a view to using the relationship to distinguish genotypes or to show the effect of experimental treatments on body composition, of knowing whether or not the relationship is affected by genotype or by the experimental treatment. Important deviations will severely affect the usefulness of the alternative estimate of carcass composition, unless the genotype or experimental differences are sufficiently well defined to allow the appropriate within-group relationships to be applied.

By providing data on animals exhibiting well defined genetic, environmental and age differences in body weight, the material to be examined was admirably suited to the present investigation. The data were, however, collected from an experiment involving just one sex, all mice being males.

A. MATERIAL AND METHODS

The material originally derived from the same base population of C-strain mice as has been used throughout the present series of experiments. It formed part of an experiment in which mice were selected for high and low liveweight gain from 3 to 6 weeks of age (Dalton 1967). Selection was carried out on both a normal laboratory diet and on a diet containing 70% cellulose.
Table 3. Distribution of Animals Available for Analysis

<table>
<thead>
<tr>
<th>Strain</th>
<th>Selection Diet</th>
<th>Rearing</th>
<th>Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Selection Line</td>
<td>Normal</td>
<td>Diluted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Normal</td>
<td>Large</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Small</td>
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<tr>
<td>Diluted</td>
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<tr>
<td></td>
<td>Small</td>
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dilution which approximately halved the rate of growth achieved on the full diet. Responses to selection were obtained in both directions and on both diets. In addition to these genotypic strain differences in liveweight growth, the experiment provided carcass data for mice killed at 3 and 6 weeks of age and for mice grown between 3 and 6 weeks on the contrasting environment to the one on which their parents had been selected. As was the case during the selection experiment, the mice tested on the diluted diet were at other times fed normally.

The carcass information available included determinations of carcass nitrogen by the conventional Kjeldahl method and estimates of carcass fat obtained by extracting the oven-dried carcass (including skin but excluding gut contents) with petroleum ether. Thus the method of estimating fat-free drymatter was essentially the same as that used throughout the present studies.

Six male mice for each of the 24 subgroups were taken at random for chemical analyses from the larger number of animals bred for the experiment. Table 3 shows the distribution of those animals on which appropriate carcass data were available. The shaded areas of this table indicate those animals that were reared on the opposite environment to the one of which they were born (i.e. the switched animals in Dalton's (1967) terms).

B. STATISTICAL ANALYSIS AND RESULTS

The data were analysed by examining the regression equations relating carcass nitrogen to the fat-free drymatter content from the point of view of assessing the strength of the association between these two measures of the non-fatty carcass component, and the generality of the relationship for animals of different strains, ages and subjected to different nutritional regimes.
Table 4. Variation About the Logarithmic Regression Lines

(Variances x $10^6$ in log e g. units)

<table>
<thead>
<tr>
<th>Strain</th>
<th>Selection Line</th>
<th>Rearing Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Large</td>
<td>Normal 3 weeks</td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td>1204 98</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>31 209</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>602 35</td>
</tr>
<tr>
<td>Diluted</td>
<td>Large</td>
<td>1781 472</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>461 15</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>34 46</td>
</tr>
</tbody>
</table>
Initially, strain differences in the regression lines were examined for each of the 4 environment x age subgroups. In each case, except for the animals reared in the dilute-diet environment and killed at six weeks of age, this revealed significant ($P<0.01$) strain differences in the variation of nitrogen content about the regression lines. That this heterogeneity remained after both the dependent and independent variates had been transformed to logarithms suggested that it was not a scale phenomenon. The squared deviations from regression for the logarithmic analyses are shown in Table 4.

Apart from a tendency for large animals to exhibit greater variability at 3 weeks of age, the mean squares of Table 4 do not demonstrate much in the way of a consistent pattern that could be attributable to strain differences or to the treatment imposed. Furthermore, there seemed to be no connection with a foreign dietary environment, such as was given to the switched animals. Indeed, considerable differences occurred at 3 weeks of age between groups of animals of the same strain but which were destined to be reared in contrasting environments between the 3 and 6 week growth period. Such differences must be attributed to sampling effects. Accordingly, this feature of the data was ignored in the analyses which follow, the deviation mean squares being pooled to test the significance of strain differences in the regression coefficients.

These analyses failed to detect any differences that reached significance at the 5% level of probability, regardless of whether the analysis was carried out on arithmetic or logarithmic scales. This was found to hold both when strain differences were examined within each of the age x environment classes and when all 24 line x environment x age differences were examined together. These analyses were also unable to detect any significant differences in the elevation of the regression lines.
Table 5.  Regression of Nitrogen on Fat-Free Drymatter
(All animals analysed)

\[ N = \bar{N} + B(F - \bar{F}) \]

<table>
<thead>
<tr>
<th></th>
<th>Arithmetic</th>
<th>Logarithmic (to base e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Nitrogen Content</td>
<td>0.418</td>
<td>-0.970</td>
</tr>
<tr>
<td>Mean Fat-free Drymatter</td>
<td>3.234</td>
<td>1.079</td>
</tr>
<tr>
<td>Regression Coefficient</td>
<td>0.134</td>
<td>1.016</td>
</tr>
<tr>
<td>Standard Error of B</td>
<td>0.0048</td>
<td>0.0019</td>
</tr>
<tr>
<td>( r^2 )</td>
<td>0.87</td>
<td>0.86</td>
</tr>
</tbody>
</table>
The pooled within-group regression equations are presented in Table 5.

The closeness and linearity of this relationship was also most apparent from a scatter diagram of individual data points. This diagram also revealed 4 points which exhibited considerable deviation from the average relationship. De-analyses of the data omitting these animals, while showing no heterogeneity of the group regression coefficients, did however demonstrate significant (P < .01) difference between the adjusted group means. Such a procedure was held to be justifiable on the grounds that the four deviant animals were omitted on the basis of a computer output which was produced with no direct reference to their group of origin. This analysis made virtually no difference to the value of the regression coefficients (B = 0.135 and 1.029 for the arithmetic and logarithmic analyses respectively) although the square of the correlation coefficient was raised to 0.98.

Significant differences between adjusted means were also evident when all available animals were analysed according to a linear model combining effects attributable to selection line, diet, environment and age along with the corresponding two factor interactions and with the weight of fat free dry matter as a covariate. Apart from the covariate the only pronounced effect contributing to variation in nitrogen content was that of the rearing environment. Animals grown on the diluted diet tended to have less nitrogen than full fed animals of similar fat-free dry matter contents. A tendency for the regressed differences between the lines selected on the diluted diet to vary according to the rearing environment was also apparent.

The pooled regression coefficients when a similar linear model was fitted to the full diet animals were 0.136 and 1.034 for the arithmetic and logarithmic analyses respectively. The pooled regression parameters over the six strains
Table 6. Regression of Nitrogen on Fat-Free Drymatter for Full Fed Mice at 6 Weeks of Age

\[ N = \bar{N} + B(F - \bar{F}) \]

<table>
<thead>
<tr>
<th></th>
<th>Arithmetic</th>
<th>Logarithmic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Nitrogen ((\bar{N})) in g.</td>
<td>0.688</td>
<td>1.652</td>
</tr>
<tr>
<td>Mean Fat-free Drymatter ((\bar{F})) in g.</td>
<td>5.255</td>
<td>-0.383</td>
</tr>
<tr>
<td>Regression Coefficient (B)</td>
<td>0.137</td>
<td>1.030</td>
</tr>
<tr>
<td>Standard Error of B</td>
<td>0.0110</td>
<td>0.1009</td>
</tr>
<tr>
<td>(r^2)</td>
<td>0.85</td>
<td>0.80</td>
</tr>
</tbody>
</table>
for those animals fed a normal diet and slaughtered at six weeks of age are shown in Table 6.

These are essentially similar to the combined results from all animals given in Table 5.

C. DISCUSSION

The results presented demonstrate the very close association between the two estimates of carcass composition, there being at least 93% of the variation between animals common to both of them ($r > 0.9$). Furthermore it was apparent that the relationship between the two was very largely independent of the age, strain or the dietary regime of the animals studied.

There appears to be no instances in the literature on the laboratory mouse of similar comparisons of such measures of carcass composition. In sheep, however, Ulyatt and Barton (1963) found the dried fat-free carcass residue to show a close relationship to N content determined by the Kjeldahl procedure. The correlation coefficient for the 39 ewes examined was 0.95, the authors concluding that the difference method based on fat-free dry matter is sufficiently accurate for estimating protein in meat.

Although the authors did not consider the question in their paper, the data of Kathburn and Pace (1945) provide further material to allow the relationship between these same two characters to be examined for their guinea pigs. An analysis gave estimates of the squared correlation coefficient of 0.96 for females and 0.99 for males. In addition, the regression coefficient was found to be significantly ($P < 0.05$) greater for the males than for the females (0.131 vs 0.119). This difference was not apparent when the regressions were re-estimated following a logarithmic scale transformation of both
Table 7. **Logarithmic Regression of Nitrogen on Fat Free Dry Matter**

(Guinea Pig Data of Pace and Rathburn 1945)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Females</th>
<th>Males</th>
<th>Sexes Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>18</td>
<td>32</td>
<td>50</td>
</tr>
<tr>
<td>$\bar{y}$</td>
<td>2.527</td>
<td>2.684</td>
<td>2.628</td>
</tr>
<tr>
<td>$\bar{x}$</td>
<td>4.590</td>
<td>4.741</td>
<td>4.687</td>
</tr>
<tr>
<td>B</td>
<td>0.973</td>
<td>1.037</td>
<td>1.030</td>
</tr>
<tr>
<td>SE (B)</td>
<td>0.0475</td>
<td>0.0157</td>
<td>0.0182</td>
</tr>
<tr>
<td>$r^2$</td>
<td>0.96</td>
<td>0.99</td>
<td>0.98</td>
</tr>
</tbody>
</table>
variates, although in this case significantly ($P < 0.01$) heterogeneous variation around the regression lines became evident. Despite this feature the pooled within-sex data has been presented along with the separate sex regression parameters in Table 7.

The value of the logarithmic regression coefficient found for male guinea pigs is strikingly similar to that found previously for full fed male mice ($1.034$). These coefficients indicate that the multiplicative growth rate of nitrogenous material is about $3\frac{1}{2}$ greater than that of the fat free dry matter. This is to be anticipated on the basis of the expected composition of these two components. Direct nitrogen determinations would seem likely to be potentially more capable of assessing the protein content of animal tissues, nitrogenous substances comprising approximately $89\%$ of true protein (Bate-Smith, 1945). Fat free drymatter estimates on the other hand would include such additional non-protein constituents as minerals, carbohydrates, lactic acid and many pigments. Of these, it would seem that ash is the component most likely to be responsible for the lower multiplicative growth rate of fat free dry matter relative to nitrogen. Tulloh's (1964a) analysis of sheep, cattle and pig data has shown that the ratio of the specific growth rate of bone weight relative to carcass weight is, for each of these species, about $20-30\%$ lower than the corresponding ratio involving the weight of dissectible muscle. The exclusion of ash from the dry fat free component might therefore be expected to lead to an even greater association with estimated carcass nitrogen. In this connection however, it is interesting to note that Russell et al. (1968) found the variation in the weight of dissectible bone for 25 mature sheep, was related more closely to variation in carcass fat-free dry matter ($r = 0.76$) than to variation in carcass ash content ($r = 0.58$).
Ulyatt and Barton (1963) also found weight dissectible bone to be rather poorly predicted by carcass ash content \( (r = 0.72) \) although in both these cases the procedure of sampling the carcasses for chemical analysis may have been responsible for the low correlations found.

D. CONCLUSIONS

The conclusion reached from this study is that the weight of fat-free dry matter provides a very good indication of protein content. The relative simplicity with which this component may be determined makes it eminently more suitable for experiments requiring determinations on large numbers of animals. In addition it would appear that little is likely to be gained from a more complex chemical analysis involving the ashing of the carcass in order that the ash-free, fat-free residue might be specified.
V. FAT DEVELOPMENT IN THE OBESE MUTANT STRAIN OF MICE

A. INTRODUCTION

Animals carrying the obese gene leading to the development of the "obese hyperglycaemic syndrome" will be referred to as "obese" animals throughout the remainder of this thesis. Some of the biochemical and physiological work that has been carried out on this mutant stock was briefly referred to in a previous section. This work has provided evidence that the greater fat content of these animals results from a disturbance to their fat metabolism. The effects of the disturbance are so gross that the animals become obviously very fat, and can be recognised as such, by the time they are 5-6 weeks of age. Because of the marked effects of the disturbance on the visible morphology of the animals, very little in the way of objective data is available on the fat contents of the obese animals in comparison with mice lacking the mutant gene. This no doubt arises because objective information is not necessary to the genetic classification of the condition and because, in physiological studies, the obese gene has been used to provide animals with markedly altered fat metabolism, there commonly being no interest taken in variation about this altered level.

The aim of the work presented in this section was to objectively compare fat development in obese mice and their normal litter mates. In particular, the obese condition provided the opportunity of examining the allometric approach to the assessment of relative carcass fatness in two groups of animals with marked differences in their fat metabolism.
Table 8. Analysis of Covariance with Log Abdominal Fat Weight (Abd. Fat) or Log Ether Extract Weight (Total Fat) as the Dependent Variate (y) and Log Carcass Weight or Log Fat-free Carcass Weight (FFCW) as the Independent Variate (x) in the Equation $y = a + bx$.

<table>
<thead>
<tr>
<th>Dependent Variate</th>
<th>Independent Variate</th>
<th>Regression Constants</th>
<th>Adjusted Means $\neq$ antilog $y$ (g)</th>
<th>F-values $\dagger$</th>
<th>$\chi^2$ Heterogeneity of Deviation M.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>a  b  a  b</td>
<td>ob  +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log Abd. Fat Wt.</td>
<td>Log Carcass Wt.</td>
<td>-5.59 1.72 -10.6 3.11</td>
<td>1.98 2.18</td>
<td>21.8++ -</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>Log FFW</td>
<td>-8.04 2.80 -11.6 3.64</td>
<td>2.69 1.15</td>
<td>1.51 48.1++</td>
<td>0.76</td>
</tr>
<tr>
<td>Log Total Fat Wt.</td>
<td>Log Carcass Wt.</td>
<td>-2.90 1.54 -5.22 2.04</td>
<td>15.2 9.33</td>
<td>7.02+ -</td>
<td>11.37++</td>
</tr>
<tr>
<td></td>
<td>Log FFW</td>
<td>-5.18 2.54 -5.68 2.33</td>
<td>20.5 6.27</td>
<td>0.48 214 ++</td>
<td>2.00</td>
</tr>
</tbody>
</table>

+ $P < 0.05$  ++ $P < 0.01$

≠ Adjusted along the common regression line to a geometric mean FFW of 25.3 g. or along the group regression lines to a geometric mean carcass weight of 33.5 g.

$\dagger$ With 1,22 d.f. for testing slope differences and 1,23 d.f. for testing elevation differences
B. MATERIAL AND METHODS

The animals were made available from the Edinburgh mutant stock over a period of 2 years. A total of 25 male mice were involved in the study; they came from 10 litters, representing the progeny of 6 parental pairs. In all litters, obese mice and their wild-type-litter mate were killed at similar times over a range of ages. The animals were dissected and processedchemically in the manner previously described.

Developmental relationships were assessed by applying regression methods to logarithmic values of the data. Since the aim was to compare the simple linear allometric equations for the two strains, most of the animals were killed at either very young (i.e. as soon as the obese condition was visibly recognizable) or very old ages. This was done in an effort to increase the precision of estimating the linear regression lines.

C. RESULTS AND DISCUSSION

The results of the logarithmic regression analyses relating abdominal fat and other extract separately to either carcass weight or to fat-free carcass weight, are presented in Table 8.

The significantly lower mean square deviation from regression for the obese mice in comparison with their normal contemporaries in the case of the regression of total fat (other extract) on carcass weight, was believed to result from the considerably larger fraction which other extract made of carcass weight in the former group. It was not evident with respect to variation about the fat-free carcass weight regression line.

The results of the analyses presented in Table 8 are illustrated by the graphs shown in Figure 2, and indicate that the greater fat content of the
Figure 2. Logarithmic Relationships ($\log_e g$ units) Between Carcass Fat and Non-fat Components for Obese (○) and Wild-type (●) Mice.

(a) Relation Between Fat and Carcass Weight  
(b) Relation Between Fat and Fat-free Dry Matter

(i) Total Fat,  
(ii) Abdominal Fat
obese animals is reflected in a greater elevation of the allometric line relating fat content to either carcass weight or fat-free carcass weight. In the case of the regression of abdominal fat on carcass weight this logarithmic elevational difference was well short of significance at the 5% level of probability. However, the slope of this line, like that relating total fat to carcass weight, was significantly lower for the mutant animals than for their normal litter mates. This indicates that relative to carcass weight the proportionate difference in fat content between the two groups is becoming reduced as growth proceeds. At the younger ages the obese animals certainly had greater proportionate amounts of their carcasses comprising total fat, but it appears from Figure 2 that at low carcass weights they were very little different from their normal litter mates in their proportionate amount of abdominal fat.

Clear positional differences in the lines relating fat content to fat-free carcass weight were demonstrated. That the proportionate differences remained constant throughout growth is shown by the absence of significant slope differences (Table 3). An analysis of the logarithmic relationships of fat content to fat-free dry matter gave identical conclusions.

Examination of the coefficients relating fat content to the fat-free component of the carcass or to carcass weight itself, revealed that the proportionate growth of abdominal fat is far greater relative to the proportionate growth of ether extract for the normal animals than for their obese litter mates. This together with the absence of clear-cut positional differences of the abdominal fat regression lines at comparable carcass weights, suggests that the relative rate of growth of the abdominal fat depot falls off as obese animals grow on past the final level of carcass weight that is
achieved by normal mice. A similar absolute average rate of growth of abdominal fat relative to carcass weight for both stocks was indicated by an arithmetic analysis of the data. This is in line with the findings discussed by Chernick (1962) who commented on plateaus in the absolute weights obtained for the epididymal and mesenteric fat depots of male rats of the Osborne and Mendel strains. The data presented by Hollman et al. (1963) on the other hand, did not indicate departures from an identical linear allelic relationship between the weights of the epididymal fat pad and of the whole body for either "Yellow-obese" mice or their normal litter mates - i.e. the same allelic line appeared to fit both genotypes equally well. Yellow-obese mice exhibit a number of similarities to the obese-hypoglycaemic mutant, the condition being due to a dominant gene which also produces a yellow coat colour and is at the agouti locus. These same authors, however, refer to some of their earlier work which, in agreement with the present findings, indicated that the maximal final weight of the epididymal fat depot is reached at a relatively young age for mice of the obese-hypoglycaemic strain.

The general conclusion reached from this investigation is that the altered fat metabolism brought about by the obese gene is reflected in a higher elevation of the allelicic line describing the growth of fat relative to carcass or fat-free carcass weight. However, the difference between the strains in the amount of fat as a proportion of carcass weight, became reduced as growth proceeded. In addition it appeared that the rate of developmental growth was greater for the abdominal fat depot than for total chemical fat.
VI.  RELATIVE FATNESS OF LINES OF MICE SELECTED FOR LARGE AND SMALL BODY SIZE

A. INTRODUCTION

This study was aimed at comparing the relative fat content of mouse carcasses from lines selected for large and small body size by expressing the growth of the chemically determined fat component (total fat) relative to the growth of the carcass as a whole using the allometric regression method described previously. In addition, the growth of the abdominal fat depot was considered in relation to the growth of total carcass fat and relative to the growth of the whole carcass for the purpose of studying the partitioning of fat deposition between this and the remaining fat depots, and in order to make an assessment of the value of the abdominal fat depot as an index of the total fat content of an animal.

B. MATERIALS AND METHODS

Mice from Professor Falconer's selection experiment were used for this study. The experiment involved mice of the C-strain, animals having been selected for a period of 14 generations from the original random mating stock. Within-litter selection for and against body weight at 6 weeks of age had been employed to produce lines with markedly different body weights in comparison with the unselected controls. The selected lines were replicated six times, each replicate having its own contemporaneous control population. Eight pair matings were used to continue the lines in each generation.

Mice surplus to requirements necessary to produce the 15th generation
Table 9. Distribution of Animals by Sex, Line, Replicate and Age Groups

<table>
<thead>
<tr>
<th>Sex</th>
<th>Line</th>
<th>Age</th>
<th>Replicate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Male</td>
<td>Large</td>
<td>4 1/2 week</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>6 week</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Large</td>
<td>9 week</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>4 1/2 week</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>6 week</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>9 week</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>4 1/2 week</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>6 week</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Small</td>
<td>9 week</td>
<td>8</td>
</tr>
</tbody>
</table>
of the selected lines were made available for this study. They were chosen at random from the total number of mice available in each of the 36 sex x line x replicate subclasses and were randomly allocated to one of three groups with the proviso that, as far as was possible, an attempt was made to distribute litter mates over each of the groups. The groups were designed for slaughter at three different ages. The aim was to analyse 5-7 first-litter mice from each sex, line and replicate sub-group at each of the 3 ages. However, some of the sub-groups required to be supplemented with second and third litter progeny produced by the re-mating of appropriate parental pairs. Even then the distribution of mice diverged from the proposed scheme as is indicated by the numbers analysed shown in Table 9.

The three ages chosen for the study were 4.5 weeks (32 days), 6 weeks and 9 weeks. These ages spanned the age at which selection had been carried out and gave roughly comparable carcass and body weight growth increments before and after 6 weeks. The mice were chemically analysed according to the method previously described.

C. METHODS OF STATISTICAL ANALYSIS

The developmental growth of the fat component relative to the whole carcass was assessed from the regression of fat weight on carcass weight, following the logarithmic transformation of the raw data using either base-ten or natural logarithms.

Group differences in the regression equation, such as for example, those due to sex, line or replicate, were evaluated for statistical significance by the general least-squares method presented by Harvey (1964). Both slope and elevation differences were tested.
The partitioning of the degrees of freedom among individual class and subclass regressions, in effect amounts to asking whether an interaction exists between the continuous independent variate and the discrete variate, for the particular dependent variate being examined. When such an interaction exists, the class or subclass means require to be adjusted to a common value of the continuous independent variate along the separate regression lines if they are to be compared in a meaningful way. The overall mean of the independent variate (i.e. \( X \)) is probably the most useful value for this purpose, although given this situation the differences among the adjusted class or subclass means will be different for each value of \( X \) chosen. In the absence of significant slope heterogeneity, the class or subclass means are best compared following adjustment along the weighted class or subclass regression line. The overall mean of the independent variate is again an appropriate point to compare the adjusted means, which in this case reflect constant elevational differences in the regression lines.

The method followed, therefore, was to fit regressions separately for the individual classes or subclasses simultaneously with the fitting of constants for the class and subclass effects. The individual class regressions were considered as deviations from the unweighted average regression, in the manner indicated by the following model for the one-way classification:

\[
y_{ij} = \alpha + a_i + b_i (x_{ij} - \overline{X}) + a_i (x_{ij} - \overline{X}) + e_{ij}
\]

where

- \( y_{ij} \) = the \( j^{th} \) observation in the \( i^{th} \) class
- \( \alpha \) = a constant common to all observations
- \( a_i \) = the effect of the \( i^{th} \) class
- \( x_{ij} \) = the value of the independent variate for the \( ij^{th} \) observation
\[ \bar{X} = \text{the overall mean of the } X_{ij} \]

\[ \bar{b} = \text{the unweighted average regression coefficient} \]

\[ b_i = \text{the deviation from } \bar{b}, \text{ of the regression coefficient for the } \]

\[ i^{th} \text{ class} \]

\[ e_{ij} = \text{a random error term.} \]

As Harvey (1964) points out, the overall mean (\( \mu \)) of the \( Y_{ij} \) for the case of equal class frequencies and for \( X_{ij} = \bar{X} \), is not directly obtainable when fitting this model. It is given by

\[ \mu = \alpha + \frac{1}{n} \sum_i b_i \sum_j (X_{ij} - \bar{X}) \]

It is, however, obtained directly if the deviations (\( X_{ij} - \bar{X} \)) are used for the average regression term in the design matrix, and the elements corresponding to the class regressions are computed as an interaction (i.e., product) between the \( a_i \) and \( b \) elements. The "F-test" for differences among the \( a_i \) then corresponds to a test of elevational differences among the regression lines at the point \( X_{ij} = \bar{X} \), both in the presence and absence of differences among the \( b_i \). The adjusted class means are given by \( \mu + \hat{a}_i \) and the individual class regression coefficients by \( \hat{b} + \hat{b}_i \).

The method may be extended to models based on more than one level of classification of the data. For each case it is appropriate to consider the sub-class regression coefficients as interactions among the regression coefficients for each of the classes.

The above general method has been employed in both the cross-sectional and static analyses of the data. The cross-sectional analyses involved the fitting and comparison of the sex, line and replicate regression equations based on the mean logarithmic values of \( X \) and \( Y \) for each of the three age groups.

The static analysis considered the sex, line, replicate and age group
regressions based on the individual logarithmic values of X and Y. Thus the cross-sectional regression estimates the average developmental relationship of fat relative to carcass weight and expresses the ratio of the percentage growth rate of fat to the percentage growth rate of the carcass as a whole. The extent to which the regression coefficient is greater than unity thus measures the degree to which the component is forming a larger percentage of carcass weight during growth. The static regression, in contrast, is the regression when variation in carcass weight due to age is eliminated. It merely specifies the average relationship of percentage differences in fat to percentage differences in carcass weight between animals of the same age. When the static regressions in the three age groups did not differ significantly they could be combined into an average or pooled, static regression. Comparison of the static and cross-sectional regressions permitted an assessment to be made of the importance of age in influencing the developmental pattern of fat growth. The main purpose of the regression analysis, however, was to provide a quantitative basis for the comparison of the strains - the selection lines and replicates - to find out in particular, if the large and small lines differed in relative fatness. In the context of this allometric approach relative fatness refers to the magnitude of the differences in fat weight after allowance is made for the differences in carcass weight. It therefore refers to the relative positioning of the regression lines for the different mouse strains.
Table 10.  F-values from the Analysis of Covariance of the Age Group Means, for Log Abdominal Fat or Log Total Fat as the Dependent Variate and Log Carcass Weight as the Independent Variate

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>d.f.</th>
<th>Abdominal Fat</th>
<th></th>
<th></th>
<th>Total Fat</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Replicate Effects</td>
<td>5</td>
<td>4.44 ++</td>
<td>2.88 +</td>
<td>4.74 ++</td>
<td>3.35 +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Line Effects</td>
<td>2</td>
<td>13.4 +++</td>
<td>16.0 +++</td>
<td>1.22</td>
<td>1.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Regression</td>
<td>1</td>
<td>366 +++</td>
<td>443 +++</td>
<td>124 +++</td>
<td>190 +++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Replicate Regressions</td>
<td>5</td>
<td>5.62 +++</td>
<td>3.19 +</td>
<td>4.11 +</td>
<td>3.01 +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Line Regressions</td>
<td>2</td>
<td>.38</td>
<td>1.25</td>
<td>1.87</td>
<td>5.43 ++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Error Mean Square (log g.)^2 units</td>
<td>38</td>
<td>.00877</td>
<td>.00692</td>
<td>.00396</td>
<td>.00438</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Regression Coefficient (b)</td>
<td></td>
<td>3.94</td>
<td>2.60</td>
<td>1.54</td>
<td>1.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.E. (b)</td>
<td></td>
<td>±.206</td>
<td>±.123</td>
<td>±.138</td>
<td>±.0981</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N.B.  In this and in the analysis of variance tables which follow, +, ++ and +++ denote statistical significance at the 5%, 1% and 0.1% levels of probability, respectively.

i.e. + = P < .05;        ++ = P < .01;        +++ = P < .001.
Table 11. Regression Coefficients and their Standard Errors for the Line and Replicate Classes

<table>
<thead>
<tr>
<th>Selection Line</th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Large</td>
<td>4.08 ± 0.323</td>
<td>2.82 ± 0.221</td>
</tr>
<tr>
<td>Control</td>
<td>4.05 ± 0.335</td>
<td>2.34 ± 0.214</td>
</tr>
<tr>
<td>Small</td>
<td>3.68 ± 0.381</td>
<td>2.65 ± 0.205</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Replicate</th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>A</td>
<td>3.97 ± 0.309</td>
<td>2.43 ± 0.201</td>
</tr>
<tr>
<td>B</td>
<td>3.13 ± 0.305</td>
<td>2.25 ± 0.241</td>
</tr>
<tr>
<td>C</td>
<td>5.17 ± 0.372</td>
<td>3.32 ± 0.241</td>
</tr>
<tr>
<td>D</td>
<td>3.78 ± 0.297</td>
<td>2.51 ± 0.208</td>
</tr>
<tr>
<td>E</td>
<td>3.75 ± 0.306</td>
<td>2.39 ± 0.225</td>
</tr>
<tr>
<td>F</td>
<td>3.82 ± 0.247</td>
<td>2.70 ± 0.180</td>
</tr>
</tbody>
</table>

Table 12. Average Elevation of the Regression Lines for the Selected Strains (log₁₀ g. units)

<table>
<thead>
<tr>
<th>Selection Line</th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Large</td>
<td>-.816 ± .0499</td>
<td>-.712 ± .0359</td>
</tr>
<tr>
<td>Control</td>
<td>-.602 ± .0222</td>
<td>-.569 ± .0198</td>
</tr>
<tr>
<td>Small</td>
<td>-.435 ± .0556</td>
<td>-.434 ± .0343</td>
</tr>
</tbody>
</table>
D. GROWTH OF THE FAT COMPONENTS RELATIVE TO CARCASS WEIGHT

1. Cross-sectional Analysis

In the absence of significant line x replicate positional (i.e. slope or elevational) differences in the regression equations, the data were reanalysed with this term deleted from the statistical model to obtain the results presented in Tables 10 and 11. The results are summarized by the average line and replicate regression equations (i.e. averaged over the 6 replicates and 3 lines respectively) presented in Figures 3 and 4.

Only in the case of the male total fat regression coefficient did line differences reach significance (Table 10), indicating with this exception, that fat development proceeds at a similar rate in each of the selected lines. The average rate of fat development was, however, greatest for the large selection line in all cases (Table 11). It was also greater for abdominal than for total fat and for female mice in comparison with the males.

All four analyses detected significant differences among the average replicate partial regression coefficients relating either of the fat components to carcass weight. The average replicate regression lines presented in Figure 4, however, clearly indicate that the differences are almost entirely due to the high slope for Replicate C and the lower slope for Replicate B. The regression coefficients presented in Table 11 show that replicates ranked in a similar order for each fat component and in each sex.

At this stage the following conclusions may be drawn concerning the developmental pattern of relative fat growth between 4½ and 9 weeks of age. Firstly, there exists genetic variation in the averaged rate of development of relative fatness as judged by the significant differences between replicates.
Figure 3. Average Cross-sectional Regression Equations for the Selected Lines (log₁₀ scale).

--- Small --- Control --- Large

Female

Male

Carcass Weight

Carcass Weight

Total Fat

Abdominal Fat

Total Fat

Abdominal Fat

1.0 1.1 1.2 1.3 1.4 20g 30g

1.0 1.1 1.2 1.3 1.4 20g 30g
Figure 4(a). Average Logarithmic Cross-sectional Regression of Abdominal Fat on Carcass Wt. for Each of the Replicates (log_{10} g scale)

**Females**

**Males**

<table>
<thead>
<tr>
<th>Carcass Weight</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>15g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25g</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 4(b). Average Logarithmic Cross-sectional Regression of Total Fat on Carcass Weight for Each of the Replicates ($\log_{10} g$ scale).

**Females**

- Females' data points and lines labeled A, B, C, D, E.

**Males**

- Males' data points and lines labeled A, B, C, D, E.

- Carcass Weight scale: 1.15, 1.25, 1.35, 1.40
- Total Fat scale: 0, 0.1, 0.2, 0.3
which represent differences arising from the effects of random genetic sampling during the course of selection. Secondly, selection for body size does not appear to have affected the developmental growth of the abdominal fat component but the rate of growth of total fat as a percentage of carcass weight does appear to have shown a positively correlated response, particularly to upwards selection, although its significance was definitely established only in the case of the males.

Figure 3 illustrates the highly significant and constant average differences in relative abdominal fatness indicated by the adjusted means presented in Table 12. These show that the selected lines deviated from the controls by a factor of 48 in the case of females and 38 in the case of the males of the average level of relative fatness in the control animals. This difference in the relative abdominal fat content of the carcasses is in line with an expectation based upon energetic considerations of animal growth and development - i.e. slow growth tends to be genetically associated with higher relative amounts of carcass fatty tissue which contains a higher energy content per unit weight than does non-fatty material. It is however, somewhat surprising that these differences were found to be present at the beginning of the growth period studied (i.e. 6 weeks of age), and suggests that they may perhaps be of maternal origin, i.e. result from environmental influences on carcass growth and development that are provided by the mother.

In contrast to relative abdominal fatness no significant differences in total relative fat content were apparent at the overall mean value of carcass weight on a logarithmic scale (Table 10). However, the adjusted means for the large and control lines tended to rank in the reverse order to the values of the regression coefficients, indicating that the average differences in
relative fatness between large and controls tended to decrease at first
during the period of development studied, i.e. the small positive correlated
response in the rate of total fat development has to overcome a negative
correlated response in the level of relative fatness present at 4½ weeks of
age before large mice exhibit greater levels of relative fatness than the
controls. Maternal effects and associated compensatory growth phenomena
(Monteiro and Falconer 1966) may be of significance to this situation.

The strong positive association found between the percentage growth of
fat relative to the percentage growth of the carcass as a whole, was evident
with respect to the selection line differences within each of the replicates.
This will become apparent from graphs presented in a later part of this
section. With only three points to estimate the relationships, it is
obvious that the linearity of the association cannot be subjected to any
particularly powerful test. Nevertheless, there did not appear to be any
marked deviations from linearity that were common to the two sexes or to the
separate lines and replicates. It should also be pointed out that the above
analyses ignore the fact that the means analysed were based upon different
numbers of individual animals because of the inequality of subclass numbers.
However, only replicate 3 is likely to suffer markedly from this influence
(Table 9).

2. Static Analyses

These analyses were carried out with the aim of establishing whether and
to what extent the developmental pattern of relative fat growth established
for the lines and replicates by the previous analyses of the data on a cross-
sectional basis, was reflected by the corresponding between-animal regression
Table 13. Results from the Analysis of Covariance. Testing Line-replicate, Sex and Age Group Regression Coefficients for Log Abdominal Fat or Log Total Fat as the Dependent Variate and Log Carcass Weight as the Independent Variate.

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>d.f.</th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Regression</td>
<td>1</td>
<td>4.64</td>
<td>2.17</td>
</tr>
<tr>
<td>Line-replicate Regressions</td>
<td>17</td>
<td>1.39</td>
<td>1.19</td>
</tr>
<tr>
<td>Sex Regressions</td>
<td>1</td>
<td>5.41</td>
<td>12.3</td>
</tr>
<tr>
<td>Age Group Regressions</td>
<td>2</td>
<td>.621</td>
<td>1.42</td>
</tr>
<tr>
<td>Interaction Regressions (sex x age)</td>
<td>2</td>
<td>1.89</td>
<td>.195</td>
</tr>
<tr>
<td>Error Mean Square (log. g.)² units</td>
<td>558</td>
<td>.0973</td>
<td>.0672</td>
</tr>
<tr>
<td>Average Regression Coefficient</td>
<td></td>
<td>2.52 ± .117</td>
<td>1.53 ± .597</td>
</tr>
</tbody>
</table>
Table 15: E-values from the Analysis of Covariance, Testing Line, Replicate and Age Differences in the Regression Coefficients and their Two-way Interactions

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>d.f.</th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Average Regression</td>
<td>1</td>
<td>117</td>
<td>+++</td>
</tr>
<tr>
<td>Regression Deviations from the Average</td>
<td></td>
<td>5.22</td>
<td>6.35</td>
</tr>
<tr>
<td>Line</td>
<td>2</td>
<td>6.70++</td>
<td>.172</td>
</tr>
<tr>
<td>Replicate</td>
<td>5</td>
<td>1.17</td>
<td>1.30</td>
</tr>
<tr>
<td>Age</td>
<td>2</td>
<td>.879</td>
<td>2.08</td>
</tr>
<tr>
<td>Line x Replicate</td>
<td>10</td>
<td>.949</td>
<td>.826</td>
</tr>
<tr>
<td>Line x Age</td>
<td>4</td>
<td>2.60+</td>
<td>.811</td>
</tr>
<tr>
<td>Rep x Age</td>
<td>10</td>
<td>1.36</td>
<td>1.39</td>
</tr>
<tr>
<td>d.f. for Error</td>
<td>231</td>
<td>237</td>
<td>231</td>
</tr>
<tr>
<td>E.M.S. (log g. units)</td>
<td>.0994</td>
<td>.0645</td>
<td>.0554</td>
</tr>
</tbody>
</table>
Table 15. *F* values from the Analysis of Covariance, Testing Adjusted Means and Line Regression Coefficients for Log Abdominal Fat or Log Total Fat as the Dependent Variate and Log Carcass Weight as the Independent Variate

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>d.f.</th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Line</td>
<td>2</td>
<td>4.69 ++</td>
<td>7.05 ++</td>
</tr>
<tr>
<td>Replicates</td>
<td>5</td>
<td>7.29 +++</td>
<td>7.96 +++</td>
</tr>
<tr>
<td>Age Group</td>
<td>2</td>
<td>15.1 +++</td>
<td>7.59 +++</td>
</tr>
<tr>
<td>Line x Rep</td>
<td>10</td>
<td>9.18 +++</td>
<td>12.20 +++</td>
</tr>
<tr>
<td>Line x Age</td>
<td>4</td>
<td>2.59 +</td>
<td>2.27</td>
</tr>
<tr>
<td>Rep x Age</td>
<td>10</td>
<td>.630</td>
<td>2.14 +</td>
</tr>
<tr>
<td>Pooled Regression</td>
<td>1</td>
<td>176 +++</td>
<td>308 +++</td>
</tr>
<tr>
<td>Line Regression</td>
<td>2</td>
<td>8.22 +++</td>
<td>1.47 +++</td>
</tr>
<tr>
<td>d.f. for Error</td>
<td></td>
<td>262</td>
<td>268</td>
</tr>
<tr>
<td>E.M.S. (log g. units)</td>
<td></td>
<td>.116</td>
<td>.0700</td>
</tr>
</tbody>
</table>

Regression Coefficients

<table>
<thead>
<tr>
<th></th>
<th>Average (b)</th>
<th>Large Line</th>
<th>Control Line</th>
<th>Small Line</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.66±.200</td>
<td>2.19±.125</td>
<td>1.54±.148</td>
<td>1.29±.122</td>
</tr>
<tr>
<td>Large Line</td>
<td>3.48±.358</td>
<td>1.95±.225</td>
<td>2.29±.264</td>
<td>1.21±.221</td>
</tr>
<tr>
<td>Control Line</td>
<td>2.99±.311</td>
<td>2.16±.228</td>
<td>1.58±.229</td>
<td>1.31±.224</td>
</tr>
<tr>
<td>Small Line</td>
<td>1.51±.370</td>
<td>2.45±.194</td>
<td>.762±.271</td>
<td>1.35±.190</td>
</tr>
</tbody>
</table>
equations at each of the slaughter ages. The establishment of the correspondence between the two types of relationship is necessary to a between-animal analysis of the genetic components of allometric growth in the case of body components which require the destruction of the animal for their assessment. This is because such data will usually be restricted to the static or mixed cross-sectional type and consequently the estimation of genetic parameters of allometric relationships in random breeding populations will be limited to a static comparison of between-animal variation for related and unrelated individuals.

The large size of the variance-covariance matrix for the linear model required to simultaneously assess the significance of effects due to sex, line, replicate and age together with their corresponding interactions, necessitated the progressive examination of different combinations of the effects, and the elimination from the model of those effects proving to be unimportant in their contribution to variation in the dependent variable. In addition, adorption of effects was employed to reduce the size of the least squares matrix, the remaining effects being examined on a within-subclass basis (Harvey 1964). This was particularly useful in the early analyses which were primarily concerned with differences in the regression coefficients rather than in the adjusted means.

The results of the analyses are presented in Tables 13, 14 and 15.

(a) Abdominal Fat

Figure 5 summarises the pertinent features of the relationships found to exist between abdominal fat carcass weight. Separate graphs are presented for each sex in view of the highly significant sex differences in the regression
Figure 5. Regression of Abdominal Fat on Carcass Weight - Static Regression Equations and Age Group Co-ordinates for Each of the Selected Strains (log $g$ scale).

- Small
- Control
- Large

**Females**

**Males**

<table>
<thead>
<tr>
<th>Carcass Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>10g</td>
</tr>
<tr>
<td>15g</td>
</tr>
<tr>
<td>20g</td>
</tr>
<tr>
<td>30g</td>
</tr>
</tbody>
</table>

Abdominal Fat

$\log g$
coefficients (Table 13). Separate regression equations for each of the selection lines are also presented, for although an overall analysis failed to demonstrate significant differences among the 18 line-replicate regression coefficients (Table 13) average selection line differences were apparent for female mice (Table 15). Average differences between replicates were, however, not apparent. The coordinates representing the line means at each of the 3 ages are also presented in Figure 5 to provide an indication of the extent to which the static regression lines differed from the average between-age cross-sectional estimates previously discussed.

The significant (P < .05) interaction of the selection line regression coefficients with age which was evident for female mice (Table 14), arose from a negative estimate (b = -.24) for female mice of the small line at 6 weeks of age. The separate estimates at each age are indicated by the dotted lines in the graph for female mice in Figure 5. The replicate differences in the regression coefficient within this sub-class were extremely variable for both fat components and the negative estimates were quite unrelated to the corresponding estimates for the male mice. The interaction observed may perhaps, therefore, best be ascribed to the fortuitous effects of sampling. In this situation the results presented in Table 15 give the best characterisation of the relationships which exist between abdominal fat and carcass weight.

The between-age regression coefficients established by the previous cross-sectional analysis were on average about 30-40% larger than the within-age estimates presented in Table 15. This indicates that age has an effect upon fat development independent of the average effect of body size - i.e. relative to carcass weight, proportionate differences between animals in abdominal fat content are greater for animals of different ages than they are for animals of
the same age. This effect of age is also demonstrated by the significant 
($p < .001$) age effect on the elevation of the selection line regressions 
(Table 15).

The effect of age over and above the effect of body size appears most 
marked for female mice of the small selection line, there in fact being evidence 
for this group that the effect of body size on abdominal fat is negative at 
six weeks of age. The significant average selection line differences in the 
regression coefficients found for female mice also rests very largely in the 
difference between mice of the small line versus those of the large and control 
stocks. With the exception shown by the female mice of the small selection 
line, the static analyses essentially confirm the pattern of differences in 
relative fatness between the lines that were established by the cross-sectional 
analyses which included the effects of age - i.e. large mice demonstrate a 
constant lower average level of relative fatness than the controls while 
females show higher levels of relative fatness than do the male mice. The 
significant line x replicate interaction for the elevation of the regression 
lines for each of the selected strains (Table 15) indicates, however, that the 
magnitude of this difference varies from replicate to replicate.

While the cross-sectional analyses revealed significant differences 
between replicates in their average pattern of developmental growth of abdominal 
fat, the static analyses showed that at the same age, differences in carcass 
weight were associated with similar differences in the weight of abdominal fat 
regardless of which replicate to which the mice belonged. Thus the greater 
slope of the between-age regressions for Replicate C and the corresponding 
lower than average slope for Replicate B indicate a different effect of age
Table 16.  **Least Squares Adjusted Age Group Means for Log Abdominal Fat**  
(Log\textsubscript{10} g units)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age Group (weeks)</th>
<th>42</th>
<th>6</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td></td>
<td>-.70 ± .022</td>
<td>-.61 ± .015</td>
<td>-.50 ± .021</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>-.63 ± .019</td>
<td>-.55 ± .012</td>
<td>-.56 ± .018</td>
</tr>
</tbody>
</table>

Table 17.  **Least Squares Adjusted Line - Replicate Class Means for Log Weight of Abdominal Fat**  (Log\textsubscript{10} g units)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Replicate</th>
<th>Selection Line</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Large</td>
</tr>
<tr>
<td>Female</td>
<td>A</td>
<td>-.57 ± .050</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>-.83 ± .053</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>-.55 ± .045</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>-.53 ± .046</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>-.67 ± .053</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>-.60 ± .048</td>
</tr>
<tr>
<td>Male</td>
<td>A</td>
<td>-.69 ± .037</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>-.76 ± .033</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>-.54 ± .033</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>-.62 ± .035</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>-.71 ± .055</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>-.61 ± .036</td>
</tr>
</tbody>
</table>
upon the average level of relative fatness in each of these groups.

In view of the somewhat complex interpretation necessitated by the lower than average static regression coefficient relating abdominal fat to carcass weight for female mice of the small line, it was decided to investigate the pattern of adjusted means under the assumption that this feature arose by chance. This was done by examining the elevation of the average within-age, within-line and within-replicate regression equations separately for mice of each sex, and gave a pattern of F-values that was very little different from that presented in Table 15. In summary, the analysis demonstrated highly significant ($P < .001$) line x replicate and average age differences in the amount of abdominal fat possessed by animals at the same carcass weight. The $F$-values testing line x age and replicate x age effects were low by comparison, although the latter interaction did reach significance at the 5% level of probability for the case of male mice. However, the interaction of the 16 line-replicate groups with age failed to reach significance in either sex when the analysis was repeated to test for line-replicate and age differences in the elevation of the regression line. The average within-age regression coefficients estimated by this analysis were 2.66 ± 0.214 for the females and 2.29 ± 0.129 for males, while the model accounted for 90% and 92% respectively, of the total sum of squares in abdominal fat weight. This was only about 5-6% less than the proportion of the sum of squares accounted for by the model which included selection line differences in the regression coefficients (Table 15). Furthermore, the reduction in sum of squares for the two models showed a very similar difference in both female mice, for which significant line differences were previously established, and in male mice for which they were not. This model has accordingly been adopted to present an
Figure 6. Average Relative Abdominal Fat Content for Each of the Selected Lines \((\log_{10} g \text{ scale})\).

\((L = \text{Large}, C = \text{Control}, S = \text{Small})\)
overall ranking of the line-replicate effects on a within-age basis. Those are presented in Table 17, while Table 16 shows the average adjusted age-group means for each sex.

The adjusted age means of Table 16 show an age trend of increasing elevation of the average regression line for female mice between 4 and 9 weeks and for male mice between 4 and 6 weeks of age. This aspect will be returned to in a later part of this section which deals with the relationships between the two fat components.

The similar pattern of line-replicate differences for both sexes was reflected in a correlation of 0.82 between the adjusted means for females and males. The pattern of differences has accordingly been summarized diagrammatically in Figure 6 which depicts the sex averages for the line-replicate means of Table 17. The figure illustrates the greater amount of abdominal fat at similar carcass weights, possessed by mice of the small selection line in comparison with mice of the large line, for the case of all replicates except replicate C; the average ranking of the selected line is reversed in this replicate. The large line has on average, a lower adjusted mean than the control line. Among the replicates, B stands out as having the greatest adjusted mean, while the line differences are greatest for replicate B, and rather small for Replicate F.

(b) Total Fat

The analyses of total fat gave results different from those of abdominal fat. With total fat, the between-age cross-sectional regressions were not consistently greater than the within-age static regressions. This means that with total fat age itself did not influence the weight of fat relative to
Table 18. **Estimates of the Average Regression Coefficients Relating Log Total Fat to Log Carcass Weight in Each of the Selection Lines**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Selection Lines</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Large</td>
<td>Control</td>
<td>Small</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.98 ± 0.157+</td>
<td>1.56 ± 0.11+</td>
<td>0.923 ± 0.160</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.64 ± 0.120+</td>
<td>1.22 ± 0.117</td>
<td>1.16 ± 0.104</td>
<td></td>
</tr>
</tbody>
</table>

*+ Significantly greater than 1.0 at P = .05*
Figure 7. Average Regression of Total Fat on Carcass Weight for Each of the Selected Lines (log g units).

- Small - Control - Large

Females

Males

Carcass Weight
crease eight. The absence of an age effect can be seen from the F-values testing the effect of age as a source of variation in Tables 13, 14 and 15.

In this situation, the best overall estimate of the regression equation relating log fat to log carcass weight is to be obtained from an analysis which ignores the age classification of the data. The regression coefficients estimated in this way are presented in Table 18, the average regression equations for each of the selection lines being shown in Figure 7.

The regression coefficients were significantly greater than unity (P < .05) for female mice of the large and control strains and for large strain male mice, indicating for these groups that the percentage of chemical fat in the carcass increases with carcass weight. It is also apparent that this increase occurs at approximately a 40% greater rate in mice of the large strain relative to the rate of increase exhibited by control strain mice of the same sex. The graphs of Figure 7 indicate that large strain mice of both sexes have a lower proportion of their carcass as chemical fat prior to carcass weights of the order of 24 g (i.e. log carcass = 3.15 approx.). At higher carcass weights, however, large strain mice demonstrate a higher level of relative fatness than the control animals of the same sex. Small strain mice do not on average exhibit a similar trend of increasing carcass fat percentage during the 4½ to 9 week growth period.

Although the above discussion described the average trend of relative fatness in mice of the different selection lines, the presence of a significant line x replicate interaction in adjusted fat weights (Table 15) indicates that the elevation of the selection line regression equations depends upon the replicate concerned. Within each of the replicates, however, their elevation was found to be independent of sex. This was reflected by a correlation of
Table 19. Elevations of the Selection Line Regressions for Log Total Fat on Log Carcass Weight (averaged over sexes) for Each of the Replicate Groups (log, g units)

<table>
<thead>
<tr>
<th>Replicate</th>
<th>Selection Line</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Large</td>
</tr>
<tr>
<td>A</td>
<td>.4579</td>
</tr>
<tr>
<td>B</td>
<td>.1057</td>
</tr>
<tr>
<td>C</td>
<td>.6270</td>
</tr>
<tr>
<td>D</td>
<td>.6653</td>
</tr>
<tr>
<td>E</td>
<td>.4835</td>
</tr>
<tr>
<td>F</td>
<td>.5321</td>
</tr>
</tbody>
</table>
Figure 8. Average Relative Total Fat Content for Each of the Selected Lines (log_10 g scale).

( L = Large, C = Control, S = Small )

Replicates
0.23 between the adjusted line-replicate means for each sex and by a non-significant F-value (F = 1.02 with 17 and 562 d.f.) testing the interaction of the adjusted line-replicate effects with sex. The adjusted line-replicate means averaged over the sexes are presented in Table 19. They were adjusted using the regression coefficients shown in Table 18. They are also presented diagrammatically in Figure 8.

Because of the similar average carcass growth increments during the 4th to 6 and 6 to 9 week periods, the adjusted means of Table 19 and Figure 8 reflect the relative ranking of the selected lines at carcass weights approximating those found for mice of the control line at six weeks of age. They thus reflect the correlated response of relative fatness close to the age at which selection was carried out. With respect to the large and control lines, the pattern of relative fatness shown by the diagram is essentially similar to that found for the abdominal fat depot, i.e. a tendency for lowered relative fatness in the large line for replicates B, D, E and F. The small line, however, tends to rank at a lower average level of relative fatness in comparison to the control line and is thus in contrast to the situation found for abdominal fat in the case of replicates J, E and F.

The adjusted means of Table 19 have been used to position the average sex regression equations for the large, control and small strains shown in Figure 9 for each of the replicates. The graphs of Figure 9 thus illustrate the average selection line regression equations for each of the 6 replicate groups. The slopes shown are based upon the average within-sex selection line regressions, the statistical analysis demonstrating that the interaction between the sex and selection line regression coefficients was just below significance at the 5 level of probability (F = 2.96 with 2 and 562 d.f.). These average regression
Figure 9. Average Positioning of the Logarithmic Regression Lines Relating Total Fat to Carcass Weight for Each of the Selected Strains (log \( g \) units).

---

**Small**  **—**  **Control**  **—**  **Large**

<table>
<thead>
<tr>
<th>Replicate A</th>
<th>Replicate B</th>
<th>Replicate C</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Graph" /></td>
<td><img src="image2.png" alt="Graph" /></td>
<td><img src="image3.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Replicate D</th>
<th>Replicate E</th>
<th>Replicate F</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image4.png" alt="Graph" /></td>
<td><img src="image5.png" alt="Graph" /></td>
<td><img src="image6.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

Carcass Weight
coefficients were 1.81, 1.39 and 1.04 for the large, control and small selection lines respectively.

The graphs of Figure 9 demonstrate the variability of the correlated response in relative fatness to selection for and against body weight at six weeks of age in each of the 6 replicates. On the whole the responses in terms of relative fat composition tend to have been very small in comparison with the response in the absolute amounts of either carcass weight or total fat content. Selection in either direction does seem however, to have altered the average allometric coefficient which has on average been increased by about 30% in the large line and decreased by a similar amount in the small line from the average value of around 1.4 for the control animals. In addition to this alteration in the average developmental trend in relative fatness between 4 and 9 weeks, there appear to be important differences among the replicates which reflect developmental differences that are already established by the age of 4 weeks. This influence, furthermore, tends to have an opposite effect on the relative fatness of the selected strains to that brought about by the positive change in the allometric coefficients. This is particularly true in replicate B, for which the large strain demonstrates a lower level of relative fatness than either the control or selected lines throughout the entire 4 to 9 week period. The same trend exists, but to a lesser degree, for the large control comparison in replicates D and F. The control-small comparison is similar in replicates A and B, but tends to be in the opposite direction for replicates C, D, E and F, i.e. small mice possess lower amounts of fat in comparison with control mice of the same carcass weight in the latter four replicates.

The variability among replicates in the developmental stage at which the
<table>
<thead>
<tr>
<th>Sex</th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>2.49 ± 0.225</td>
<td>1.48 ± 0.156</td>
</tr>
<tr>
<td>Male</td>
<td>1.76 ± 0.176</td>
<td>1.30 ± 0.140</td>
</tr>
<tr>
<td>Average</td>
<td>2.11 ± 0.178</td>
<td>1.38 ± 0.137</td>
</tr>
</tbody>
</table>

Table 20. Between-strain Genetic Regression Coefficients Relating Log Fat Components to Log Carcass Weight
relative ranking of the selection lines is reversed by the joint effects of those two development patterns, might possibly be interpreted as a temporal alteration in the onset of the different average relative growth rates found to characterise the three selection lines between 4 and 9 weeks of age. It could, however, also result from a growth dependent pattern of changes in the relative growth coefficients which varied for each of the 3 strains. The choice between those two possibilities would require the analysis of a greater number of developmental stages than was used for the present investigation in order that departures from the linearity of the allometric relationship might be adequately assessed.

3. Genetic Regression of Fat Components on Carcass weight

Estimation of the between-strain coefficients of genetic allometry for each sex and for each fat component of the carcass from the regression of log fat component on log carcass weight using the within-age least-squares means for the 36 sex-line-replicate subclasses, confirmed the average pattern of selection responses already established. The estimates of the genetic regression coefficients for total fat (Table 20) were of similar magnitude of the average phenotypic regressions previously reported (Table 18) and indicate that selection has produced no changes in relative fatness on average over the 4 to 9 week growth period. The estimates for abdominal fat were, however, somewhat lower than their phenotypic counterparts indicating that positive genetic changes in carcass weight have on average been accompanied by lower concomitant changes in relative abdominal fatness than would be expected from the phenotypic relationship. Conversely, negative carcass changes have on average resulted in carcasses containing greater amounts of fat than carcasses
Table 21.  F-values from the Analysis of Covariance, Testing Line-replicate, and Sex x Age Differences in the Regression Coefficient Relating Log Total Fat to Log Abdominal Fat

<table>
<thead>
<tr>
<th>Source</th>
<th>d.f.</th>
<th>F-Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Regression</td>
<td>1</td>
<td>224.1+++</td>
</tr>
<tr>
<td>Line-replicate regressions</td>
<td>17</td>
<td>1.30</td>
</tr>
<tr>
<td>Sex Regressions</td>
<td>1</td>
<td>61.5+++</td>
</tr>
<tr>
<td>Age Regressions</td>
<td>2</td>
<td>33.3+++</td>
</tr>
<tr>
<td>Sex x Age Regressions</td>
<td>2</td>
<td>15.9+++</td>
</tr>
<tr>
<td>E.M.S.</td>
<td>558</td>
<td>0.019</td>
</tr>
</tbody>
</table>

Regression Coefficients (*S.E.*)

<table>
<thead>
<tr>
<th>Sex</th>
<th>4.5 weeks</th>
<th>6 weeks</th>
<th>9 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>0.55±0.022</td>
<td>0.55±0.021</td>
<td>0.71±0.020</td>
</tr>
<tr>
<td>Male</td>
<td>0.56±0.025</td>
<td>0.79±0.028</td>
<td>0.83±0.027</td>
</tr>
</tbody>
</table>
Table 22. *F*-values from the Analysis at Covariance. Testing Sex, Age and Line Differences in the Partial Regression Coefficients for Total Fat on Log Abdominal Fat at the same Value of Log Carcass Weight

<table>
<thead>
<tr>
<th>Source</th>
<th>d.f.</th>
<th>F-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Carcass Regression</td>
<td>1</td>
<td>3.43</td>
</tr>
<tr>
<td>Average Abdominal Fat Regression</td>
<td>1</td>
<td>1620</td>
</tr>
<tr>
<td>Sex Regressions</td>
<td>1</td>
<td>13.6</td>
</tr>
<tr>
<td>Age Regressions</td>
<td>2</td>
<td>21.8</td>
</tr>
<tr>
<td>Line Regressions</td>
<td>2</td>
<td>5.45</td>
</tr>
<tr>
<td>Sex x Age Regressions</td>
<td>2</td>
<td>7.88</td>
</tr>
<tr>
<td>Sex x Line Regressions</td>
<td>2</td>
<td>3.25</td>
</tr>
<tr>
<td>Age x Line Regressions</td>
<td>4</td>
<td>1.34</td>
</tr>
<tr>
<td>E.M.S.</td>
<td>575</td>
<td>.0220</td>
</tr>
</tbody>
</table>

% Reduction in Total S.S.                     | 97%  |

Regression Coefficients (± S.E.)

<table>
<thead>
<tr>
<th>Sex</th>
<th>4.5 weeks</th>
<th>6 weeks</th>
<th>9 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>.57±.029</td>
<td>.61±.029</td>
<td>.78±.028</td>
</tr>
<tr>
<td>Male</td>
<td>.62±.035</td>
<td>.81±.036</td>
<td>.83±.034</td>
</tr>
</tbody>
</table>
Table 23.  
E-values from the Analysis of Covariance. Testing Line x Age Differences in the Partial Regression Coefficients Relating Log Total Fat to Log Carcass Weight and Log Abdominal Fat Weight

<table>
<thead>
<tr>
<th>Source</th>
<th>d.f.</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Carcass Regression</td>
<td>1</td>
<td>.379</td>
<td>2.70</td>
</tr>
<tr>
<td>Age Regressions</td>
<td>2</td>
<td>.460</td>
<td>1.70</td>
</tr>
<tr>
<td>Line Regressions</td>
<td>2</td>
<td>3.90</td>
<td>2.54</td>
</tr>
<tr>
<td>Age x Line</td>
<td>4</td>
<td>.490</td>
<td>.919</td>
</tr>
<tr>
<td>Average A. Fat Regression</td>
<td>1</td>
<td>955</td>
<td>620</td>
</tr>
<tr>
<td>Age Regressions</td>
<td>2</td>
<td>10.7</td>
<td>8.13</td>
</tr>
<tr>
<td>Line Regressions</td>
<td>2</td>
<td>9.5</td>
<td>7.31</td>
</tr>
<tr>
<td>Age x Line</td>
<td>4</td>
<td>.30</td>
<td>.45</td>
</tr>
<tr>
<td>E.M.S. (d.f.)</td>
<td></td>
<td>.0172 (272)</td>
<td>.0261 (278)</td>
</tr>
</tbody>
</table>
Figure 10. Logarithmic Regression of Total Fat on Abdominal Fat for Each Sex and at 4½, 6 and 9 weeks of Age.

(log_e g scale)

---

Females

Males

---

Total Fat

Abdominal Fat

b=1.0
of similar weight in the base population. The scatter of the individual line-replicate means about the average genetic regression lines merely confirmed the particular pattern of correlated responses that was previously found to characterise the separate replicates.

2. **RELATIONSHIP BETWEEN ABDOMINAL FAT AND TOTAL FAT**

Regression relationships with log total fat as the dependent variate have been used to assess the average pattern of developmental growth of total fat relative to the abdominal component and of the value of abdominal fat as an index of total carcass fat content. Figure 10 summarises some of the pertinent features revealed by the results presented in Tables 21, 22 and 23.

The regression coefficients relating total to abdominal fat were consistently less than unity for each sex and at each age (Table 21) indicating that percentage differences in the abdominal fat content of different mice were greater than the corresponding percentage differences in total fat content. Important sex differences were, however, found to exist in the developmental pattern of the two fat components. This was revealed by the significant sex x age effect upon the regression coefficients (Table 21).

At 4 weeks the percentage differences between mice were about twice as large for abdominal fat in comparison with the percentage differences in total fat content. This was true for either sex although male mice exceeded the females by 20% with respect to the proportion of their total fat in the abdominal depot. The average trend of developmental growth for the two fat components (dotted lines in Figure 10) remained rather linear for male mice, but females mice on the other hand, showed a progressively faster rate of development of abdominal relative to total fat and became similar to the males.
in the proportion of total fat in the abdominal depot at total fat weights of around 2\textsubscript{g} g. However, at this point of equality of relative fat distribution between the abdominal and non-abdominal sites, the females were on average about one week older (7 weeks of age) than the males (6 weeks of age). This developmental trend continued to at least 9 weeks of age, by which stage the sex difference was the reverse of that which existed at \( \frac{1}{2} \) weeks of age - i.e. the females now possessed greater amounts of abdominal fat relative to their total fat content than did the males.

At 6 and 9 weeks of age the slope of the within-age regressions of ether extract on abdominal fat were greater than the average developmental patterns described above. This reflects the importance of age in influencing the developmental pattern of relative fat growth in the abdominal and non-abdominal depots. Between mice of the same age greater differences existed in the total amount of fat relative to the amount of abdominal fat, or conversely, smaller differences exist in the proportion of fat in the abdominal depot, than would be expected from the average developmental trend of fat distribution. The within-age regression coefficients for male and female mice indicate that this age effect on the between animal variation in fat distribution is small for female mice between \( \frac{1}{2} \) and 6 weeks of age (i.e. similar within-age coefficients which are of the same order as the between age trend); the age effect is, however, relatively large but very little different at 6 and 9 weeks of male mice (i.e. regression coefficients of 0.8 which are greater than the between-age trend of approximately 0.5).

The existence of a highly significant sex x age interaction in the regression of total on abdominal fat, means that the within-sex and age relationship must be known in order that the total fat content of the carcass can be
accurately predicted from a knowledge of abdominal fat weight. In addition the appearance of significant differences between selection lines in the slope of this relationship (Table 22) suggests that the prediction equation is likely to be different for different genotypes. This would seem to be particularly true on arithmetical scales of measurement, for when the analysis presented in Table 21 was repeated without the transformation of the data to the logarithmic scale, highly significant ($P < .01$) line-replicate differences in the regression coefficient were evident in addition to the significant ($P < .01$) differences between the sex x age sub-classes.

The inclusion of carcass weight in the logarithmic prediction equations failed to eliminate the sex x age and line heterogeneity (Tables 22, 23). Apparently, once abdominal fat is known, carcass weight is on average of little additional value in predicting total fat content (partial regression for carcass weight not significant), although carcass weight does appear to be of some advantage in predicting the differences in total fat weight for female mice belonging to different selection lines. Conversely, if carcass weight is known, knowledge of the weight of abdominal fat is still important in predicting total fat content. In this case also, the prediction equations for male mice are likely to vary markedly with such genotype differences as those which are reflected by the differences between the selection lines.

f. RELATIVE GROWTH OF THE FAT COMPONENTS TO MATURITY

The data were re-analyzed on a cross-sectional basis following the inclusion of one additional observation in each subclass to represent the weights of the carcass and its fat components taken on a different sample of C-strain measured at an average age of 48 weeks. The animals were the progeny
Table 24. Cross-sectional Regression Coefficients Estimating the Average Trend of Fat Development to Maturity for Each of the Selection Lines

<table>
<thead>
<tr>
<th>Line</th>
<th>Abdominal Fat</th>
<th></th>
<th>Ether Extract</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\hat{b}$</td>
<td>$\sigma^*$</td>
<td>Within-sex</td>
<td>$\hat{b}$</td>
</tr>
<tr>
<td>Large</td>
<td>3.31</td>
<td>3.07</td>
<td>3.19</td>
<td>1.91</td>
</tr>
<tr>
<td></td>
<td>±.297</td>
<td>±.234</td>
<td>±.223</td>
<td>±.194</td>
</tr>
<tr>
<td>Control</td>
<td>3.30</td>
<td>2.63</td>
<td>3.05</td>
<td>1.78</td>
</tr>
<tr>
<td></td>
<td>±.264</td>
<td>±.203</td>
<td>±.192</td>
<td>±.172</td>
</tr>
<tr>
<td>Small</td>
<td>2.61</td>
<td>2.51</td>
<td>2.54</td>
<td>1.32</td>
</tr>
<tr>
<td></td>
<td>±.244</td>
<td>±.175</td>
<td>±.168</td>
<td>±.160</td>
</tr>
<tr>
<td>Unweighted</td>
<td>3.08</td>
<td>2.74</td>
<td>2.92</td>
<td>1.67</td>
</tr>
<tr>
<td>average</td>
<td>±.155</td>
<td>±.118</td>
<td>±.113</td>
<td>±.101</td>
</tr>
<tr>
<td>regression</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
of an earlier generation of the same selection experiment and were included with the present data for an overall cross-sectional analysis in order to gain some idea of whether the patterns of allometric growth established between 4.5 and 9 weeks of age continued during later life. In view of the somewhat smaller strain differences in relative fatness in comparison with the absolute differences in the fat and non-fat components, it was considered that the three generation gap between these two samples of mice would be unlikely to seriously detract from the value of such an analysis.

An examination of line, replicate and line x replicate effects on the slope of the logarithmic regression lines relating the fat components to carcass weight, revealed the existence of significant line effects only. In contrast to the earlier analyses, there was no evidence of important slope differences in the average replicate regression equations for either character or for either sex. Re-analysis using a statistical model which fitted just the line differences in the regression coefficients gave the estimates shown in Table 24.

The results broadly confirmed the average previously established pattern of line and sex differences. The sex difference in the abdominal fat regression coefficient was somewhat less than found previously, while average line differences remained similar and still failed to reach significance at the 5% level of probability. The pattern of significant selection line differences for the total fat regression coefficients was also similar to that previously established, although the coefficients were a little greater in all cases.

The least squares means on which these analyses were based are presented graphically in Figures 11 and 12 as a pictorial summary of the development trends of relative fatness in these strains of mice. They are based upon the within-
Figure 11. Average Within-Sex Logarithmic Relationships Between Abdominal Fat and Carcass Weight in Each Replicate (log_{10} g units).

---

**Small**  
**Control**  
**Large**
Figure 12. Average Within-Sex Logarithmic Relationships Between Total Fat and Carcass Weight in Each Replicate ($\log_{10} g$ units)

- **Small**
- **Control**
- **Large**

**Replicate A**

**Replicate B**

**Replicate C**

**Replicate D**

**Replicate E**

**Replicate F**

<table>
<thead>
<tr>
<th>Carcass Weight</th>
<th>Total Fat Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>10g</td>
<td>0</td>
</tr>
<tr>
<td>20g</td>
<td>1</td>
</tr>
<tr>
<td>30g</td>
<td>2</td>
</tr>
</tbody>
</table>
sex line-Replicate age group means using all available animals. While the patterns of relative fat development to maturity are seen to be remarkable linear for all the strains, there is a suggestion in the graphs of Figure 12 that the pattern of relative growth for total fat may have a tendency towards curvilinearity in large strain animals such that relative fat development proceeds at a higher than average rate as these animals approach their final body size. One further interesting trend suggested by Figure 12 is a lower than average rate of developmental growth for total fat as a proportion of carcass weight between the ages of 6 and 9 weeks. This feature is evident for a number of the control and small strain graphs, but is not apparent for any of the large strains. Such a trend agrees with the low within-age regression coefficients previously established for the regression of abdominal fat on carcass weight amongst small strain female mice at six weeks of age. Similar decreases in the average rate of relative fat development during early post-natal life were evident in Zucker and Zucker's (1963) study of fat accretion and growth in the rat.

G. SUMMARY

(i) Growth of both the abdominal depot fat and total chemical fat were found to be closely associated with total carcass weight between 6 and 9 weeks of age.

(ii) The relationships were remarkably linear on a logarithmic scale and indicated that the fat components formed an increasing proportion of the carcass as development proceeded. The percentage rate of increase of the fat components was found to exceed the percentage growth of carcass weight by a factors of the order of 3 for abdominal fat and 1.5 for total fat.
Female mice increased the proportion of fat in the carcass at a higher rate than males between 4 and 9 weeks of age. The rate of increase of abdominal fat relative to carcass weight was about 50% greater in females than in males, and the rate of increase of total fat about 25% greater.

In contrast to the positive correlated responses in the absolute amounts of abdominal fat, the relative abdominal fat content decreased as a result of selection for large body size, and increased as a result of selection for small body size. The changes were of similar magnitude in both directions and represented an alteration of the order of 30-40% from the average level of relative fatness in the control populations. The correlated responses in the level of relative abdominal fatness varied considerably from replicate to replicate; they were most marked for replicate B which exhibited a low average level of relative fatness and were in the opposite direction in replicate C which exhibited a fast rate of increase in relative fatness.

Both the static and cross-sectional analyses led to similar conclusions with respect to the comparative levels of relative fatness. Together they indicated an age effect on the relative amounts of abdominal fat and that the magnitude of this age effect varied from replicate to replicate.

In contrast, the relative growth of total fat in the carcass did not demonstrate a similar regular age trend. It did, however, vary from strain to strain. Although the average rate of percentage growth of chemical fat was about 40% greater for mice of the large strain in comparison with the average rate for the controls, the mice of large strain were found to possess a lower level of carcass fat percentage when carcass weights were less than about 24 g. Small strain mice did not on average show a similar trend of increasing fat percentage with carcass weight during this same growth period.
Significant variation was found to exist between the replicates in the extent to which selection for increased body size had resulted in a lowered relative fatness at the beginning of the growth period investigated. However, as a net result it was apparent that selection had on average resulted in virtually no change in the relative total fat content of the carcasses at the age at which selection had been carried out - i.e. the large strains possessed amounts of total fat at 6 weeks of age that were similar to those possessed by control line animals of the same carcass weight.

(vii) An extended analysis of relative fat growth to carcass weights close to their maximum mature value essentially confirmed the conclusions based on relative growth to 9 weeks of age.

(viii) The effect of age upon the relative proportion of carcass weight comprised of abdominal fat resulted in a different age pattern of relationships between the two components in each sex. Female mice were found to possess a lower proportion of (total) fat in the abdominal depot at 4 weeks of age but subsequently exhibited a progressively faster rate of fat growth in the abdominal depot than did the males. Sex equality in relative fat distribution between the abdominal and remaining depots was found to occur at total fat weights of the order of 21/2 g, at which stage the female mice were approximately one week older than the males. By 9 weeks of age the females had a considerably greater relative amount of their total fat in the abdominal depot.

The presence of this sex x age interaction in the regression of total fat on abdominal fat limits the usefulness of the latter component as an index of the total fat content of individual animals. This is further hampered by the existence of a different regression relationship for each of the selected
strains. Carcass weight was found to be of little additional value to the prediction of total fat content once information on the abdominal fat content was available.
VII. GENETIC EVALUATION OF GROWTH CURVE PARAMETER

A. INTRODUCTION

Section II summarized the recent attempts that have been made by a number of workers to describe growth patterns in mice in terms of the parameters of specific mathematical functions. The basis of the approach rests in the possibility of being able to condense a large amount of data representing the extended pattern of growth in time, by means of a relatively small number of mathematical parameters. The extent to which such a practice may be useful biologically, depends both upon the ability of the mathematical model chosen to smooth out unimportant irregularities of the growth process but to leave undistorted the essential systematic trends representing the basic underlying pattern of growth in time. Four different growth functions - namely, the asymptotic, Gompertz, von Bertalanffy and logistic - have been used to describe patterns of growth in mice. However, very little accurate assessment has been made of the usefulness of those functions and even less has been done with respect to the evaluation of alternative growth functions.

A comparison of genotypic differences with respect to the estimated growth parameters would seem to be a useful approach to these two problems and has been undertaken as a part of this investigation. The attempt has involved an estimation of genetic parameters of the logistic growth constants for a randomly bred population of mice, and a comparison of the estimated parameters of the asymptotic growth function for lines of mice that had been selected for large or small body size. In the latter case the study also involved an assessment of the value of the asymptotic growth parameters in estimating the chemical components of the mouse carcass, in an effort to
discover whether or not the knowledge of an animal's growth pattern affords a better prediction of body composition than does a knowledge of its final body size alone.

B. GROWTH FUNCTIONS

The asymptotic regression function, \( y = \alpha + \beta e^{\gamma x} \), represents a relation between \( x \) and \( y \), when \( y \) tends asymptotically to a limit as \( x \) tends towards infinity. The relation is a form of the exponential curve as can be seen if it is written in the equivalent form

\[
y = \alpha + \beta e^{-\gamma x}
\]

where \( \gamma = -\log_e \epsilon \)

The equation contains three parameters: \( \alpha \) representing the asymptotic value of \( y \), \( \beta \) the change in \( y \) when \( x \) passes from 0 to \( +\infty \), and \( \gamma \) the factor by which the deviation \( (y - \alpha) \) is reduced per unit change in \( x \). For the case of body weight growth in time (i.e., where \( y \) = body weight and \( x \) = age), \( \alpha \) represents asymptotic mature weight, while \( \gamma \) represents a parameter describing the rate of change of body size, as a proportion of the amount of growth remaining. This is evident from the first differential,

\[
\frac{dy}{dx} = -\gamma \beta e^{-\gamma x} = \gamma (\alpha - y)
\]

which describes the exponential decay of growth rate to zero as body weight increases asymptotically to mature weight \( \alpha \). The third parameter, \( \beta \) establishes the position of the growth curve along the time axis, being the value of \( y \) at \( t = 0 \). The two parameters \( \alpha \) and \( \gamma \), effectively act as weight-scaling and age-scaling parameters respectively. This is evident on rearrangement of the asymptotic function to the form

\[
(\alpha - y) = -\beta e^{-\gamma x}
\]

from which the time taken to halve the deviation \( (\alpha - y) \) is given by the time interval \( t \) in the equation

\[
e^{-\gamma t} = \frac{1}{2} \quad \text{i.e.} \quad t = \log_e \frac{2}{\gamma} = \frac{0.69}{\gamma}
\]
Thus the deviation \((d - y)\) is halved every 0.694 \(t\) units of time.

An equivalent form of the asymptotic regression curve is the following equation considered by Brody (1945) and Taylor (1965):

\[

t = A \left[ 1 - e^{-k(t-t^*)} \right]
\]

where \(t\) = body weight at age \(t\), \(A\) is mature body weight and \(t^*\) the time origin of the curve. This equation is equivalent to the previous form for

\[
 k = \lambda \quad \text{and} \quad t^* = \log_e \left( \frac{-\beta}{\alpha} \right) / \lambda
\]

Therefore, in this form the three parameters \(A\), \(k\) and \(t^*\), represent live weight scaling, age scaling and time origin parameters (respectively) of the growth function.

Stevens (1951) has pointed out the connection which exists between the asymptotic regression equation and the Gompertz and logistic functions.

Taking the reciprocal of \(y\) converts the asymptotic regression equation to

\[
 z = 1/y = 1/(\alpha + \beta e^{-\lambda t})
\]

which converts to the usual logistic form of

\[
 z = A/(1 + B e^{-kt})
\]

for \(z = 1/y\), \(t = x\), \(A = 1/\lambda\), \(k = k\) and \(B = B/\lambda\).

The Gompertz function is generated by taking the exponential function of

\[
y = \exp(y) = \exp(\alpha + \beta e^{-\lambda t})
\]

Thus the parameter estimates obtained by fitting \(y = \log_e(1/e^{\alpha + \beta e^{-\lambda t}})\) satisfy the Gompertz relation

\[
y = \exp(\alpha + \beta e^{-\lambda t}) = \exp[-b \exp(-kt)]
\]

for \(y = \log_e k\), \(x = t\), \(j = k\), \(a = e^{\alpha}\) and \(b = -\beta\).

This demonstrates the functional relationships which exist between the growth forms which have been used to describe body weight growth in the mouse. Richards (1959) has shown that these functions can be derived as special cases of a more general function, differing only with respect to the fraction of mature body size at which the inflexion in the growth curve occurs.
C. GENETIC PARAMETERS OF THE LOGISTIC GROWTH CURVE

1. Materials and Methods

The C-strain mouse data collected by Monteiro and Falconer (1966) were used for this investigation. Weekly body weight records between birth and 8 weeks of age were available on 656 female and 702 male mice which represented the progeny of 71 sires and 132 dams. The data were collected over a period of 2 generations, all matings having been made at random.

The logistic growth function \( W = \frac{A}{1 + Be^{-kt}} \) was fitted directly to the untransformed body weights (g) and ages (weeks) of individual mice by least squares using the Simplex method of iteration (Nelder and Mead 1965).

The linear form of the logistic function is given by

\[
\log_e \left( \frac{A-W}{A} \right) = \log_e B -kt
\]

where, \( W \) = weight (in grams) at age \( t \) (in weeks)

\( A \) = final adult weight

\( k \) = the exponential rate of change in weight

In this context, therefore, parameter \( k \) may be visualised as the regression coefficient of \( \log_e (A-W)/A \) on age, parameter \( B \) corresponding to the regression constant and specifying the value of \( \log_e (A-W)/A \) at \( t = 0 \). Parameter \( B \) thus represents the positioning of the growth curve along the time axis. Age at the point of inflexion \( t_i \) is given by

\[
t_i = \frac{\log_e B}{k}
\]

This age corresponds to an estimated body weight equal to \( A/2 \) in the case of the logistic curve.

Because of the exponential nature of this growth function, animals may be considered to have effectively reached their final mature size when \( (A-W)/A \).
Table 25. Means and Components of Variation of the Parameters of the Logistic Growth Equation,

\[ W = \frac{A}{1 + Be^{-kt}} \]. Refer to Text for the Definition of the Growth Parameters

(\( V_A \) = Additive genetic, \( V_{Ec} \) = Between litter environment, \( V_{Ew} \) = Within litter environment)

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>( V_A )</td>
<td>( V_{Ec} )</td>
<td>( V_{Ew} )</td>
<td>Total Variance</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d.f. for M.S.</td>
<td>70</td>
<td>131</td>
<td>483</td>
<td>684</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-wk.weight (g)</td>
<td>24.12</td>
<td>3.60 ± 1.77</td>
<td>2.33 ± 0.799</td>
<td>0.962 ± 0.903</td>
<td>6.89</td>
<td></td>
</tr>
<tr>
<td>A (g)</td>
<td>25.75</td>
<td>3.98 ± 1.59</td>
<td>1.38 ± 0.672</td>
<td>1.06 ± 0.819</td>
<td>6.42</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>13.06</td>
<td>2.66 ± 3.11</td>
<td>6.63 ± 1.63</td>
<td>3.30 ± 1.58</td>
<td>12.79</td>
<td></td>
</tr>
<tr>
<td>( k )</td>
<td>.6923</td>
<td>.0014± .0010</td>
<td>.0012± .0005</td>
<td>.0026± .0005</td>
<td>.0053</td>
<td></td>
</tr>
<tr>
<td>( t_i )</td>
<td>3.67</td>
<td>.0027± .0568</td>
<td>.1481± .0330</td>
<td>.1105± .0292</td>
<td>.2613</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>( V_A )</td>
<td>( V_{Ec} )</td>
<td>( V_{Ew} )</td>
<td>Total Variance</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d.f. for M.S.</td>
<td>70</td>
<td>130</td>
<td>500</td>
<td>699</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-wk.weight (g)</td>
<td>29.61</td>
<td>3.95 ± 2.61</td>
<td>4.07 ± 1.28</td>
<td>3.76 ± 1.35</td>
<td>11.79</td>
<td></td>
</tr>
<tr>
<td>A (g)</td>
<td>32.01</td>
<td>3.97 ± 2.53</td>
<td>2.48 ± 1.26</td>
<td>8.47 ± 1.42</td>
<td>14.92</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>18.62</td>
<td>7.86 ± 5.00</td>
<td>7.19 ± 2.44</td>
<td>8.48 ± 2.62</td>
<td>23.53</td>
<td></td>
</tr>
<tr>
<td>( k )</td>
<td>.7186</td>
<td>.0001± .0012</td>
<td>.0028± .0007</td>
<td>.0039± .0007</td>
<td>.0067</td>
<td></td>
</tr>
<tr>
<td>( t_i )</td>
<td>4.06</td>
<td>-.621 ± .0795</td>
<td>.2464± .0508</td>
<td>.2191± .0414</td>
<td>.4034</td>
<td></td>
</tr>
</tbody>
</table>
has attained a value close to 1.0. For \((A-\bar{b})/\bar{b} = 0.98\), the linear form of the logistic becomes 
\[-0.0202 = \log_e B - kt\]

Therefore, the time to reach this degree of maturity \(t_{0.98}\) is given by

\[t_{0.98} = \frac{\log_e B + 0.0202}{k}\]

showing that time to mature is directly proportional to \(1/k\).

Components of variation and covariance were estimated for each of the growth parameters and for age at the point of inflexion, on the basis of a nested design specifying sires, dams with sires, and individuals within litters. All calculations were based on deviations from the generation means to allow for the effects of environmental differences between the two generations, and were carried out separately for each sex. The additive genetic component was estimated directly, the environmental components being separated into between-litter and within-litter terms on the assumption of negligible non-additive genetic effects (Monteiro and Falconer 1966).

2. Results and Discussion

The mean growth parameters and the causal components of variation estimated by the analysis are given in Table 25. Corresponding results for eight-week body weight are also given. The growth parameters were calculated for body weight in grams and age in weeks, the parameters \(B\) and \(k\) being presented dimensionless in Table 25 and those which follow.

The sex differences for the growth parameters are in general agreement with those estimated for 8-strain mice by Timon (1968) who fitted a logistic function to 12 weeks of age. They indicate a positive relationship between the age and weight-scaling parameters, the regression of \(\log \left(\frac{1}{k}\right)\) on \(\log A\)
### Table 26. Logistic Growth Parameters - Components of Variation as a Percentage of Total Phenotypic Variation

<table>
<thead>
<tr>
<th></th>
<th>$V_A$ (♀)</th>
<th>$V_A$ (♂)</th>
<th>$V_Ec$ (♀)</th>
<th>$V_Ec$ (♂)</th>
<th>$V_{Ew}$ (♀)</th>
<th>$V_{Ew}$ (♂)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-wk. weight</td>
<td>52±24</td>
<td>34±22</td>
<td>34</td>
<td>35</td>
<td>14</td>
<td>32</td>
</tr>
<tr>
<td>A</td>
<td>62±23</td>
<td>27±17</td>
<td>22</td>
<td>17</td>
<td>17</td>
<td>57</td>
</tr>
<tr>
<td>B</td>
<td>22±24</td>
<td>33±21</td>
<td>52</td>
<td>31</td>
<td>26</td>
<td>36</td>
</tr>
<tr>
<td>$k$</td>
<td>27±18</td>
<td>1±18</td>
<td>23</td>
<td>42</td>
<td>49</td>
<td>58</td>
</tr>
<tr>
<td>$t_1$</td>
<td>1±22</td>
<td>-15±20</td>
<td>57</td>
<td>61</td>
<td>42</td>
<td>54</td>
</tr>
</tbody>
</table>

### Table 27. Phenotypic Correlations Among Logistic Growth Parameters

(females = upper triangle, males = lower triangle)

<table>
<thead>
<tr>
<th></th>
<th>8-week</th>
<th>A</th>
<th>B</th>
<th>$k$</th>
<th>$t_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-wk.</td>
<td>0.91</td>
<td>-0.28</td>
<td>0.08</td>
<td>-0.32</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.71</td>
<td>-0.17</td>
<td>-0.22</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>-0.20</td>
<td>0.05</td>
<td>0.24</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>$k$</td>
<td>0.31</td>
<td>-0.19</td>
<td>0.13</td>
<td>-0.63</td>
<td></td>
</tr>
<tr>
<td>$t_1$</td>
<td>-0.38</td>
<td>0.28</td>
<td>0.50</td>
<td>-0.75</td>
<td></td>
</tr>
</tbody>
</table>
being of the order of -0.17. This is in contrast to the estimates obtained by Timon (1969) for the logistic function fitted to a random bred control population with body weight data to 14 weeks of age, which indicated a negative between-sex relationship for two parameters, and thus a positive between-sex relationship between mature size and the time to mature. Taylor (1968) also presented evidence of a strong positive association between mature size and time to mature both for mice and for other mammalian species.

Also in agreement with the results of Timon (1968) is the low between-additive component found for the age-scaling parameter, k. The relative partitioning of the variance components for the characters is, however, more obvious from the ratios which the variance components made to the total phenotypic variance. These are presented in Table 26. From this table, parameter k is seen to provide a further point of contrast to the results obtained by Timon (1969). On the assumption that maternal influences were not likely to be important for this parameter, Timon (1969) interpreted the large full-sib component as providing evidence of considerable genetic variation for this parameter. It is apparent from the present data, however, that this parameter may indeed exhibit an important maternal component, this also being indicated by the results of Cannon (1965).

Age at the point of inflexion of the growth curve also showed evidence of a strong maternal component, as is to be expected from the large maternal component found for age at sexual maturity by Monteiro and Falconer (1966) and the strong positive between-litter association they found between age at sexual maturity and age at the point of growth inflexion. In contrast to the present results however, Timon (1968) obtained an estimate of 0.51 ± 0.27 for the between-additive heritability of age at inflexion. The large full-sib
heritability found for $t_1$ by Timon (1969) ($h^2 = 1.32 \pm 0.11$) is however, compatible with a small component of additive genetic variance for this trait, the corresponding full-sib intra-class correlations for the present data being $1.14 \pm 0.07$ for females and $1.07 \pm 0.07$ for males.

In contrast to the traits discussed above, nature body weight was found to exhibit a large additive heritability, the partitioning of the phenotypic variance for this trait being in line with that expected from an extrapolation of the age trends in variance components demonstrated by Monteiro and Falconer (1966) for the same body of data. The lower heritability of nature body weight found for male mice is in correspondence with the lower estimate found for 8-week body weight in that sex.

A comparison of the fitted and actual growth curves for individual mice, however, revealed a number of animals with unusual growth patterns from which the least squares method estimated a disproportionately large value for asymptotic size relative to actual 8-week body weights. These animals were found to be characterised by a growth pattern exhibiting more than one inflexion point. Such abnormal growth patterns were also found to occur to a greater extent amongst males than females. Elimination of six of the most extremely deviant male mice from the analysis, raised the heritability estimate for nature body weight to $0.45 \pm 0.20$, a value which is in better agreement with the female estimate. Such exclusion made little change to the relative size of the common environmental component for this trait or to the partitioning of the variance components for 8-week body weight. It did however, slightly alter the partitioning of the variance components for the growth parameters $B$ and $k$, making them more similar to the corresponding female estimates.
In view of the large sampling errors for the estimates presented in Table 25, the data were not able to provide meaningful estimates of genetic correlations among the growth parameters. Estimates of the phenotypic correlations are presented in Table 27, and indicate reasonable agreement between the sexes. The estimates were affected very little when the six previously mentioned male mice were excluded from the analysis.

The negative phenotypic correlation coefficient \( r = -0.20 \) between growth parameters \( \lambda \) and \( k \) indicates a slight tendency for mature body size to be positively associated with the time taken for individuals to mature, and is to be compared with the estimate of \( -0.40 \) found by Timon (1969) for mouse body weight data to 14 weeks of age. The corresponding genetic correlation was very similar in the case of female mice \( r = -0.20\pm0.36 \) while for the males exclusion of the 6 most deviant mice reduced the estimate from +1.55 to +0.27. In both sexes there was a high positive correlation between 8-week body weight and estimated mature size, \( \lambda \). The corresponding genetic correlations were +1.00±0.03 for females and +1.10±0.09 for males which are not significantly different from unity. Large negative correlations between \( k \) and \( t_1 \) are to be expected in the case of the logistic curve, since the inverse of the former parameter represents the maturing interval while \( t_1 \) estimates age at half asymptotic size.

The above discussion must, however, be tempered by the fact that although the logistic function gave a reasonable statistical description of post-natal body weight growth to 8 weeks of age, its biological description of the growth process is evidently less satisfactory. This was evidenced by the very deviant individuals already mentioned and by the under-estimation of mature body weight. The latter feature is one which was also found by Timon (1969)
Figure 13. Logistic Growth Curves Fitted to the Body Weight Means for Each Sex.
and it is one which will become more apparent in a later section when the full cycle of growth to maturity is further examined for Q-strain mice. In the case of the present data evidence of a poor biological fit is also provided by the lower estimates for age at the point of inflexion in comparison with those obtained by Monteiro and Falconer (1966) from a consideration of the connection between prior body weight and subsequent body weight gains.

The overall logistic growth function fitted to the mean body weights of each sex is presented in Figure 13. Although the residual variation about the fitted curves was less than 1% of the variation between the body weight means, the fitted curves tended to alternate between periods of underestimation and periods of overestimation of body weight. This feature of the logistic function was also apparent in the curves fitted by Timon (1968 and 1969) and suggests that investigations may need to include body weight measurements that are made over extended growth periods up to a point close to final maturity in order that growth patterns may be usefully described by such simple growth functions as the logistic.

D. PATTERN OF ASYMETRIC GROWTH TO MATURITY IN MICE SELECTED FOR LARGE AND SMALL BODY SIZE

1. Material and methods

This investigation was undertaken on a sample of Q-strain mice which were surplus to the requirements of another experiment not reported in the present thesis. The animals represented progeny of Professor Falconer's selection experiment, being the product of duplicate matings that were made in the tenth generation of the experiment in addition to the normal matings required
Table 28. **Distribution of Animals for the Study of Asymptotic Growth to Maturity**

<table>
<thead>
<tr>
<th>Replicate</th>
<th>Large</th>
<th>Control</th>
<th>Small</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>B</td>
<td>7</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>D</td>
<td>3</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>E</td>
<td>6</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>F</td>
<td>11</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>35</td>
<td>50</td>
<td>34</td>
</tr>
</tbody>
</table>


Figure 14. Graphs of the Body Weight Means of the Selected Lines to 294 Days of Age.

( L = Large, C = Control, S = Small )

Females

Males

Age (days)
for the continuation of the selected body weight lines. As is indicated by
the distribution shown in Table 28, the available animals were rather poorly
representative of the line x replicate sub-groups. Nevertheless, it was
considered that selection had brought about a sufficiently marked genotypic
divergence in body weight between the lines for the material to be useful
for an investigation of the patterns of asymptotic growth to maturity and of
their relationship with final body composition (see Figure 14).

The animals were reared according to routine laboratory practice and
were weighed at regular intervals from weaning until some 46 weeks of age, at
which stage they were killed and processed in the manner previously described
for body composition analysis. The asymptotic curve of body weight growth
considered by Taylor (1965) was fitted to a regular sequence of body weight
records of individual mice. These weights were estimated by linear inter-
polation from the larger number of body weights recorded during the experiment.
Only animals with at least 17 of the possible 19 weight records corresponding
to the ages of 21, 25, 28, 32, 35, 42, 49, 56, 70, 84, 98, 126, 154, 182, 210,
233, 266, 294, and 322 days have been considered in the statistical analyses
which follow. The asymptotic growth curve was fitted using the same general
Simplex least squares method that was used for the logistic function of the
last section.

2. Results and Discussion
(a) Patterns of Asymptotic Growth

Figure 14 presents the mean growth curves to 294 days for mice of the
large, control and small selection lines calculated for each sex without
regard to their replicate status. The asymptotic pattern of the post-natal
Figure 15. Body Weights and Fitted Growth Curves (Asymptotic Regression Curves) for Three Individual Mice.
Figure 16. Distribution of the Residual Variation (Standard Deviation in g)

About the Fitted Growth Curves for Individual Mice.

(L = Large, C = Control, S = Small)

Females

Males
growth process is clearly evident from these graphs, a sigmoid pattern really only being obvious in the case of the female mice. A further noteworthy feature of these graphs is the extremely slow approach to asymptotic body weight, the curves for the large lines suggesting that the mice of this strain may still have some way to go before maximum body weight is reached. This interpretation would agree with the results of Roberts (1961) which indicated that some male mice of his large body weight strains take as long as 60 weeks for maximum body size to be attained.

The asymptotic function varied from animal to animal in the success with which it described the growth patterns. This is evident from the sample growth curves and fitted functions for individual mice shown in Figure 15, and by the histograms depicting the residual standard deviation about the fitted curves for all individual mice, presented in Figure 16. The tendency for the asymptotic function to underestimate body weights between 5 and 8 weeks and to overestimate body weights over the 12-15 week growth period occurred to a variable extent for many of the individual growth functions. The distribution of residual variation about the fitted curves (Figure 16) tended to be flatter for large strain mice of both sexes and for control line males. The flatness of the distribution was accompanied by a longer tail at the positive end of the distributions. This tendency towards a less good a fit of the asymptotic function in the case of a number of animals from these groups may be due to a failure of such animals to have attained maximum body size by 322 days of age. This is suggested, for example, by the relatively poor fit for the middle sample curve presented in Figure 15.

Preliminary analyses indicated that a linear model made up of line-replicate and sex effects represented a suitable description of the variation
in each of the growth parameters \( A, k \) and \( t \). Statistical analysis ignoring the interaction between these two effects (which reached significance at the 5% level of probability only in the case of parameter \( k \)), showed that sex differences were highly significant \( (P < .01) \) for all three parameters, as were the average within-sex line-replicate differences for the parameters \( A \) and \( t \). The absence of significant genotypic differences in parameter \( k \) indicates that selection for body weight has on average not been instrumental in including any consistent alteration in the rate at which very different mature body sizes are attained. This was also apparent when the graphs presented in Figure 14 were redrawn with body weight expressed as a fraction of the average of the 266 and 294 day mean body weights. Expressed in this way the average growth curves of the selected strains were very similar.

From these results it must be concluded that selection for body size at six weeks of age has not produced any consistent change in the shape of the mean curve of body weight growth to maturity. This is in agreement with Timon and Eisen's (1969) study of body weight growth to 14 weeks in a strain of mice selected for fast post-weaning body weight gain to six weeks of age.

(b) Relationships between mature size and Time to Maturity

In view of the general relationship that has been found to hold between mature size and time to mature for species, sexes, and strains (Taylor 1965, 1968), the association between the growth parameters \( A \) and \( k \) has been examined for the present data. The correlation between these two parameters for the line-replicate means estimated on a within-sex basis was found to be \(-0.21\), the regression of \(-\log k \) on \( \log A \) (which is the same as the regression of \( \log(1/k) = \log \tau \) on \( \log A \)) being \(0.13\), and \(0.016\). This is only about half the
Figure 17. Relationships Between the Least Squares Means for Mature Size and Time to Mature ($\log_e$ scale)
average between strain estimate reported by Taylor (1968). In addition, the
ever value of the correlation coefficient suggests that the between strain
relationship is not very strong in the present data. However, a scatter
diagram of the mean parameters revealed some interesting trends (see Figure 17).
It showed that the relationship between the logarithms of the least squares
means tends to be rather linear in replicates A and B, and close to Taylor's
between strain estimate. In contrast there existed a negative estimate
between the large and control lines in the case of replicates D, E and F.
This general pattern of relationships was also revealed when the strain means
were plotted separately for each sex. The findings indicate that the
selection responses in the first two replicates has been in accordance with
Taylor's general relationship, a ten-fold difference in mature size being
assumed with a 3-4 fold difference in time taken to mature. By comparison
it would appear that the increase in mature size produced by selection in
replicates D, E and F has been accompanied by a decrease in the time required
for this mature body size to be attained. This indicates that although on
average there was seen to be little difference in the shape of the mean growth
curves of the large body-weight strains in comparison with the average for the
controls, shape differences might be more pronounced in the case of replicates
D, E and F. Large mice of this line would be expected to have a more sharply
curved asymptotic growth pattern than their controls. This tendency is
indeed apparent from the mean growth curves plotted for male mice in Figure 18(a).
The first set of graphs in this figure gives the absolute mean growth curves
for male mice of the large strain averaged over replicates A to C inclusive
\( (L_A \rightarrow L) \) and over replicates D to F inclusive \( (L_D \rightarrow F) \). Both these groups
show similar average absolute growth rates to 42 days of age, but exhibit a
Figure 18. (a) Mean Body Weight Growth Curves to 266 Days Averaged for Male Mice of the Large Strain Over Replicates A to C (L_{A+C}) and D to F (L_{D+F}) and for Male Mice of the Control Strain Over Replicates D to F (C_{D+F}).

(b) Body Weight Growth for L_{D+F} and C_{D+F} as a Percentage of Final Size (males only).
final body weight difference of around 4 g (± 0.45) at 266 days of age. The greater
curvature of the mean growth curve for L_{j} \rightarrow p males in comparison with the
control line male mean for the same three replicates (C_{j} \rightarrow p), is more apparent
in Figure 18(b) in which body weight, expressed as a percentage of final body
weight, is plotted against age.

The residual within-subclass variation obtained from the analysis which
gave rise to the estimates plotted in Figure 17, indicated a correlation of
-0.45 between the asymptotic growth parameters A and k. This is twice as
high as the average between-strain relationship and indicates a positive
relationship between mature size and time to mature for individual animals.
Further analysis of the between-animal regression of log (1/k) on log
A revealed a significant (P < .01) sex difference in the regression coefficient.
line differences in the regression coefficient failed to attain statistical
significance (i.e. P < 0.05), although significant (P < .001) average line
differences in the elevation of the average regression lines for each sex
were apparent. The unweighted average regression coefficient was 1.47 ± 0.18,
the sex deviation being +0.50 ± 0.18 for females and -0.50 ± 0.18 for males.
This average regression is very similar to the average between strain value
of 1.5 reported by Taylor (1968) for the Gompertz growth parameters of the
strains of mice studied by Laird and Howard (1967). Its standard error is
however, considerably lower than that of Taylor's estimate which does suggest
that the within-strain relationship for mice may be even more different from
the average between species value than was suggested by Taylor's (1968)
analysis. Indeed, the regression coefficients indicate that within-strain
differences in mature body size are associated with similar percentage
differences in maturing time in the case of males, and a 2-fold difference in
Table 29. Phenotypic Correlations Between Growth Curve Parameters and Carcass Components

<table>
<thead>
<tr>
<th></th>
<th>Total Fat</th>
<th>Abdom. Fat</th>
<th>Fat-free Carcass</th>
<th>Carcass Weight</th>
<th>A</th>
<th>k</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Fat</td>
<td>1.00</td>
<td>.35</td>
<td>.83</td>
<td>.69</td>
<td>-.57</td>
<td></td>
</tr>
<tr>
<td>Abdominal Fat</td>
<td>.96</td>
<td>.36</td>
<td>.81</td>
<td>.69</td>
<td>-.61</td>
<td></td>
</tr>
<tr>
<td>Fat-free Carcass</td>
<td>.37</td>
<td>.42</td>
<td>.77</td>
<td>.77</td>
<td>-.27</td>
<td></td>
</tr>
<tr>
<td>Carcass Wt.</td>
<td>.80</td>
<td>.81</td>
<td>.84</td>
<td>.91</td>
<td>-.59</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>.63</td>
<td>.65</td>
<td>.83</td>
<td>.90</td>
<td>-.66</td>
<td></td>
</tr>
<tr>
<td>k</td>
<td>-.42</td>
<td>-.37</td>
<td>-.09</td>
<td>-.32</td>
<td>-.30</td>
<td></td>
</tr>
</tbody>
</table>

(females = upper triangle, males = lower triangle)
maturing time in the case of females. Thus there exists a larger sex difference in the time taken to mature, the greater the mature size of the individual animals; it tends to zero around asymptotic body weights of the order of 20 g this being at the low end of the range of individual variation in the case of the present data. This overall tendency for females to mature more slowly than males of the same asymptotic body size is in contrast to the finding of Taylor (1968) for the data of Laird and Howard (1967). However, the negative between-sex regression was a consistent finding in the present data, being apparent, for example, within each of the selection lines.

(c) Relationships of Asymptotic Growth Parameters to Body Composition

Table 29 presents the correlation coefficients describing the association between the asymptotic regression curve parameters \( \lambda \) and \( k \) and the fat and non-fat components of the carcass. The correlations are presented separately for each sex and were estimated on a within line x replicate subclass basis following the transformation of the data to base ten logarithms.

On the whole the male and female estimates agreed well, the agreement being least close in the case of the correlations involving growth parameter \( k \). For this character the absolute magnitude of the estimates tended to be lower for the females although the relative ranking of the correlation coefficients involving \( k \) and the remaining characters tended to be similar in both sexes. The estimates suggest a tendency for growth parameter \( k \) to be more strongly associated with the fat component of carcass weight than with the non-fat component; to a lesser extent the reverse tends to be true for the case of growth parameter \( \lambda \). In this case one might expect that a knowledge of both growth components might go some way towards usefully predicting the relative
fat content of the carcasses. The correlations involving the mature size parameter tended to be only slightly lower than the corresponding correlations involving carcass weight; they were however, consistently greater in absolute value than the corresponding correlations involving growth parameter k.

The value of the asymptotic growth curve parameters A and k to a prediction of relative carcass fat content was assessed using multiple regression methods, by including the growth parameters as covariates along with carcass weight. In this way both the single and joint effects of parameters A and k could be considered with respect to their accuracy in predicting the fat content of carcasses adjusted to the same carcass weight. A line-replicate classification was included in the statistical models as a fixed main effect in order to focus attention on between animal variation within the line-replicate classes. It also permitted an examination to be made of the relative extent to which the different models were able to discriminate between the line-replicate classes, this being assessed from the value of the F-ratios in the analysis of variance test for the significance of the line-replicate effects.

All models were fitted after the data had been transformed to logarithms. The model containing line-replicate effects plus carcass weight alone accounted for 81.5, 81.7 and 94.0 of the total variation between animals for the characters total fat, abdominal fat and fat-free carcass weight respectively. This situation was very little improved by the inclusion of either or both of the growth parameters as additional independent variables. The addition of either growth parameter accounted for around 1 more of the total variation of the fat characters and about 1 more of the variation in fat-free carcass weight.

This is perhaps a little surprising, for in view of the high correlation between carcass weight and mature size, A, it might have been anticipated that
Table 30.  \( F \)-values Testing the Significance of Line-Replicate Differences and the Partial Regression Coefficients, for a Statistical Model Expressing the Dependent Variable as a Function of Line-Replicate Effects and the Partial Regressions on Carcass Weight, Growth Parameter \( A \) and Growth Parameter \( k \)

| Dependent Variate | Sex | Line-Replicate Differences | Regression on Carcass Weight | Regression on \( A \) | Regression on \( k \) | % Reduction in Total Sum of Squares | Standard Error of Estimate \( (\sigma_{y,x}) \) Log_{10} g \ units |
|-------------------|-----|-----------------------------|-----------------------------|------------------|------------------|----------------------------------|---------------------------------
| Total Fat         | ♀   | 4.07 ++                     | 90.1 +++                    | 18.7 +++         | 10.4 +++         | 87.5                             | 0.113 |
|                   | ♂   | 1.99 +                      | 84.3 +++                    | 13.0 +++         | 11.2 ++          | 82.1                             | 0.107 |
| Abdominal Fat     | ♀   | 3.45 +++                    | 63.4 +++                    | 12.58 +++        | 16.8 +++         | 86.9                             | 0.160 |
|                   | ♂   | 2.52 ++                     | 75.5 +++                    | 8.70 ++          | 5.43 ++          | 82.4                             | 0.139 |
| Fat-free Carcass  | ♀   | 5.58 +++                    | 6.91 +                      | 19.1 +++         | 26.1 +++         | 95.2                             | 0.0175 |
| Weight            | ♂   | 2.37 ++                     | 23.6 +++                    | 13.4 +++         | 15.0 +++         | 95.8                             | 0.0177 |
Table 31. *Single and Joint Contributions of Growth Parameters A and k to Variability in the Relative Amounts of the Fat and Non-fat Components of Carcass Weight*

<table>
<thead>
<tr>
<th></th>
<th>Total Fat</th>
<th>Abdominal Fat</th>
<th>Fat-free Carcass</th>
</tr>
</thead>
<tbody>
<tr>
<td>A alone</td>
<td>10.4%</td>
<td>6.0%</td>
<td>8.0%</td>
</tr>
<tr>
<td>k alone</td>
<td>5.8%</td>
<td>6.5%</td>
<td>12.1%</td>
</tr>
<tr>
<td>A and k</td>
<td>20.0%</td>
<td>16.3%</td>
<td>25.0%</td>
</tr>
</tbody>
</table>
would have made a somewhat greater contribution than \( A \) to the additional variation explained over and above that associated with carcass weight. Jointly the gain in terms of explained variation was \( 2\% \) and \( 1\% \) of the variation in the fat and fat-free weights, respectively. The \( F \)-values testing the differences among the line-replicate classes were not greatly different for each of the three models.

Despite the rather small differences in the fraction of the total variation explained by each of the models, the separate independent variables all tended to make a significant contribution over and above the joint effects of the remaining two. This is indicated by the results presented in Table 30. As judged from the size of the \( F \)-values in this table, carcass weight made the greatest contribution over and above the effects of the other two characters with respect to explaining the variability in fat weight; on average all 3 characters contributed similarly in terms of explaining additional variability in fat-free carcass weight.

With particular regard to the prediction of within-class variability in relative fat content (i.e., within the line-replicate groups), the additional variability accounted for by the single and joint effects of \( A \) and \( k \) have been expressed as a percentage of the variability remaining after fitting line-replicate effects and the carcass regression term. Averaged over both sexes this revealed the situation presented in the following table (Table 31).

Taken together the asymptotic growth curve parameters \( A \) and \( k \) were able to account for around 20% of the variability in relative fatness at maturity. On their own the indication was that parameter \( A \) was perhaps of slightly greater value for the prediction of relative carcass fat content and parameter \( k \) was superior for the estimation of amounts of non-fat tissue at constant
Table 32. Simple and Partial Regression Coefficients Relating Growth Parameters A and k to Relative Carcass Fat Content

<table>
<thead>
<tr>
<th></th>
<th>Total Fat</th>
<th>Abdominal Fat</th>
<th>Fat-free Carcass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple Regression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>-1.81</td>
<td>-2.00</td>
<td></td>
</tr>
<tr>
<td>Coefficients</td>
<td>-0.152</td>
<td>-0.230</td>
<td></td>
</tr>
<tr>
<td>k</td>
<td>-0.295</td>
<td>-0.242</td>
<td></td>
</tr>
<tr>
<td>Partial Regression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>-2.47</td>
<td>-2.10</td>
<td></td>
</tr>
<tr>
<td>Coefficients</td>
<td>-0.295</td>
<td>-0.242</td>
<td></td>
</tr>
<tr>
<td>k</td>
<td>-0.295</td>
<td>-0.242</td>
<td></td>
</tr>
</tbody>
</table>
carcass weights. This was the reverse of the tendency suggested by the simple correlations for the prediction of the absolute amounts of these two carcass components.

While both mature size and time to mature were positively associated with absolute levels of the fat and fat-free components of the carcass, the simple partial regression coefficients relating these characters to relative fat and non-fat contents (Table 32) indicate that mature size \( A \) is negatively, and time to mature \( 1/k \) is positively associated with relative carcass fat content. The partial regression coefficients show that animals taking longer than average to grow to the same mature size have greater than average relative fat contents. This situation is thus compatible with an expectation based upon the relative energetic densities of fat and non-fatty tissue. It indicates that variation in the time to reach identical mature sizes is to some extent related to the relative partitioning of energy available for growth into the fat and non-fat components of the carcass, the constant of proportionality on a logarithmic scale being of the order of \( J \). Nevertheless, the small proportion of variation in relative fatness that is accounted for by the joint effects of \( A \) and \( k \), indicates considerable flexibility in the association between carcass composition and the shape of the body weight growth curve.
VIII. GENETIC VARIATION AND COVARIATION OF RELATIVE FATNESS IN A
RANDOM BREEDING POPULATION

A. INTRODUCTION

This study was concerned with an analysis of some genetic parameters of fatness and relative fatness characters in a random breeding population of mice in order to gain an insight of their expected direct and correlated responses to selective breeding. In particular, attention was focussed upon the relative importance of genetic variation about the regression line relating the fat components to carcass weight in order to assess the extent that such a measure of relative fatness is amenable to genetic modification by selection.

B. NICK AND METHODS

The animals used were drawn from the control lines of the C-strain selection experiment and were expanded in three distinct randomly mated groups which represented the original samples of the base population from which the selected lines were derived. The three groups will be referred to as the AB, CD and LF strains, this coding indicating their respective origins - i.e. the AB strain derived from the control lines of replicates A and B. Twenty-four pair matings were used for the establishment of the strains in the first generation, the parents coming from generation 15 of Professor Falconer's C-strain selection experiment. They were subsequently maintained using a harem mating plan in order to provide both full-sib and half-sib families. In any one generation each of 10 males of each strain were mated to 4 females and, as far as was possible, up to 3 offspring of each sex were randomly chosen from each litter for body composition analysis. The complete litter was,
however, left with the mother to be reared until weaning at 3 weeks of age. The parents were selected at random but with an effort being made to choose one male from each sire-family and one female from each full-sib family, in order to minimise the effects of inbreeding. The harems were also formed at random within each of the strains, but with the avoidance of any full-sib matings.

Matings were made at around 7 weeks of age, the male mice being left in the mating cages until they were slaughtered along with their full and half-sibs at 9 weeks of age. The aim of the mating plan was to obtain body composition information on 3 mice of each sex from each of 3 of the 4 litters produced by a harem. This gave some latitude to cope with infertile matings and small litter sizes and also allowed the work of dissecting the mice to be spread. A spread of work was also facilitated by the practice of staggering matings for each of the strains by one week, and by forming the harems of a strain in two batches separated by an interval of two days.

The experimental design allowed the estimation of the additive genetic variance from the variation between sires, the 3 generations over which data were collected providing a total of 57 sire-families and involving 1507 individual mice. The number of sires and offspring for each of the strain x generation subgroups is shown in Table 33.
Table 34. **Estimates of Genetic Variation at 9 Weeks of Age for Each of the Random Bred Strains - (log_10 grams)**

<table>
<thead>
<tr>
<th></th>
<th>AB</th>
<th>CD</th>
<th>EF</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Fat</td>
<td>.01576</td>
<td>.009841</td>
<td>.01214</td>
<td>.01258</td>
</tr>
<tr>
<td>Total Fat</td>
<td>.01211</td>
<td>.005814</td>
<td>.009129</td>
<td>.009018</td>
</tr>
<tr>
<td>FFCW</td>
<td>.001624</td>
<td>.002069</td>
<td>.001561</td>
<td>.001751</td>
</tr>
<tr>
<td>Carcass Wt.</td>
<td>.001420</td>
<td>.001614</td>
<td>.001356</td>
<td>.001463</td>
</tr>
</tbody>
</table>

Table 35. **Estimates of Phenotypic Variation at 9 Weeks of Age for Each of the Random Bred Strains (log_10 scale)**

<table>
<thead>
<tr>
<th></th>
<th>AB</th>
<th>CD</th>
<th>EF</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Fat</td>
<td>.03759</td>
<td>.03201</td>
<td>.03430</td>
<td>.03463</td>
</tr>
<tr>
<td>Total Fat</td>
<td>.02497</td>
<td>.02669</td>
<td>.02218</td>
<td>.02461</td>
</tr>
<tr>
<td>FFCW</td>
<td>.002613</td>
<td>.002988</td>
<td>.003335</td>
<td>.002979</td>
</tr>
<tr>
<td>Carcass Weight</td>
<td>.002553</td>
<td>.002535</td>
<td>.003420</td>
<td>.002836</td>
</tr>
</tbody>
</table>

Table 36. **Heritability Estimates at 9 Weeks of Age for Each of the Random Bred Strains (log scale)**

<table>
<thead>
<tr>
<th></th>
<th>AB</th>
<th>CD</th>
<th>EF</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Fat</td>
<td>0.42±0.15</td>
<td>0.31±0.13</td>
<td>0.35±0.15</td>
<td>0.36</td>
</tr>
<tr>
<td>Total Fat</td>
<td>0.49±0.17</td>
<td>0.22±0.11</td>
<td>0.41±0.16</td>
<td>0.37</td>
</tr>
<tr>
<td>Fat-free Carcass Wt.</td>
<td>0.62±0.19</td>
<td>0.69±0.20</td>
<td>0.47±0.17</td>
<td>0.59</td>
</tr>
<tr>
<td>Carcass Weight</td>
<td>0.56±0.18</td>
<td>0.64±0.19</td>
<td>0.40±0.15</td>
<td>0.53</td>
</tr>
</tbody>
</table>
Table 33. Distribution of Animals for Half-sib Analysis of Variation

<table>
<thead>
<tr>
<th>Strain</th>
<th>AB</th>
<th>CD</th>
<th>EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generation</td>
<td>2 3 4</td>
<td>2 3 4</td>
<td>2 3 4</td>
</tr>
<tr>
<td>Ko.Sires</td>
<td>10 8 10</td>
<td>10 8 12</td>
<td>10 9 10</td>
</tr>
<tr>
<td>Ko.Offspring</td>
<td>181 133 202</td>
<td>173 125 210</td>
<td>143 131 204</td>
</tr>
<tr>
<td>Ko.Offspring/ sire</td>
<td>18.1 17.3 20.2</td>
<td>17.3 15.6 17.5</td>
<td>14.3 14.6 20.4</td>
</tr>
</tbody>
</table>

Sire components of variation and co-variation were estimated separately for each strain using a linear model in which the random sire effects were combined with the fixed effects of sex - i.e. they were estimated on a within-sex basis ignoring any environmental differences between generations. The data were transformed to base ten logarithms prior to analysis in order that the results could be directly compared with the previously established allometric relationships for the selected body weight lines of C-strain mice.

C. RESULTS AND DISCUSSION

1. Phenotypic and Genetic Parameters

The separate estimates within each of the strains and their unweighted means are presented in Tables 34 to 39. The phenotypic and genetic variances (Tables 34 and 35) show reasonable agreement between each of the strains but indicate lower genetic variation for the fat components and higher genetic variation for fat-free carcass weight in the CD strain. Their ratios (Table 33) indicate heritabilities of the order of 0.5 for carcass weight, 0.4 for the fat component and 0.6 for fat-free carcass weight. The heritability estimates
### Table 37. Estimates of Genetic Correlations at 9 Weeks of Age for Each of the Random Bred Strains (log scale)

<table>
<thead>
<tr>
<th></th>
<th>AB</th>
<th>CD</th>
<th>EF</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.Fat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Fat</td>
<td>0.95±0.03</td>
<td>0.84±0.09</td>
<td>0.81±0.09</td>
<td>0.87</td>
</tr>
<tr>
<td>FFCW</td>
<td>0.10±0.26</td>
<td>0.29±0.26</td>
<td>0.16±0.28</td>
<td>0.18</td>
</tr>
<tr>
<td>Carcass</td>
<td>0.37±0.23</td>
<td>0.52±0.20</td>
<td>0.31±0.25</td>
<td>0.42</td>
</tr>
<tr>
<td>T.Fat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFCW</td>
<td>-0.01±0.26</td>
<td>-0.05±0.30</td>
<td>0.03±0.28</td>
<td>-0.01</td>
</tr>
<tr>
<td>Carcass</td>
<td>0.27±0.24</td>
<td>0.25±0.28</td>
<td>0.30±0.26</td>
<td>0.27</td>
</tr>
<tr>
<td>FFCW</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcass</td>
<td>0.96±0.02</td>
<td>0.96±0.03</td>
<td>0.96±0.02</td>
<td>0.96</td>
</tr>
</tbody>
</table>

### Table 38. Estimates of Environmental Correlations at 9 Weeks of Age for Each of the Random Bred Strains (log scale)

<table>
<thead>
<tr>
<th></th>
<th>AB</th>
<th>CD</th>
<th>EF</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.Fat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Fat</td>
<td>0.90</td>
<td>0.94</td>
<td>0.96</td>
<td>0.93</td>
</tr>
<tr>
<td>FFCW</td>
<td>0.58</td>
<td>0.66</td>
<td>0.67</td>
<td>0.44</td>
</tr>
<tr>
<td>Carcass</td>
<td>0.75</td>
<td>0.59</td>
<td>0.81</td>
<td>0.72</td>
</tr>
<tr>
<td>T.Fat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFCW</td>
<td>0.40</td>
<td>-0.05</td>
<td>0.54</td>
<td>0.30</td>
</tr>
<tr>
<td>Carcass</td>
<td>0.64</td>
<td>0.53</td>
<td>0.72</td>
<td>0.63</td>
</tr>
<tr>
<td>FFCW</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcass</td>
<td>0.96</td>
<td>0.80</td>
<td>0.97</td>
<td>0.91</td>
</tr>
</tbody>
</table>
obtained for the weight of abdominal fat at 9 weeks of age (0.36) is somewhat lower than the corresponding half-sib estimate (0.56±0.17) found by Hull (1960) for the weight of abdominal fat at 6 weeks of age. The estimates found for 9 week body weight were very similar to those presented for carcass weight (0.5) and are thus in agreement with an expectation based on the 3-strain data analyzed by Monteiro and Falconer (1966).

In the light of their standard errors, the genetic correlations presented in Table 37 show very good agreement between the strains which reinforces the confidence than can be placed upon their average values. The two fat measurements showed a high genetic correlation but were both poorly correlated with fat-free carcass weight and only moderately correlated with carcass weight. The latter correlations were greater (by 0.15 to 0.19) in the case of abdominal fat component. Fat-free carcass weight showed a very high genetic correlation with carcass weight. The average genetic correlation found between body weight at 9 weeks of age and abdominal fat weight was 0.45 and it thus similar to the genetic correlation between this fat component and carcass weight. Hull's (1960) selection responses on the other hand, indicated the corresponding genetic correlation at 6 weeks of age to be only 0.29. However, Hull's results gave estimates for the genetic correlation between 3 and 4.5 week body weight and 6 week abdominal fat weight of 1.0 and 0.45 respectively, suggesting that his estimate involving 6 week body weight may be somewhat lower than expected.

In contrast to the genetic correlations, the between-strain agreement was less good in the case of the environmental and phenotypic correlations (Tables 38 and 39). This was due to a much lower environmental correlation between the fat and fat-free components of the carcass in the CD strain. The
Table 39. Estimates of Phenotypic Correlations at 9 Weeks of Age for Each of the Random Bred Strains (log scale)

<table>
<thead>
<tr>
<th></th>
<th>A.Fat</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Fat</td>
<td>AB</td>
<td>CD</td>
<td>EF</td>
<td>Average</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.92</td>
<td>0.91</td>
<td>0.90</td>
<td>0.91</td>
</tr>
<tr>
<td></td>
<td>FFCW</td>
<td>0.32</td>
<td>0.16</td>
<td>0.46</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>Carcass</td>
<td>0.56</td>
<td>0.53</td>
<td>0.65</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T.Fat</td>
<td>FFCW</td>
<td>-0.05</td>
<td>0.32</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.45</td>
<td>0.38</td>
<td>0.55</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>Carcass</td>
<td>0.96</td>
<td>0.90</td>
<td>0.97</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
average of the estimates indicate the environmental correlation between the fat and fat-free components to be about 0.3 higher than the genetic correlation. The same average difference is apparent with respect to the correlations between the fat components and carcass weight.

2. **Expected Selection Responses in Relative Carcass Fat Content**

The moderately low genetic correlation between fat weight and carcass weight, coupled with the existence of considerable genetic variation in fat weight indicates the existence of genetic variation in fat weight that is independent of carcass weight. In addition, the presence of greater environmental than genetic correlations between fat weight and carcass weight, suggests that selection using an index designed to alter fat content without altering carcass weight might not sacrifice much genetic progress in comparison with straightforward mass selection for absolute amounts of fat - i.e. selection for relative fatness might not result in very different responses in absolute amounts of fat in comparison with mass selection for fat weight alone. Purser (1960, 1966) found that selection for relative cannon bone length in sheep actually gave a genetic response that was about 25% greater than could be obtained by mass selection. He used an index which put positive selection pressure on cannon bone length but which aimed at maintaining body weight constant, the genetic and environmental correlations between these characters being 0.23 and 0.85 respectively. This occurred because body weight was able to provide a considerable amount of information on the environmental variation in cannon bone length relative to the amount of genetic variation in cannon bone length that was lost by requiring that body weight did not alter under selection.
The general theory of restricted selection indices has been dealt with by Kempthorne and Nordskog (1959) while a useful summary of the work of Kendal (1954) and Osborne (1957) which is relevant to a two component restricted selection index is given by Purser (1960). In the case of a two component system the theory provides for the construction of an index of the form: \( I = Y - aX \).

In the context of the present study, \( Y \) represent fat weight and \( X \) carcass weight the aim being to alter the fat weight without change in carcass weight - i.e. to change relative carcass fat content in either direction by selective breeding. It can be shown (Purser 1960), that the appropriate weighting factor (\( a \)) for this situation is given by the genetic regression of \( Y \) on \( X \) \( b_{(y|x)} \), and that the ratio of the genetic progress in \( Y \) when selection is based on \( I \), to the progress that is possible from direct selection on \( Y \) ignoring \( X \), is given by

\[
RELS = \left(1 - r^2_g \right) \frac{\sigma_Y}{\sigma_I}
\]

with \( \sigma_I = \sigma_Y \left(1 - 2r_g r_p \frac{h_y}{h_x} + r^2_g \frac{h^2_y}{h^2_x} \right)^{1/2} \)

where \( r_g \) is the genetic correlation between \( X \) and \( Y \), \( \sigma_Y \) is the phenotypic standard deviation of \( Y \) and \( \sigma_I \) is the phenotypic standard deviation of the index (\( I \)). The ratio may thus be called the relative efficiency of restricted selection (RELS).

Application of the above theory to the average within-strain parameters estimated for the present data, gave the results shown in Table 40. Both the abdominal and total fat components of the carcass were considered.
Table 40. Restricted Selection for Carcass Fat Content using the Genetic Regression Coefficient

<table>
<thead>
<tr>
<th></th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic Regression Coefficient ($b_{\text{G}<em>{\text{N}</em>{\text{A}}}}$)</td>
<td>1.23 ± 0.30</td>
<td>0.67 ± 0.27</td>
</tr>
<tr>
<td>Relative Efficiency ($u_{\text{E}<em>{\text{D}</em>{\text{R}}}}$)</td>
<td>0.97</td>
<td>1.01</td>
</tr>
<tr>
<td>Heritability of Index</td>
<td>0.42</td>
<td>0.40</td>
</tr>
</tbody>
</table>

The results indicate that the expected progress is very little different regardless of whether or not an effort is made to maintain carcass weight constant. They also indicate the presence of considerable genetic variation about the genetic regression line. This genetic variation equals $\sigma^2_{g}(1 - r^2_{g})$, where $\sigma^2_{g}$ is the genetic variance of fat weight. The genetic correlation between the deviations from the genetic regression line and the absolute levels of fat content can be shown to be equal to $\sqrt{1 - r^2_{g}}$, $r_{g}$ being the genetic correlation between fat weight and carcass weight. With the latter genetic correlations being of the order of 0.30 and 0.40 for the present data it is obvious that the former genetic correlations will be very large (greater than 0.90). These large genetic correlations do not however, represent genetic correlations between absolute and relative levels of fatness. Relative fatness relates to the pattern of developmental growth of individual animals and can be represented by the variation about the phenotypic regression line relating fat to carcass weight.

Then measured in terms of the deviations about the phenotypic regression...
line the heritability of relative fatness is given by the ratios of the genetic to the phenotypic variation in $I$, which equals:

$$h^2_I = h^2_Y \left(1 - 2r_p r_g \frac{h_Y}{h_Y} + r_p^2 \frac{h_Y^2}{h_Y^2}\right) / (1 - r_p^2)$$

For the present data $h^2_I$ works out at 0.47 for total fat and 0.50 for abdominal fat. The genetic correlation between the absolute and relative fat contents is in turn given by

$$r_{g_y a_y'} = \left(1 - r_p r_g \frac{h_Y}{h_Y}\right) / \left(1 - 2r_p r_g \frac{h_Y}{h_Y} + r_p^2 \frac{h_Y^2}{h_Y^2}\right)^{1/2}$$

and equals 0.80 and 0.66 for total fat and abdominal fat respectively. The rate of progress in the absolute levels of fat using this restricted index, as a ratio to the rate of progress from simple mass selection for fat weight, is given by the following formula (Osborne 1957):

$$E = \left(1 - r_p r_g \frac{h_Y}{h_Y}\right) / (1 - r_p^2)^{1/2}$$

For the present data these relative efficiencies turn out to be 0.97 and 0.83 respectively. These are less than unity indicating that the phenotypic regression index is less than optimal with respect to maximising genetic improvement in the absolute level of $Y$. The appropriate formula for calculating the optimum index coefficient is given by Purser (1960), who also shows that it is equal to the phenotypic regression coefficient when $r_g = 0$. Table 41 summarizes these results for the case of selection for relative carcass fat content using the phenotypic regression of fat on carcass weight in a selection index.
Table 41. Selection for Relative Carcass Fat Content Using the Phenotypic Regression Coefficient

<table>
<thead>
<tr>
<th>Phenotypic Regression Coefficient (by.x)</th>
<th>Abdominal Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenotypic Regression Coefficient (by.x)</td>
<td>2.03±.073</td>
<td>1.36±.068</td>
</tr>
<tr>
<td>Relative Efficiency (I)</td>
<td>0.88</td>
<td>0.97</td>
</tr>
<tr>
<td>Heritability of Index</td>
<td>0.50</td>
<td>0.47</td>
</tr>
<tr>
<td>Genetic Correlation between Absolute and Relative Fat Contents</td>
<td>0.76</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Restricted selection for relative fatness on the basis of the phenotypic regression coefficient will however, cause a correlated change in carcass weight (X) whenever the genetic correlation between fat and carcass weight is not zero. The ratio of the response in fat weight to the response in carcass weight is given by the ratio:

\[
R = \frac{\text{cov}(\varepsilon_Y, I)}{\text{cov}(\varepsilon_X, I)} = \frac{\sigma^2_{\varepsilon_Y}/\sigma^2_{\varepsilon_X} - a b_G}{(b_G - a)}
\]

where \(\sigma^2_{\varepsilon_Y}\) and \(\sigma^2_{\varepsilon_X}\) are the genetic variances of Y and X, while a and b_G are the phenotypic and genetic regressions of Y on X respectively. The ratio (R) turns out to be -7.63 for abdominal fat and -7.61 for total fat using the previously presented parameter estimates. Thus, a positive 7.6% change in absolute fat weight is accompanied by a negative 1% change in body weight - i.e. selection for higher relative fatness is expected to decrease body weight to some extent.
The phenotypic regression coefficients presented in Table 35 are very similar to the average values found for the body weight strains in Section VI of this thesis. An interesting situation is, however, revealed by the genetic regression coefficients presented in Table 40. Their values are low relative to the corresponding phenotypic estimates. Indeed, they suggest that a genetic change of 10% in the level of expression of carcass weight would be accompanied by only a 6.7% change in total fat content and only a 12.3% change in abdominal fat content. These are considerably less than the corresponding changes expected during the normal developmental growth of individual animals (14% and 20%, respectively) and indicate that selection for increased carcass weight would result in a lowered level of relative carcass fat content. This is somewhat surprising in view of the findings presented in Section VI which showed that selection for body weight at 6 weeks of age brought about little change in relative total fat content of the carcasses at this age but did tend to increase relative fatness at later ages.

The situation is thus somewhat reminiscent of the findings of Hull (1960) that selection for body weight at three weeks of age gave a greater correlated response in abdominal fat weight at 6 weeks of age than did selection at 6 weeks, and that selection at 6 weeks of age was intermediate in this respect. It is not, however, unequivocally clear that Hull's body weight lines were in fact different in relative fatness. His experiment gave the surprising result of considerably greater genetic responses in six week body weight following selection at 3 weeks of age even in comparison with the line directly selected for six week body weight, and it is difficult to assess whether his three week line contained any more fat than control mice of similar body weights would be expected to possess. An analysis of covariance of the
Figure 19: Between-Generation Relationships Between Abdominal Fat and Carcass Weight for the Selected Line Means of Hull (1959) - $\log_e g$ units.
logarithms of the body weight and abdominal fat means presented by Hull (1959) (ignoring the significant between-line heterogeneity of variation about the regression lines - P < .01) was unable to detect significant slope or elevation differences in the respective selection line regression equations, suggesting that the selection responses were merely shifting the populations along the phenotypic regression line. Ignoring the selection line classification, the data gave an estimate of 2.77 for the overall regression of abdominal fat on carcass weight. This line is shown along with the scatter of the individual generation means in Figure 18. It is seen to give a reasonable fit to the overall scatter of the data points. The diagram does, however, indicate an important lower than average slope of the relationship (β = 1.2) for mice of the six week line, the relationships for the other lines not being so consistently different but suggesting that the three week line is perhaps indeed of greater relative fatness than the others as Hull concluded.

The results of Hull thus also reveal a low genetic regression of fat on body size, this being evident at 6 weeks of age in his case and occurring at 9 weeks of age in the present data - i.e. at the age at which fat is being measured in both cases. The associations between fat weights at 9 weeks of age and body weights at earlier ages have accordingly been examined in the present data to see if this also was similar to the pattern demonstrated by Hull (1960). The results are presented in Table 42.
Table 42. Genetic Correlations Between BodyWeights at 3, 4½, and 9 Weeks of Age and Fat Weights at 9 Weeks

<table>
<thead>
<tr>
<th></th>
<th>4½ weeks</th>
<th>6 weeks</th>
<th>9 weeks</th>
<th>Abd. Fat</th>
<th>Total Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 weeks</td>
<td>0.88±.03</td>
<td>0.85±.04</td>
<td>0.65±.08</td>
<td>0.23±.14</td>
<td>0.05±.15</td>
</tr>
<tr>
<td>4½ weeks</td>
<td>0.94±.02</td>
<td>0.66±.08</td>
<td>0.13±.15</td>
<td>-0.01±.15</td>
<td></td>
</tr>
<tr>
<td>6 weeks</td>
<td></td>
<td>0.80±.05</td>
<td>0.21±.15</td>
<td>0.00±.16</td>
<td></td>
</tr>
<tr>
<td>9 weeks</td>
<td>0.43±.13</td>
<td></td>
<td>0.29±.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abd. Fat</td>
<td></td>
<td></td>
<td></td>
<td>0.88±.04</td>
<td></td>
</tr>
</tbody>
</table>

While the inter-age genetic correlations of body weight agree very closely with those found by Hull, there is no evidence of corresponding high genetic correlations between fat weights at 9 weeks and body weight measurements taken at younger ages. This feature therefore seems unable to provide a clue to explaining the lower genetic regression of fat on carcass weight at 9 weeks of age.

In summary the results indicate that selection for increased carcass weight at 9 weeks of age is expected to result in animals of lower than average relative fat content at this age, and that selection using an index designed to hold carcass weight constant would not materially alter the rate of genetic progress in absolute fatness. It was further shown that genetic variation exists in relative carcass fat content defined in terms of the deviations about the phenotypic regression line and that selection for relative fatness would induce a negative response in carcass weight, and would sacrifice a little progress relative to that possible from straightforward mass selection for fat weight alone.
IX. GENERAL DISCUSSION

A. THE ALLOMETRIC APPROACH TO BODY COMPOSITION ANALYSIS

A consequence of the widespread usefulness of the allometric equation is that simple allometry has often been credited with representing a fundamental law of growth. The conclusion reached by Reeve and Huxley (1945) in their review of such claims was that no satisfactory basis for allometric relationships could be inferred from postulates concerning mechanisms of growth. The hypotheses they reviewed were clearly rather limited in their approach and were either unable to provide mathematical laws of differential growth or they merely substituted a number of biological parameters which were difficult or impossible to measure, in place of the allometric coefficient which is at least able to be estimated.

A number of workers have, however, been able to deduce mathematical connections between the allometry equation and equations of time growth. Huxley himself (Huxley 1932) considered the allometric equation in terms of the declining rate of tissue multiplication with time, while Lummer (1937), Kavanagh and Richards (1942) and Sorra (1958) further developed the relation between body components when both follow the same type of growth function in time. The latter two publications have shown that the equation of relative growth may be directly deduced mathematically from time growth functions of the simple exponential or sigmoid form, without the need of any a priori assumptions concerning the physiological mechanisms. The relationship has been formalised in a recent paper by Laird et al. (1968) who show, with the assumption of identical exponential rates of decay in the specific growth rates of two body components, that the coefficient of allometry represents an index of the
displacement in time of the Gompertz growth process of one part relative to the other. The time displacement ($\Delta t$) is given by:

$$\Delta t = \frac{1}{\lambda} \log_b$$

where $\lambda$ is the common rate of exponential decay of specific growth rate and $b$ is the coefficient of allometric growth.

The value of this formalisation depends upon the assumption of equality in the rate of decay of the specific growth rates. Laird (1965) concluded from a study of the specific growth rates of the parts of human and chick embryos that in many cases the assumption would appear to be justified but that where it does not hold a curved allometric relationship would result. Rate of change in specific growth rate is directly estimable as the time scaling parameter of the Gompertz growth function and the conclusion reached by Laird and co-workers of similar rates of decay for the different parts of an organism was based on the finding that the time scaling parameters were several fold less variable from part to part than were the Gompertz parameters which represented the weight of the parts at time zero. The time scaling parameters nevertheless demonstrated a range of $\pm 25\%$ about the mean value.

Their conclusion was, furthermore, based on an analysis of Gompertz growth parameters estimated from the mean growth trend for a number of animals, rather than upon any considerations of between-animal variability in the Gompertz growth parameters. The value of their formalisation is thus somewhat limited, although it does indicate one of the circumstances in which linear allometric relationships might arise. It is, however, conceivable that linear relationships might also result from a joint variation of the Gompertz growth parameters for each part. Indeed, these same authors indicate in a companion paper (Barton and Laird 1969) that deviations from linearity of relative growth
equations are likely to be hard to detect and that a "20 percent difference in the values for (the time scaling parameter of the Gompertz growth function) will produce a curvature that might easily pass unnoticed in an allometric plot." The authors accordingly favour a separate characterisation and comparison of time growth functions for each of the components on the grounds that these may more readily indicate departures of the observed growth processes from any particular growth model chosen to represent the data. To some extent, the advantage to be gained from this alternative approach to the description of relative growth, will rest upon the extent to which the time growth model chosen to best represent the data can be interpreted biologically.

The biological interpretation of mathematical models of time growth has always been a subject of considerable speculation and the fact that no formula of time growth could be given a secure physiological basis led Reeve and Huxley (1945) to further question the value of the allometric formula as a fundamental law. Blaxter (1968) has, however, recently been able to derive an equation of body weight growth in time from biological parameters of energy metabolism and has shown this to be very similar to the empirically derived time growth functions studied by Brody (1945) and Taylor (1965 and 1968). Perhaps in the future further advances will be possible in this direction and will allow the allometric coefficient to be elevated from its empirical descriptive status to something that is more biologically revealing.

Until such a stage has been reached it would seem important to remain alive to the possibility of circumstances in which the allometric approach fails to provide a useful description of relative growth phenomena. The detection of such deviations is however likely to require studying developmental relationships over extended time periods and calls attention to the need for careful
experimental design, whereby the average developmental trend is accurately specified by ensuring that the measurements are taken over an extended growth period, and additional measurements are made over these key growth periods which prior knowledge reveals as the most likely points at which important deviations might arise.

Of importance to the allometric approach to the measurement of developmental growth is the dispute which exists concerning the relevance of fat deposition to the regular developmental changes occurring during growth. Adsley et al. (1964) and Fowler (1968) have given a good historical review of the classical work on body development in domestic animals that has arisen largely from the Cambridge School of Workers under Sir John Hammond, and favour the view that fat deposition is controlled more by nutrition than are the other components of the body. They argue that because fat is a unique tissue with functions very different from those of the other major tissues, the inclusion of such a variable component in any measurement of growth may thwart attempts to fit precise developmental equations to the data. Accordingly, they suggest that all developmental comparisons should be made relative to either a fat-free or fat-corrected baseline of growth. Their argument is based on the concept of fat deposition being largely a means of dealing with surplus energy and claim support for the developmental uniqueness of fatty tissue from a re-analysis of some Cambridge data which failed to detect differences between nutritional treatments in the weight of either bone or muscle relative to the combined weight of bone plus muscle, but which did indicate important nutritional differences in the relative fatness of pigs using this baseline of growth.

Fowler (1968) therefore promotes the view that the allometric concept is most useful when it is applied to anatomical components which form integral parts
of the same functional unit. It is worth noting however, that the allometric approach adopted by these workers is somewhat restricted in its outlook, in that it would appear to be limited to situations in which the same linear coefficient of relationship exists for all the treatment groups being compared, attention being confined to differences in the adjusted mean values of the dependent variables.

Seebeck's (1968) argument against this approach is that fat is inevitably part of the animal irrespective of its age and size and that subtraction of one component from the growing aggregate can only be justified if the absence of this component does not disturb the relationship between each of the other components and the weight of the whole less the subtracted component. Thus the exclusion of fat weight in a three component system of bone + muscle + fat, could only be justified if fat weight were found to have no effect upon the amount of bone and or the amount of muscle at constant weight of bone + muscle. Seebeck's own re-analysis of the same pig data examined by LeRoy et al (1964) did indicate that intermuscular fat was probably having a significant effect upon the muscular content of the remainder of the carcass.

Further reasons for not leaping blindly into the fat-free approach come from work indicating that some lipid has functional significance other than as a metabolically inert concentrated energy store. For example, Pomroy (1955) provides evidence of specific insulating properties in the pig. It is also known that fat depots possess a certain individuality in their rate of developmental growth relative to total carcass fat content and total carcass weight (Liebelt et al 1965, Seebeck 1968), suggesting that each of these depots has its own intrinsic rate of metabolic activity, which shows a proportional relationship to total body lipid content. Liebelt et al (1965) have also shown
that a decrease in potential lipid storing capacity caused by the removal of
the gonadal fat organs did not reduce the amount of fat present in mouse
carcasses following the development of ATG obesity. Further work by the same
authors on the development of ATG obesity suggests the operation of a feedback
control mechanism by which the hypothalamic regulation of food intake is itself
regulated by the extent to which the potential lipid storing capacity of adipose
tissue has been reached. The reviews of Adler and Wartheimer (1968) and
Kinsell (1962) also provide additional evidence that adipose tissue itself
should be regarded as a dynamic center of energy regulation which is integrated
with neural, hormonal and other physiological mechanisms.

Despite the difficulties of interpretation discussed above, the allometric
approach to the study of relative fatness was used throughout the present work
and led to meaningful and interesting conclusions which will now be discussed.

B. FAT DEVELOPMENT IN THE OBESE MUTANT

Application of the allometric approach to the assessment of differences in
fat development between obese mutants and their normal litter mates revealed
that the gross physiological difference in adipose tissue metabolism that results
from the presence of the obese gene was reflected in a clear positional difference
in the linear logarithmic regression line relating fat content to either carcass
weight or to the fat-free carcass component. The analysis showed that on
average there existed the same ratio between percentage growth increments for
the fat and fat-free components of carcass weight in each of the two strains but
that the obese animals had considerably greater amounts of fat relative to non-
fat tissue. The large ratio for the average percentage growth rates of these
two components (logarithmic regression coefficient for total fat on fat-free
carcass weight = 2.5), resulted in the allometric line relating fat weight to carcass weight being of lower slope for animals carrying the obese gene. This in turn indicated that the percentage which the fat component made of carcass weight, increased during growth at a slower rate for these animals in comparison with their normal litter mates. Consequently the difference in fat percentage between the two strains was found to decrease during growth, being at a maximum at the earliest stage of the growth period investigated.

The youngest mouse in this study was killed at an age of 6 weeks, this being about as young as one can expect to visually recognise the presence of the mutant gene with any certainty. The results obtained thus suggest that the allometric method could be of considerable practical value to a classification of animals for the presence of the mutant gene during an early stage of their post-natal life. While this method of classification is likely to be of little advantage to the proving of heterozygosity in parental pairs required for breeding purposes, apart from a possible saving of cage space in the mouse laboratory, it could be of considerable benefit to physiological studies requiring young animals. For such purposes, however, a more accurate specification of the allometric relationships for the obese mutants and their wild-type contemporaries will be required than has been accomplished by the present analysis. This is especially true with respect to the specification of regression relationships prior to 6 weeks of age if a dangerous amount of extrapolation is to be avoided. While such a task will be beset with the problem of recognising the genetic constitution of animals prior to 6 weeks of age, it is suggested that the technique of discriminant function analysis (Seal 1966) preferrably in conjunction with a concurrent assessment of enzymatic parameters (Bulfield 1968) may well lead to profitable results being obtained.
Figure 20. Arithmetic Relationships Between Fat Weight and Carcass Weight in the Large and Small Body Weight Selection Lines of N-strain Mice.

(taken from Fowler (1958))
Although the primary lesions responsible for the genetically determined obese conditions have not yet been identified, this field of research along with those studies that are concerned with the development of NPG obesity, is proving extremely valuable to the untangling of the complex biochemical pathways involved in the control of fat metabolism. Bulfield (1968) has suggested that progress may well profit from a further broadening of research into the genetic control of the biochemical processes of fat metabolism. He specifically suggests an examination of variations in the levels of activity of lipogonic enzymes for inbred strains of mice, and that this could be followed by selective breeding using lipogonic parameters as the criteria of selection in an attempt to produce new genetic combinations of lipogenic characters. The pronounced difference in the developmental pattern of fat growth found between the two strains of mice examined by Fenton (1956) would emphasize the possible value of the first of these approaches. It is suggested that allometric studies of fat development may provide a useful screening technique that would permit a choice of those strains most likely to lead to profitable results, and may also provide a valuable quantitative criterion for use in selection studies.

C. FAT DEVELOPMENT IN BODY WEIGHT STRAINS OF MICE

The close developmental association between the fat content of mouse carcasses and their carcass weight found from the material analysed in Sections V and VI was also apparent for the selected strains studied by Fowler (1958). It was evident, for example, from the scatter diagram she presented for male mice of the b-strain and which is reproduced here in Figure 20. It was also revealed by a plot of the means for fat and carcass weight at 6, 9 and 12 weeks.
Figure 21. Arithmetic Relationships Between the Mean Fat and Carcass Weights at 6, 9 and 12 Weeks of Age for the C and N-strain Selected Lines of Mice
(taken from Fowler (1958) - Table 4)
Figure 22. Logarithmic Relationships Between the Mean Fat and Carcass Weights at 6, 9 and 12 Weeks of Age for the C and N-strain Selected lines of Mice - log_e g scale. (taken from Fowler(1958)).
of age extracted from Table 4 of her publication. Those are presented in Figure 21, the corresponding plots on a logarithmic scale being given in Figure 22. A regression analysis fitted the following pooled within-strain regression line to the logarithims of the age means of Figure 22.

\[ y = 1.20 + 2.42 \log (x - \bar{x}) \]

where \( y = \log(\text{fat weight (g)}) \) and \( x = \log(\text{carcass weight (g)}) \). This indicates the following arithmetic relationship:

\[ Y = 2.15 \times 10^{-3} x^{2.42} \]

or \( 100 \left( \frac{Y}{x} \right) = 0.215 x^{1.42} \)

which quantifies the exponential relationship between fat percentage and carcass weight for this material.

With respect to her comparison of the selected strains, Fowler (1958) noted that "the amount of fat in the small line was approximately similar to, though slightly higher than, that of the large line for identical carcass weights despite large age differences." This is indeed apparent from her data shown in Figure 20. The age means for her data (Figure 22) in fact reveal a similar allometric pattern of relative fat growth for the large and control strains, the linearity of the relationship being very apparent. A greater amount of fat relative to carcass weight for animals of the small selection line is also revealed by both sets of graphs given for the N-strain in Figures 21 and 22.

A close association between fat weight and carcass weight was also apparent for Fowler's C-strain material, the age means for which are also given in Figure 22. On the basis of the graphs presented, and of Fowler's (1958) covariance analysis, it is evident that fat was growing at a faster relative rate in comparison to the percentage rate of carcass growth, in the large line
of the N-strain than in the large C-strain line. Although the slope difference appears to be slight, a covariance analysis indicated significance at the 5% level of probability. The estimates were 2.84 for the NL line and 2.46 for the CL line. This difference is therefore in broad agreement with the conclusions reached by Fowler (1958). Fowler concluded that for both the large and small lines of the C-strain, protein and water were deposited at a fairly constant rate up to 12 weeks of age and that the rate of fat deposition increased only slowly. The large mice of the N-strain, however, were held to exhibit a marked increase in the rate of fat deposition at 5 weeks of age. This difference between the large lines of the two strains was, however, based merely on a visual inspection of the absolute growth curves in time for each of the carcass components. The present statistical examination of the relative growth rates suggests that there exists a characteristic difference between the two strains in the relative growth rate of the fat component throughout the 6 to 12 week period. Whether this difference is an accurate reflection of that existing at earlier ages cannot be determined from the data presented in her publication. Differences in the genetic constitution of the base population, the selection criteria and the duration of selection were put forward by Fowler as possible explanations of the difference in relative fatness between the two strains.

Comparison of the graphs for the large and small selected lines within Fowler's C-strain material does not reveal such marked differences as were apparent for the N-strains. However, a covariance analysis of the logarithms of the age group means indicated a significantly different (P < .05) slope of the logarithmic regression line relating fat content to carcass weight, the estimates being 2.45 for CL mice and 1.70 for the small Cs animals. This is
to some extent contrary to the situation existing in the B-strains, for which a covariance analysis was unable to detect significant strain differences in the slope of the regression lines, although the slope was least for the small line mice (b = 1.83).

The results obtained from this allometric re-analysis of some of Fozdar's data is thus compatible with the results obtained from the B-strain material examined in Section VI of this thesis. The difference found for Fozdar's C- and B-strains are in general agreement with the variation in the selection responses that was found to exist between the different replicates of the B-strain material. It is apparent however, that these coefficients of allometry for relative fat growth in her material are somewhat higher than the corresponding average values found for the B-strain selection lines over the 4 to 9 week growth period. The B-strain cross-sectional coefficients for fat development to 4 weeks of age were, however, less different from those estimated from Fozdar's material, the differences between the N and C-strains being of a similar order but of opposite sign, to the differences between and C and B-strains.

It thus appears that selection for body weight at six weeks - i.e. for increase in immature body size - increases the rate of fat development by about 6 weeks but often results in animals of lower relative fatness during the early post-weaning growth period. The net result at the age of selection therefore depends upon the extent to which these two effects balance one another. It is suggested from Figure 22 for the B-strains examined by Fozdar (1953) and by the average results presented in Section VI for the B-strains, that the two effects have more-or-less cancelled one another by about 6 weeks of age. It is worth recalling, however, that the relative importance of the two effects varied
Table 43. Ratio of the Percentage Response in Weight of Fat to the Percentage Responses in Carcass

<table>
<thead>
<tr>
<th>Source of Data</th>
<th>Sex</th>
<th>Lines</th>
<th>Age at Carcass Analysis (weeks)</th>
<th>Percentage Response</th>
<th>Ratio of Fat Response to:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fat Wt. Carcass Wt.</td>
<td>Carcass Response</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Body Wt.</td>
<td></td>
</tr>
<tr>
<td>Fowler (1958)</td>
<td>Male</td>
<td>L-C</td>
<td>6</td>
<td>125</td>
<td>37.4</td>
</tr>
<tr>
<td>N-strains</td>
<td></td>
<td></td>
<td>8-9*</td>
<td>97.9</td>
<td>25.8</td>
</tr>
<tr>
<td>Hull (1959)</td>
<td>Mixed</td>
<td>3wk-C</td>
<td>6 *</td>
<td>76.0*</td>
<td></td>
</tr>
<tr>
<td>Generations 4 and 5</td>
<td></td>
<td>4 1/2</td>
<td>6 *</td>
<td>14.0*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 -C</td>
<td>6</td>
<td>9.9*</td>
<td></td>
</tr>
<tr>
<td>Lang (1967)</td>
<td>Male</td>
<td>L-C</td>
<td>6</td>
<td>17.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>L-C</td>
<td>6</td>
<td>-ve</td>
<td></td>
</tr>
<tr>
<td>Biondini et al (1968)</td>
<td></td>
<td>Line 1-C</td>
<td>16-21</td>
<td>52.6</td>
<td>12.1</td>
</tr>
<tr>
<td>(Based on within sex</td>
<td></td>
<td>Line 2-C</td>
<td>16-21</td>
<td>33.9</td>
<td>11.3</td>
</tr>
<tr>
<td>regress for Gen. 2-9)</td>
<td></td>
<td>Line 3-C</td>
<td>16-21</td>
<td>41.2</td>
<td>17.9</td>
</tr>
<tr>
<td>Timon et al (1969)</td>
<td>ad.lib feeding</td>
<td>Male</td>
<td>L-C</td>
<td>8</td>
<td>32.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Female</td>
<td>L-C</td>
<td>8</td>
<td>32.2</td>
</tr>
</tbody>
</table>

1 Based on abdominal fat weight rather than total fat content.

* Carcass analysis carried out at older ages than the age at selection.
from replicate to replicate in the case of the Q-strain animals.

In the case of the Q-strain material examined in this thesis, the tendency for selection to have had little overall effect upon relative fatness at six weeks of age was reflected by a similar estimate for the average between-strain coefficient of genetic allometry to that found to summarise the phenotypic differences between individual animals of the control line (Section VI).

Table 43 presents a number of estimates for coefficients of genetic allometry that have been extracted from published reports presenting results on correlated responses in fat content to selection for increased body size. The table also presents some corresponding ratios of correlated responses. The genetic allometry coefficients have been calculated from the ratio of the indirect to the direct responses after expressing the responses as a percentage of the level of the character in the control population (Reeve 1950). With the exception of the results of Lang (1967) it is clear that the coefficients are of the order of 2.0 - 3.0, and are thus somewhat higher than the average of 1.4 which was found to characterise the Q-strain mice. The separate ratios of the percentage responses to positive body weight selection in the different Q-strain replicates ranged, however, from -0.29 for Replicate B to 2.39 for Replicate A. The corresponding ratios of the correlated responses at 9 weeks of age ranged from 0.92 to 4.19 - i.e. were higher, a feature which is also apparent for Fowler's results at 12 weeks of age.

J. GENETIC PROPERTIES OF GROWTH CURVES

Taylor (1965, 1966 and 1968) has developed a thesis of the genetic properties of mammalian growth curves based upon the knowledge that exists concerning the patterns of changes in genetic variance with age and of interage genetic
correlations, for the generally found situation of continued slow increases in the heritability of post-weaning body weight with age until final mature size is reached, and the presence of large inter-age genetic correlations. He has also considered the consequences of selection at a given age on the pattern of body weight growth for a population of cattle.

Since weight at every age is fairly highly genetically correlated with mature weight, a large portion of the genetic variation in body weight at any age will be removed when mature weight is held constant, and selection for increased weight at a given age will result in considerable associated changes in mature size. Taylor's approach is aimed at a separation of the predicted selection responses in the mean growth curve into those due to mature weight and those due to changes in the shape of the growth curve. He does this by expressing body weights as a proportion of mature weight, such a fraction being referred to as the average degree of maturity at the stage of development being considered. No matter at what age body weight was measured, Taylor showed that positive selection pressure would result in large predicted increases in mature body weight, but that these would not result in marked changes in the maturity curves. This was seen to be especially true when the expected responses were considered in relation to the amount of selection pressure applied. Thus, while selection at an immature age leads to earlier maturing animals in comparison with unselected animals of the same mature size - i.e. results in animals that are more mature at a given age - this small effect tends to be offset by the slower rate of maturing of the larger animals - i.e. by the longer time required for mature size to be attained.

In view of the broad similarities between mice and cattle in the pattern of change of body weight heritabilities and genetic correlations with age (Hull 1960),
(Monteiro and Falconer 1966), a similar situation is to be expected for the former species. The results of Timon and Bisen (1969) and those presented here in Section VII do indeed agree with Taylor's hypothesis of the relative inflexibility of mammalian growth curves to changes in shape following selection for an immature body weight. For the case of the selected strains studied in Section VII the most pronounced shape changes that were apparent were for large mice of Replicates D, E and F which demonstrated a greater curvature in their post-natal growth pattern to maturity, than did their respective controls. The significant variability among the line-replicate means presented in Figure 17 does, however, provide evidence for the existence of genetic variability in the shape of mouse growth curves. This is in line with the results of Johnson and Gowe (1962) and Abplanalp et al (1963) for turkeys.

While the results of Section VII tended to verify the general inflexibility of the shape of mouse growth curves to changes following selection at six weeks of age, the data on which they were based were not ideal for demonstrating the detailed pattern of the small changes that are expected to occur. This is because the data did not extend beyond an age of 46 weeks, there in fact being evidence that body weight was still increasing in some of the large and control lines at this time. The individual growth curves presented by Roberts (1961) for male mice of the N-strain examined by Fowler (1958) show the extended pattern of body weight growth in time for animals of the large selection line.

Figure 1 of Roberts (1961) suggests mature sizes in the region of 54, 31 and 22 grams for the large, control and small selection lines respectively, and corresponding maturing times being of the order of 400, 320 and 225 days. Using these estimates of mature size to adjust the growth data on this same strain of mice (N-strain) presented by Fowler (1958) gave rise to the maturity
Figure 23. Age Changes in the Degree of Maturity for the Selected Lines of N-strain Mice.
(taken from Fowler (1958) and Roberts (1961))

- Small line
- Control line
- Large line
curves presented in Figure 23. These curves indicate that the overall effect of selection for increased body weight at six weeks of age has been a reduction in the degree of maturity at all ages between birth and 12 weeks. Selection for low body weight has had the reverse effect. Furthermore, the similar pattern of growth (i.e. shape of their growth curves) for all three strains is apparent from this graph.

Taylor has also recently considered (Taylor 1969) the relative usefulness of such simple growth functions as Brody's asymptotic, the logistic and the Gompertz, to the description of growth patterns over extended periods of time. He shows that the asymptotic function gives a useful description of post-natal growth beyond 30% of mature weight provided that growth measurements extend to beyond 80-90% of final weights, an absence of measurements close to maturity resulting in an underestimation of mature body weight. Because the logistic function is also unable to give an accurate description over extended growth periods Laird (1965) was led to favour an equation of the Gompertz type. However, as Taylor (1969) shows, even this growth function is unable to give an adequate description of growth beyond 80% of final weight. To cope with this feature, Laird et al. (1965) have developed a derived form of the Gompertz function by including an additional parameter which represents a linear growth process over and above the basic sigmoid growth form represented by the Gompertz. They have shown that this function gives a very much better fit to mouse growth data which includes measurements beyond 70% of final mature size. However, because of the interpretational complexities introduced by this additional parameter, the general conclusion reached by Taylor (1969) must be upheld - i.e. no general growth function exists which has all the attributes required to give a broad baseline to mammalian growth in order that short-term measures of growth
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might be set within a broad undistorted framework.

Despite their deficiencies the above mentioned simple growth functions have aided the establishment of a number of useful generalizations concerning mammalian growth patterns. Of particular importance is the association which has been found to exist between mature size and the time to mature.

Apart from its biological interest, the value of knowing the relationship between these two growth criteria lies in being able to separate variation in rate of maturing that is associated with mature size from that which is not and which, accordingly, represents variability in the shape of the growth pattern. Taylor (1965 and 1966) has shown that a close positive relationship exists between the two criteria, both between species, between breeds and strains and between sexes within a breed or strain.

The studies that were made of this relationship in Section VII in general tended to confirm the associations established by Taylor. The main exceptions were with respect to the between sex relationships, and to the magnitude of the regression coefficients between individuals within strains. Although the analyses indicated that the relationship did not appear to be particularly strong for these data, its usefulness was made evident from the manner in which it allowed the strains selected for large body size to be separated into two broad groups differing in their pattern of body weight growth relative to their controls. The analysis of Montiero and Falconer's (1965) data using the logistic function did not prove to be particularly revealing, most probably because of the short period of growth for which data were available. The data were not able to provide reliable estimates of the strength of the genetic association between the two characters, but did indicate that the heritability of mature size is likely to be considerably larger than the heritability of
time to mature. Taylor and Craig (1967) also found low heritabilities for earliness of maturing of linear body measurements in cattle, although their analysis did suggest the presence of plenty of genetic variation as evidenced by genetic coefficients of variation of a similar order (5%) to those found for mature skeletal measurements.

Although it is apparent that further work is needed to discover the relative phenotypic and genetic relationships between mature size and time to mature the analyses undertaken were able to highlight the general inflexibility of mouse growth patterns, and emphasise the need for fairly sophisticated selection criteria if the shape of mammalian growth curves is to be altered by breeding.

A further value of knowing the relationship between mature size and time to mature that has been put forward by Taylor (1963) is the provision of a scale of metabolic age which would allow mature animals to be compared with respect to their body composition. The relationships examined in Section VII showed, however, that only about 20% of the variation in relative fatness could be explained on such a scale - i.e. was associated with the joint effects of mature size and time to mature and therefore with differences in the shape of the body weight growth curve. The associations revealed were nevertheless compatible with an expectation based upon energetic considerations of body development. The between strain relationships (Figure 17) however, bore no obvious association with the average between-strain levels of relative fatness at maturity, all large lines, for example, tending to exhibit a lower level of relative fatness than their respective controls.

b. GENETIC VARIATION IN RELATIVE FATNESS

The results of the half-sib analysis of fat and non-fat components of the
carcass that was undertaken in Section VIII demonstrated the presence of
 genetic variation in relative carcass fat content at 9 weeks of age and indicated
 that genetic progress could be expected if it were desired to alter fat weight
 without at the same time causing any change in total carcass weight. The
 parallel that the expected changes in relative fatness following selection for
 body or carcass weight made with Hull's (1959) results, suggested, however,
 that while positive selection at a given age may bring about little change in
 relative carcass fat content at that age, and may even be expected to reduce it
 somewhat in the case of abdominal fatness, it may lead to increased levels of
 relative fatness at later ages. This would seem to be the main reconciling
 feature common to the great majority of results from research into the genetics
 of fat development in the mouse.

 The tendency for selection for fast body weight growth to result in lowered
 levels of relative fat content is compatible with nutritional considerations if
 there exists genetic variation in the metabolic partitioning of the energy
 available for growth between the fat and non-fat tissues of the body. The
 results found for the obese mutant would support this view, while the results
 given in Section IV indicate that variation in the non-fat carcass component
 closely reflects variation in protein composition. Under this influence there-
 fore, genetic variation in growth rate would be positively associated with
 genetic variation in a protein-biassed metabolism.

 However, fast growth may also come about from variation in appetite leading
to variation in the amount of energy that is available for growth. Indeed,
 Elaxter's (1968) considerations of the consequences of variations in food energy
 intake upon growth, indicate that the shape of the growth curve is clearly
 dependent upon the time pattern of energy supply. Animals of average energy
partitioning ability that are growing fast by virtue of having a large energy intake would be expected therefore, to be of greater relative fatness to an extent that depends upon the degree to which the energy for their growth exceeds the growth potential of their lean body mass and must be diverted into fat stores (Fowler 1968). The effect of selection at any given age upon relative fatness at this or any other age would thus depend upon the net outcome of these two influences and of the extent to which maxima in the rates of protein deposition (Blaxter 1968) are under genetic control.

Knowledge of the pattern of change in the phenotypic expression of all these influences and of the degree to which they are under genetic control would therefore be needed for a complete description of the genetics of developmental growth under even this over-simplified growth model. These features highlight the importance of analysing patterns of development over extended growth periods and indicate that our knowledge of the processes involved is in fact lamentably lacking at the genetic level. An important practical consequence of the findings presented in this thesis would, however, seem to be that if selection for immature body weights is not to be accompanied by increases in relative fatness at later ages, then selection may have to be carried out close to the age at which the desired responses in relative fatness are required to be realised.
1. A review of the literature on the genetic control of growth and development in the mouse indicated a lack of knowledge of the degree to which variation in the shape of the curve of body weight growth reflects variation in the developmental pattern of fat and non-fat tissue growth and of the precise extent to which these two growth processes are under independent or under common genetic control. The review also indicated the allometric equation to be a useful method of quantifying the developmental changes associated with normal body weight growth.

2. Preliminary investigations confirmed the utility of the allometric method by its characterisation of fat development in the genetic obese strain of mice relative to their normal litter mates, and showed the fat-free dry matter component of the carcass to be useful indicator of phenotypic variation in carcass nitrogen content.

3. The allometric coefficients of linear relationship on a logarithmic scale showed, for normal mice, that fat development occurred at a $2^{1/2}$ to 3-fold greater rate in the case of the gonadal fat depot, and at a 1-fold greater rate for total chemical fat, relative to the percentage rate of growth of the carcass as a whole.

4. In contrast to the positive correlated responses in absolute amounts of fat, relative carcass fat content was altered little at a given age by selection for high or low body weight at that age in the case of total fat, but was decreased
in the case of gonadal depot fat, selection also resulted in a positively correlated response in the rate of development of total fat relative to carcass weight, with the result that the large strain mice tended to be relatively leaner prior to the age of selection and relatively fatter at older ages. Significant variation was found to exist among replicates in the extent of these responses. Important effects of sex, age and genotype were established for the extent to which variation in the weight of gonadal depot fat reflected variation in total chemical fat weight.

5. Selection for body weight at six weeks of age was found to have had very little effect upon the shape of the growth curve to 46 weeks of age. Genetic variation in growth curve parameters was very largely confined to genetic variation in mature body size. Mature body size was positively related to the time which individual mice took to mature, and variation in relative fat content was found to be associated with the joint variation in these two growth curve parameters.

6. A half-sib analysis demonstrated the presence of genetic variation in relative carcass fat content at 9 weeks of age, — heritability of the order of 0.5 in comparison with an estimate of 0.4 for absolute fat content. Selection for relative fatness — defined in terms of the deviations about the phenotypic regression of fat on carcass weight — was expected to result in a negative correlated response in carcass weight and to sacrifice a little of the progress in absolute fat content relative to that possible from straightforward mass selection for fat weight alone. Selection about the genetic regression line maintained carcass weight constant and made no such sacrifices. Selection for
carcass weight at 9 weeks of age was expected to produce animals of lower than average relative fat content at that age.
I wish to thank Professor D.S. Falconer for laboratory facilities and for his encouragement and advice during the period of this study.

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