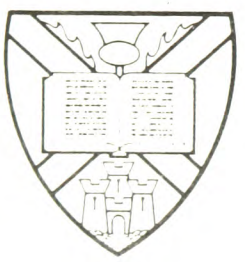

Influence of Selection for Body Weight and Testis Weight on the Growth of Mice.

by

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DEDICATION

To a mouse.....

"Nelson", who livened up the

hours in the Mouse House.

We patronise them for their incompleteness, for their tragic fate of having taken form so far below ourselves, and therein we err, and greatly err.

For the animal shall not be measured by man. In a world older and more complete than ours they move finished and complete, gifted with extensions of the senses we have lost or never attained, living by voices we shall never hear. They are not brethren, they are not underlings, they are other Nations, caught with ourselves in the net of life and time, fellow prisoners of the splendour and travail of the earth.

HENRY BESTON (1928).

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SUMMARY

A potential means of improving the efficiency of meat production was tested. This was a technique to alter the shape of the growth curve by selection. Within family selection on males was practised for 6 generations within 2 replicates of each of 8 lines of mice for combinations of 5 week body weight (W) and 5 week testis weight (T). There were 8 single pair matings per generation within each line. Selection criteria were: high W (HX), low W (LX), high T (XH), low T (XL), high W and high T (HH), low W and low T (LL), high W and low T (HL), low W and high T (LH). Control lines were also maintained. In the double trait lines W and T were combined in an index which weighted each trait by the reciprocal of its phenotypic standard deviation. Realised within family heritabilities were: W, 0.24 ± 0.10, T, 0.48 ± 0.07, HH/LL index, 0.36 ± 0.09, HL/LH index, 0.60 ± 0.07. The realised genetic correlation between W and T in the single trait lines was 0.70 ± 0.25. Responses in W and T in the index lines were in the desired directions and about the same sizes as direct responses in the single trait lines. In the HL/LH lines responses were larger than predictions based on parameters estimated in the single trait lines. Selection had little effect on litter size. In an unselected 7th generation growth curves of mice in the HH and LL lines diverged up to 6 weeks of age and then converged. HL and LH lines continued to diverge to 15 weeks of age. The difference in weight between HX and LX mice remained constant, and between XH and XL mice it converged with age. Growth patterns of males, females and castrates were similar within lines. There was no response in the pattern of tail growth. There was a significant

change in the testis weight to body weight ratio in all but the HX and LX lines. It was concluded that selection on combinations of W and T may be useful in breeding programmes designed to alter the shape of the growth curve, but that further research is necessary before the technique could be applied to agricultural practice.

I INTRODUCTION AND REVIEW

The value of an animal for meat production is determined by its growth rate, feed conversion and carcass quality. Growth rate is most important for the economy of meat production because feed costs and most of the fixed costs decrease with increasing growth rate (Bakker, 1974). It is possible to select to improve the rate of growth but the high positive genetic correlations which exist between body weights at different ages (Bichard, 1968; Taylor, 1968) mean that any increase in early growth will be accompanied by an increase in mature weight (Bichard, 1968; Brinks, Clark, Kieffer and Urick, 1964; Taylor, 1968; Taylor and Craig, 1965). Brinks (1968) pointed out that a heavier mature weight would cause an increase in the maintenance costs of breeding stock. It is desirable to restrict increases in mature size when selecting on growth rate to avoid these extra costs. It is generally agreed that one way to improve the efficiency of meat producing animals would be to breed a strain with an increased growth rate up to slaughter weight but with a minimum increase in mature size (Bichard, 1968; Dickerson, 1970; Taylor, 1968). Therefore it is of economic interest to find an effective method of breeding strains of animals which have modified patterns of growth.

1.1 Direct selection to alter the shape of the growth curve.

1.1.1 Predicted responses.

Expected responses to selection on the shape of the growth curve have been predicted by several workers. Taylor (1968) evaluated the effects of various types of selection on the degree of maturity in body weight of cattle.He concluded that genetic changes in the shape of the growth curve may be achieved but the size of the expected change is small compared to the amount of selection pressure exerted. Dickerson (1982) suggested that index selection for faster growth and lighter birth weight in cattle can be expected to limit the increase in both birth weight and mature size with little reduction in post-natal growth. Timon and Eisen (1969) estimated heritabilities and genetic correlations amongst the parameters of theoretical functions fitted to the growth curves of mice. They suggested that direct selection for a change in the shape of the growth curve would be moderately successful. Thus theoretical predictions are that it should be possible at least to make small genetic changes in the pattern of growth.

1.1.2 Realised responses.

In practice the few experimental attempts to genetically alter growth patterns have met with varying degrees of success. Table 1.1 summarises these experiments, all of which involved either poultry or mice. In all of the experiments quoted, selection was on combinations of early and late weights. Selection indexes were

Table 1.1 Summary of selection experiments designed to alter the shape of the growth curve.

Species	Type of Selection	Aim of selection	Number of generations of selection	Summary of results	Source
Turkeys	Index	To increase 8 week wgt. without increasing 24 week weight.	7	Mean 8 week weight increased by 0.58kg(males) and 0.40kg(females). Mean 24 week weight remained fairly constant.	Ablanalp, Ogasawara and Asmundson (1963).
Chickens	Index	High 63 day and low 147 day weights.	First 7	63 day weight increased, 147 day weight remained constant.	Merritt (1974)
			Second 7	63 day weight continued to increase, 147 day weight also increased.	
Chickens	Independent culling levels	Combinations of high and low weights at 8 and 36 weeks.	12	8 week and 36 week weights increased and decreased in the desired directions.	Ricard (1975)
Mice	Direct	To increase the ratio of weight gain between 3 and 6 weeks (G3-6) to the gain between 6 and 9 weeks (G6-9).	8	Percentage of total gain occurring between 3 and 6 weeks increased significantly ($p<0.05$) from 79.5% to 83.8% (replicate 1) and 77.3% to 89.6% (replicate 2). Estimates of realised h^2 of G6-9 were 0.05 (replicate 1) and 0.13 (replicate 2).	Wilson (1973)
Mice	1) Index	a) To hold 10 week weight constant and i) increase 5 week weight. ii) decrease 5 week weight. b) To hold 5 week weight constant and i) increase 10 week weight. ii) decrease 10 week weight.	14	Generally successful. In lines a(ii) and b(ii) there were some correlated responses in the restricted weights.	McCarthy and Doolittle (1977), and McCarthy and Bakker (1979)
	2) Independent culling levels	a) High 5 week weight and low 10 week weight. b) Low 5 week weight and high 10 week weight.		a) No demonstrable response. b) Body weight decreased at both ages.	
Mice	Index and independent culling levels	High 3 to 5 week weight gain, and low 8 week weight.	5	No response in the desired directions under either type of selection.	Butler, Willeke and Pirchner (1980)

calculated using estimates of genetic parameters obtained from unselected populations. In these index selected lines the amount of selection pressure placed on each of the body weight measurements was weighted according to their variances in the unselected populations. One of the problems with this type of work is that, as selection proceeds, the variances of the critical body weights may change and consequently the selection pressure placed on each weight alters. This could explain why Merritt (1974) achieved the desired response in his first seven generations of selection but obtained an unwanted increase in the later weight as well as the increase in early weight in the latter seven generations. McCarthy and Bakker (1979) fitted growth curves to the growth data from the lines selected by McCarthy and Doolittle (1977) and showed that index selection produced lines of mice with quite different patterns of growth. The growth curves of the lines selected by independent culling levels remained largely unaltered. From the results of the experiments listed in table 1.1 it would appear that it is easier to alter the pattern of growth of poultry than that of mice, and also that selection on an index based on genetic parameters of the relevant traits has been the most successful type of selection. Eisen (1976) reviewed the experiments on mice and concluded that the results of selection experiments designed to change the growth pattern of the mouse have been moderately successful, but the realised responses tend to be low, and also responses in early post weaning gain are less than if selection is directly for post weaning gain or body weight.

In general the results from experimentation would appear to

verify the predictions that selection to alter the shape of the growth curve is possible but with some difficulty. The main drawback is that responses tend to be low and responses in rate of early gain are less than if selection is directly for gain or body weight. The latter problem is not considered directly in this study. However, this may not be such a big problem because in the long term a slow change in the pattern of growth may bring about greater improvements in the overall efficiency of animal production than a faster increase of gain coupled with increasing mature size.

1.2 Indirect selection to alter the shape of the growth curve.

The results of the experiments reviewed above suggest that the most effective means of selection to alter the growth curve has been to use an index based on two or more characteristic traits of the growth curve combined with the relevant genetic parameters. Taylor and Craig (1965) concluded that without an efficient index based on genetic correlations and involving the full record of each individual's size at a long succession of ages, selection would be ineffective and progress very slow. However, if selection is based on an index of weights taken over a long age period then the generation interval will be correspondingly long and will mean that progress is still slow. To speed up the rate of response Taylor (1968) suggested the use of indirect selection to avoid the necessity of measuring mature size.

1.2.1 Testis size as a measure of degree of maturity in body weight.

Land (1981) proposed a way to speed up the rate of genetic change in the growth curve. He suggested that selection should be on body weight as a measure of body size, combined with testis size as a measure of degree of maturity with both traits measured at an immature age. Direct evidence to support this hypothesis comes from two sources. The main one is an experiment described by Land, Carr and Lee (1980) in which two lines of sheep were selected for high and low testis size respectively. Ram lambs were chosen on the basis of their testis diameter, which was the mean of 3 measurements taken and corrected for body weight at 6, 10, and 14 weeks of age and expressed in standard deviation units. One of the correlated responses to selection was observed in the adult weights of females, which were lighter in the high testis size line than in the low line at 18 and 30 months of age. Land *et al* (1980) suggested that selection for large testes at a fixed weight at a young age may favour more mature animals while selection for animals with small testes at the same weight and age could favour those which mature more slowly. The second piece of evidence to support Land's (1981) proposal is quoted by him and is a personal communication by C.Legault made in 1979. This is the observation that pigs with small testes at a given weight were very young, sexually immature, lean animals, whereas pigs with large testes at the same weight were very old, sexually mature and fat.

Apparently there have been no further direct investigations into the relationship between testis size and degree of maturity in body

weight. The results of selection experiments on growth and correlated responses in male reproductive traits should yield some evidence to support or refute the possibility of a relationship. However, published papers which contain the necessary information to derive such evidence are rare. One such paper is by Johnson and Eisen (1975) who measured the body weight and testes weights of mice at ages from 3 to 16 weeks. Two lines were involved, one selected for post-weaning gain and the other a control line. The selected line was heavier than the control and continued growing for longer than the control so it was apparently later maturing. When expressed per gramme body weight the testes weights of the selected line were lighter than those of the control. Therefore, it would be expected that in a group of mice all at the same body weight, the ones with the lightest testes would also be the ones which continued growing over a longer period and matured the latest, i.e. the mice with the lightest testes would be the least mature in body weight.

1.2.2 Hormonal relationships between testis size and growth.

Work on the regulation of growth by hormones gives indirect evidence for a relationship between testis size and degree of maturity in weight and is briefly reviewed here.

There may be a direct relationship between thyroxine levels and testis size as shown in an extensive review by Maqsood (1952): lowered levels of thyroxine reduced testis weights in young male mice, young rats, and cockerels, whereas elevated levels produced increases in testis weights of young mice and mallard drakes. There

was no direct information on the relationship between thyroxine and testis weight in sheep but thyroxine therapy produced precocious sexual maturity and prolonged the ram breeding season. It might therefore be expected that testis size would also be influenced in the ram. It is well known that thyroxine is important in the control of growth. The level of thyroxine optimal for sexual development in the mouse and rabbit was also optimal for body growth (Maqsood,1952). Testis size may therefore reflect the thyroxine levels which are regulating overall body growth.

The hormones produced by the testis, especially testosterone, are themselves involved in regulating growth. The rise in the levels of sex hormones (including testosterone) which occurs at puberty, may inhibit growth hormone (somatotrophin) production which will reduce growth in the epiphyseal cartilage at the ends of the long bones and thus reduce and perhaps stop long bone growth (Trueta,1974). Before this the low levels of sex hormones apparently stimulate bone growth (Short,1980). A similar phenomenon can be seen in the growth of the deer antler which is actually true bone (Wislocki, Weatherford and Singer, 1974). Normal growth of the antlers in velvet (a vascularised, innervated layer of skin) occurs when testicular testosterone secretion is low but gradually rising (Lincoln, Youngson and Short, 1970). When the androgen levels exceed a certain value the velvet is shed and the antlers stop growing (Miararchi, Scanlon, Kirkpatrick and Schreck, 1973). In young male cattle castration caused an increase in the growth of long bones (Muzikant and Podany, 1977; Robertson, Paver and Wilson, 1970). Removal of the testes apparently removed the calves' capacity to

produce inhibitory high levels of testosterone. Robertson et al (1970) castrated 18 male calves at about 13 weeks of age. On average these 18 steers reached a significantly greater withers height, greater chest depth, and greater foregirth than 18 comparable entire animals. In a similar experiment in which twins were used, steers had significantly longer metacarpal and metatarsal bones than their entire brothers (Muzikant and Podany, 1977). Short (1980) summarised the effects of sex hormones on bone growth by suggesting that they have a "double threshold" effect: low levels stimulating long bone growth and high levels inhibiting it.

The sex hormones also play a part in regulating rate of weight gain. Castration has been shown to reduce the rate of gain of male cattle (Robertson et al, 1970; Gortesma, Jacobs, Sasser, Gregory and Bull, 1974), sheep (Wilson, Ziegler, Rugh, Watkins, Merritt, Simpson and Kreuzberger, 1970; Glimp, 1971; Wilson, Varela-Alvarez, Rugh and Borger, 1972), pigs (Salomon, 1976; Rajamahendran, Ravindran and Rajaguru, 1978), and deer (Drew, Fennessy and Greer, 1978). Turton (1962) and Robertson (1966) who reviewed work on the effects of castration on cattle , sheep and pigs, concluded that in all cases growth rate was affected. Evidence that endogenous testosterone is involved in promoting the growth of entire animals in relation to castrates comes from Gortesma et al (1974) who compared blood plasma testosterone levels and the growth performances of bulls with those of steers from birth up to slaughter. Bulls had much higher levels of plasma testosterone than castrates and they also had increased growth compared to the castrates. Similar evidence has been produced from sheep using exogenous testosterone in silastic

capsules implanted into wether lambs (Schanbacher, Crouse and Ferrell, 1980). The implants produced the same blood testosterone levels and growth rates in the wethers as those in entire ram lambs, whereas non-implanted wethers had low testosterone levels and poorer growth rates.

The male steroids apparently influence carcass composition. In general the carcass of a castrated animal contains a higher percentage of fat and lower lean percentage than that of the entire equivalent (Turton, 1962; Robertson, 1966; Field, 1971). Application of exogenous testosterone to steers affected their carcass characteristics in a manner opposite to the effect of castration (Hale and Oliver, 1973). It would therefore appear that testosterone is important in determining the type of growth, as well as regulating growth rate, and the limits of growth. However there is a lack of information on the connection between the level of testosterone secretion and testis size. One piece of positive evidence for a relationship between the two comes from an experiment by Setchell, Waites and Lindner (1965) in which the testosterone ouput of both underfed and well-fed rams was closely related to the weights of their testes.

Assuming that levels of hormones secreted by the testis <u>are</u> connected to testis size, then the involvement of testosterone in the control of growth indicates that a relationship between testis size and degree of maturity in weight could be possible. Thus there is a physiological basis to support the suggestion that there is a connection between testis size and the regulation of body growth

either through thyroxine and/or via the hormones secreted by the testis. The study described in the following pages investigated the possibility of using this connection in selection designed to alter the shape of the growth curve.

1.3 Experimental aims and predictions.

The aim of the study is to test the hypothesis that selection on a combination of body weight and testis weight measured on the immature animal can be effective in breeding programmes designed to influence early gains and mature weights. The hypothesis was tested on the mouse. Lines of mice were selected for the four combinations of high and low body weight and high and low testis weight. The two traits were measured at an immature age which was determined before selection was started (section II). Testis weight was measured directly by hemicastrating each male mouse at selection age and weighing the excised testis. The selected males were subsequently able to breed with sperm from the remaining testis. The correlation between right and left testes weights was measured in the preliminary experiment described in section II, to check that it was feasible to use the weight of one testis as an expression of the total testis weight of a mouse.

The lines of mice selected for large testes were expected to show less growth after selection age since large testes should indicate a relatively high degree of maturity in overall growth. Conversely the lines selected for small testes were expected to show more growth after selection age. It was predicted that the lines should

respond as follows:

- High body weight, high testis weight: high early gain but little subsequent gain.
- Low body weight,low testis weight: low rates of gain and delayed maturity.
- High body weight,low testis weight: high early gain, delayed maturity and high mature weight.
- Low body weight, high testis weight: low rates of gain and low mature weight.

Unselected control lines were also included in the experiment, plus divergent selection on body weight and testis weight separately. This made it possible to 1) estimate genetic parameters of the two traits, and 2) compare the responses to selection on a combination of weight and testis weight with the responses obtained when only one is the object of selection. Two replicates of each line were maintained so that account could be taken of the effects of random drift on the responses.

Selection was practised for 6 generations. The responses in body weight and testis weight at selection age were measured in each generation. Measurements of the body weights of hemicastrated males and of females were taken at later ages in the sixth generation to test for responses in the shape of the growth curve. Selection was relaxed in a seventh generation so that the effects of selection on the growth of entire males could be measured and the validity of the hypothesis could be tested.

Indirect responses in litter size were measured throughout the experiment to check for any favourable or deleterious effects of selection on the reproductive rate of the mice. Selection on body weight and testis weight as single traits in previous experiments has influenced female ovulation rate and/or litter size. Selection for large size can increase the frequency of sterility in mice, but large selected mice which do give birth generally have greater litter sizes than control or small mice (Roberts, 1979). The ovulation rate of females in lines in which males were selected for high testis weight at 11 weeks of age was increased, although litter size was not affected (Islam, Hill and Land, 1976). No general predictions were made about responses in litter size in this study, but it was expected that the litters produced in the high body weight lines would be larger than in the low body weight lines.

II DETERMINATION OF THE AGE AT WHICH TO SELECT

2.1 Introduction.

The age at which body weight and testis weight should be measured was considered to be an important factor in determining the responses to selection. For the purposes of this study the "best" age at which to select should be when:

- both traits are still growing rapidly (i.e. are immature).
- the variability, both genetic and phenotypic, of each of the traits is high to allow a high intensity of selection.
- the heritabilities of both traits are high.
- the genetic correlation between body weight and testis weight is low to permit selection of the two traits in opposite directions.
- the genetic correlation between testis weight and degree of maturity in body weight is high.
- the correlation between right and left testes weights is high so that it is feasible to use the weight of one testis as a measure of total testis weight.

The growth of 256 unselected mice from 0 to 9 weeks of age was measured to provide information for the first two and the last criteria (below), and estimates of some of the genetic parameters for the two traits were obtained from the literature (section 2.4).

Data on male growth in body weight, skeletal size, body fat, testis weight, and an associated sex gland (the Cowper's gland)

weight, were obtained using a serial slaughter technique. Body length and tail length were used as indirect measures of skeletal size, total body fat was estimated by the gonadal fat pad weight since the two are highly correlated (Jagot, Webb, Rogers and Dickerson, 1980; Rogers and Webb, 1980), and the weight of the Cowper's gland was used to indicate degree of sexual maturity.

2.2 Materials and methods.

The parents of the male mice which were used in this preliminary study were from the second generation of a random-bred control line of the "G-strain". The formation of the G-strain is described by Sharp (in press). Mice from later generations of G-strain control lines were used subsequently to generate the base populations for the main selection programme (section 3.2). To generate the experimental animals, twenty-five pair matings were set up and twenty-five more were set up three weeks later. Thus the 3 to 9 week old progeny from the first set of matings experienced the same environment as 0 to 6 week old progeny from the second set.

At birth, litter sizes were adjusted to 8 offspring by adding or removing female pups. Litters were weaned at 3 weeks of age. Only male progeny were kept and they were allocated 6 to a cage in such a way that each cage contained representatives of several different litters. Male mice were killed by cervical dislocation at weekly ages from 1 to 9 weeks of age. The individuals to be killed at weaning, and pre-weaning were generally chosen randomly, on average 1.5 mice per litter, so that by 3 weeks of age the average litter

size was reduced from 8 to 6.5 pups. Mice slaughtered post-weaning were killed 6 at a time, all from the same cage.The number of mice measured at each age ranged between 15 and 49 (table 2.1)

Table 2.1 Number of mice measured at each age.

Age (weeks)	Number of individuals measured
0	49
1	22
2	26
3	24
4	36
5	25
6	24
7	18
8	15
9	17

The following measurements were recorded for each mouse at slaughter: liveweight, right and left testis weights, and body and tail lengths measured using the device illustrated in figure 2.1. Additionally, for mice slaughtered at 2 weeks old and upwards, records were taken of the weights of Cowper's gland, and the gonadal fat pad. The liveweights and body- and tail lengths of 49 newborn mice (age 0) were also recorded.

2.3 Results.

The mean values of each trait with age are shown in table 2.2. Mean testis weight at 8 weeks of age was lower than that at 7 weeks due to the measurement of a mouse with a very low testis weight. A growth curve was drawn out for each trait by plotting the mean values of the trait against age (figure 2.2). Measurements of all

FIGURE 2·1 DEVICE TO MEASURE THE BODY- AND TAIL LENGTHS OF A DEAD MOUSE.

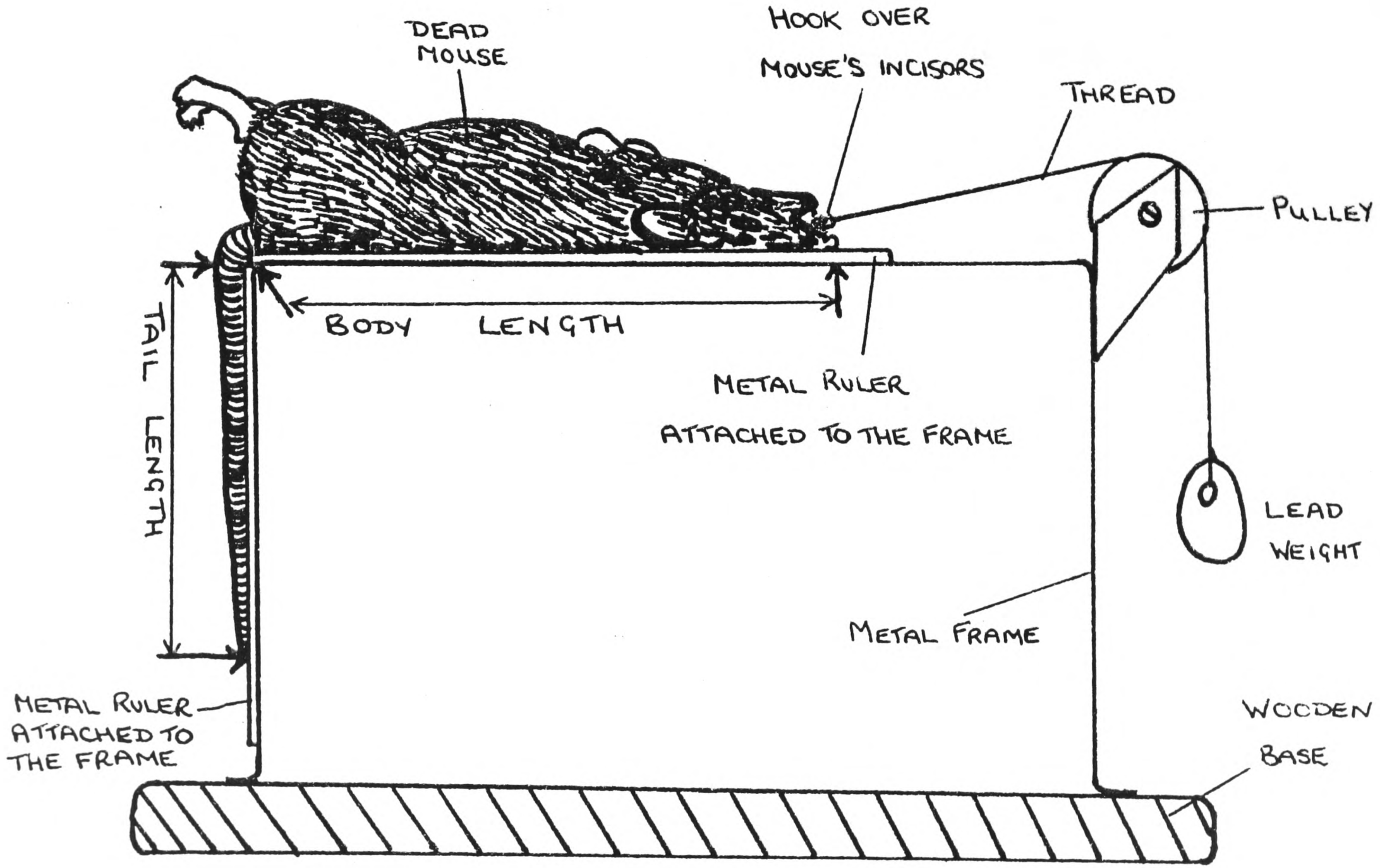
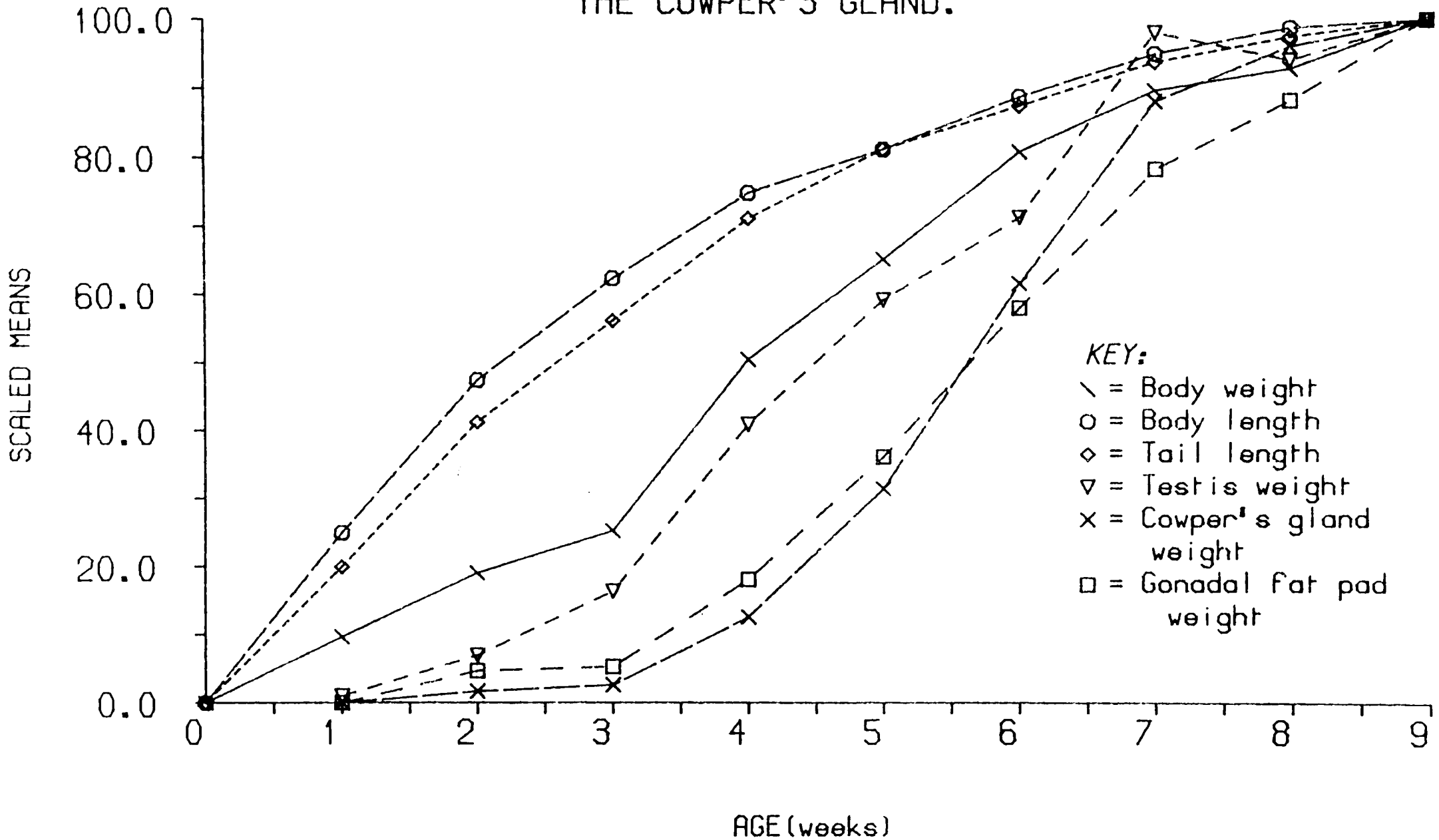


Table 2.2 Growth of body weight, body length, tail length, testis weight, gonadal fat pad weight and the Cowper's gland.

Trait	Age (weeks) 0	1	2	3	4	5	6	7	8	9
Body weight (g.)	1.6	5.0	8.2	10.3	18.9	23.9	29.2	32.2	33.3	35.7
Body length (cms.)	3.3	5.3	7.1	8.3	9.3	9.8	10.4	10.9	11.2	11.3
Tail length (cms.)	1.2	2.8	4.5	5.7	6.9	7.7	8.2	8.7	9.0	9.2
Testis weight (mg.)		7.4	19.0	37.1	84.6	119.8	143.2	194.8	187.0	198.4
Cowper's gland (mg.)		0.0	2.6	4.0	19.8	49.3	96.6	138.0	150.5	156.6
G.F.P.W.* (mg.)		0.0	23.2	26.3	88.9	178.0	285.9	385.5	434.8	492.3

* Gonadal fat pad weight.

FIGURE 2.2 GROWTH CURVES OF BODY WEIGHT, BODY LENGTH, TAIL LENGTH, GONADAL FAT PAD WEIGHT, AND WEIGHT OF THE COWPER'S GLAND.



the traits were adjusted to the same scale so that they could be plotted on one graph. Body weight increased most rapidly between 3 and 6 weeks of age. Total body fat, as indicated by the gonadal fat pad weight, began to increase from 3 weeks in parallel with body weight up to 6 or 7 weeks, but continued with a rapid increase after 7 weeks whereas the rate of growth in body weight began to decline. Presumably lean growth slowed by 7 or 8 weeks of age in these mice and subsequent growth was due mainly to increases in fatness. The pattern of skeletal growth adds weight to this argument: body and tail lengths increased between 0 and 8 weeks and began to plateau between 8 and 9 weeks suggesting that the rate of growth in body size independent of fatness had fallen by 8 weeks of age.

The testes increased in weight most rapidly between 3 and 7 weeks of age. The Cowper's gland followed the same pattern but about one week later. Therefore, it was assumed that sexual maturity was reached some time after 6 or 7 weeks.

Mean body weight and mean testis weight at each age were expressed as percentages of the mean values at 9 weeks to give some idea of the rate of maturing of each trait (table 2.3). The mice were more mature in body weight at pre-weaning ages than in testis weight. However, body weight matured more slowly than testis weight and so by 7 or 8 weeks of age the two traits were at a similar state of maturity. The figures would suggest that both traits are immature at least up to 6 weeks of age.

Relevant correlations and coefficients of variation were

Table 2.3 Relative maturity in body weight and testis weight, and estimates of correlations and coefficients of variation calculated from the data of mice at ages between 1 and 9 weeks.

ESTIMATE OF	Age (weeks) 1	2	3	4	5	6	7	8	9
Degree of maturity (%)*									
1) Body weight	14.0	23.0	28.9	52.9	66.9	81.8	90.2	93.3	100.0
2) Testis weight	3.7	9.6	18.7	42.6	60.4	72.2	98.2	94.3	100.0
Coefficient of variation:									
1) Body weight	0.12	0.15	0.16	0.15	0.17	0.12	0.10	0.11	0.08
2) Testis weight	0.27	0.30	0.30	0.26	0.26	0.26	0.17	0.19	0.24
Within age phenotypic correlation between:									
1) Body weight and testis weight	0.32	0.89	0.91	0.64	0.50	0.41	0.54	0.25	0.23
2) Right and left testis weights	0.82	0.97	0.97	0.98	0.99	0.99	0.98	0.99	0.99

* As a percentage of the mean 9 week measurement.

calculated at each age and are presented in table 2.3. The coefficients of variation of body weight and testis weight remained fairly constant at about 0.16 and 0.26 respectively over the observed period. It was not possible to estimate genetic correlations between body weight and testis weight from the data in this experiment. However, phenotypic correlations were calculated within each age and these were used to give an indication of the underlying genetic correlations. The correlation between the two traits fell steadily from 0.9 at 2 to 3 weeks old to 0.2 at 9 weeks. The within-age correlation between right and left testes weights was over 0.97 at all ages above 1 week.

2.4 Genetic parameter estimates.

The genetic control of body weight has been the subject of many published papers which have been reviewed by Roberts (1965), Eisen (1974), and McCarthy (1982). McCarthy (1982) presented a table of realised heritability estimates of body weight at different ages, which were obtained in a number of selection experiments. The table is repeated in table 2.4. Monteiro and Falconer (1966) estimated components of the variance of body weight of male and female Q-strain mice from 0 to 8 weeks of age. Heritability was estimated as additive genetic variance/phenotypic variance and values are given in table 2.5.

Table 2.4 Summary of experiments with several generations of selection for increased weight (from McCarthy, 1982).

Weight at week	Realised heritability (%)*	Duration (generations)	Population size	Reference
3	17(W)	14	3 x 30	Frahm and Brown (1975)
5	39(W)	15	64	McCarthy and Doolittle (1977)
6	22(W)	11	32	Falconer (1953)
6	25(M)	7	2 x 26	Rutledge *et al* (1973)
6	40(W)	10	6 x 32	Falconer (1973)
6	13(M)	14	2 x 30	Cheung and Parker (1974)
6	55(M)	12	49	Eisen (1978)
6	42(M)	12	184	Nagai *et al* (1978)
8	28(M)	14	32	Bakker (1974)
10	32(W)	15	64	McCarthy and Doolittle (1977)

* Overall h^2 following mass (M) or within family (W) selection.

Table 2.5 Estimates of the heritability of body weight from random bred Q-strain mice (from Monteiro and Falconer, 1966).

Age	Heritability (%) Females	Males
0	0	0
1	33	28
2	6	0
3	18	2
4	10	0
5	15	4
6	34	22
7	42	32
8	52	34

The results of this study would suggest that it is useless to try and select for body weight in male mice at 2, 3, 4, or 5 weeks of age because the estimates of heritability at these ages are all very low or zero. However lines of mice have been successfully selected for body weight at these ages previously as noted in the reviews of Roberts (1965) and Eisen (1974), and accordingly the heritability estimates of Monteiro and Falconer (1966) were regarded with caution.

Studies on the genetic control of mouse testis weight and genetic relationships between body weight and testis weight are more difficult to come by. Islam, Hill and Land (1976) practised mass selection for high and low testis weight in the mouse and obtained a

realised heritability of 11 week testis weight of 0.52 ± 0.07. They give a figure of 0.20 for the genetic correlation between body weight and testis weight at 11 weeks. Eisen and Johnson (1981) selected mice for litter size and body weight and calculated the realised genetic correlation between body weight and testis weight at 6 weeks of age. This was 0.60 ± 0.03. Therefore it would appear that testis weight in the mouse is a heritable trait which is positively correlated genetically with body weight.

2.5 Conclusions.

- Body weight and testis weight both increase rapidly between 3 and 6 weeks of age.
- Variability of the two traits remains fairly constant with age.
- Estimates of the heritability of body weight lie between zero and 0.42 between 3 and 6 weeks of age.
- The genetic correlation between body weight and testis weight is positive and fairly high at 6 weeks of age and at 11 weeks.
- The phenotypic correlation between body weight and testis weight declines from 0.91 at 3 weeks to 0.50 by 5 weeks of age.
- The genetic correlation between testis weight and degree of maturity in body weight is unknown.
- The phenotypic correlation between right and left testes weights is over 0.97 from 3 weeks of age upwards and therefore high enough to use the weight of one testis as a reflection of total testis weight

Taking all these factors into consideration it was decided to select mice at 5 weeks of age when the phenotypic correlation

between body weight and testis weight is relatively low but the two traits are still immature.

III SELECTION PROGRAMME - MATERIALS AND METHODS

3.1 Experimental design.

Lines were selected for 6 generations for the following characteristics, selection being practised only on males at 5 weeks of age:

High body weight (HX)

Low body weight (LX)

High testis weight (XH)

Low testis weight (XL)

High body weight, high testis weight (HH)

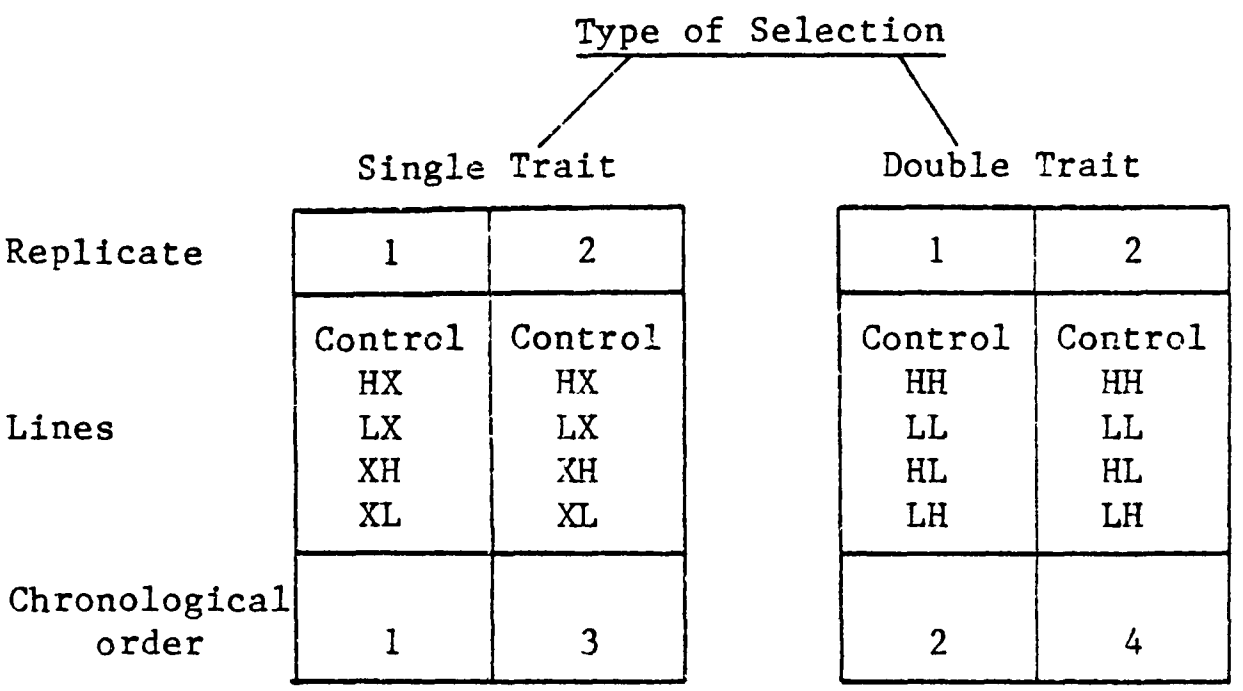
Low body weight, low testis weight (LL)

High body weight, low testis weight (HL)

Low body weight, high testis weight (LH)

There were two replicates of each line. The 16 lines were grouped into four groups of four selected lines with a time lag of three weeks between each group within each generation so that the technical work load could be spread out. Each group consisted of two pairs of divergent lines, and a control line was also maintained with each set. Selection was not practised in the control lines. The overall design of the experiment is illustrated in figure 3.1

Figure 3.1 Experimental design.



3.2 Breeding stock.

Mice to begin the lines were the progeny of crosses made between random-bred control lines of the G-strain, which itself originated from crosses between two inbred and one outbred strain of mice (Sharp, Hill and Robertson, in press). The G-strain was at the end of its third and beginning its fourth generation at this time.

The procedure to start the lines was the same for each of the four groups of five lines shown in figure 3.1 and was as follows: Two sets of twelve pair matings (24 matings in all) were made between mice from two of the G-strain control lines. Within each set of twelve pairs no more than one male and one female came from any one control line litter. Progeny of the matings formed the zero generation of this project. Each set of 12 litters contributed to the formation of a pair of divergent selected lines: the "highest"

male in each litter was selected to sire the first generation of a high line, and the "lowest" male in each litter picked to sire the first generation of the corresponding low line. The pairs of divergent lines were HX/LX, and XH/XL in groups 1 and 3, and HH/LL and HL/LH in groups 2 and 4. The females to be mated to these males were taken randomly, one from each litter for each of the two lines. The control line in a group was begun with 12 randomly selected males and 12 randomly selected females. Six of the males and 6 of the females were from 6 of the 12 litters used to supply one pair of divergent lines, and the other 6 of each sex came from 6 of the 12 litters used to supply the second pair of divergent lines. The control line mice were picked after the mice had been selected for the selected lines. This whole procedure was repeated four times with an interval of 3 weeks between each repeat, and beginning the four groups in figure 3.1 in the chronological order shown.

3.3 Selection.

Selection was within family, on males only and was carried out at 5 weeks of age. Within family selection was practised to minimise the effect of maternal environment on the progress of selection, and also to increase the effective population size since the choice of one male and one female from each family to be parents of the next generation makes the variance of family size zero and the effective number of individuals twice the actual number (Falconer, 1981). Selection for high and low body weight alone (HX and LX), and high and low testis weight alone (XH and XL) was based on the simple measurements of the relevant trait. In the double trait selection

lines (HH, LL, HL and LH) selection was based on an index in which body weight and testis weight were each weighted by the reciprocal of their within family phenotypic standard deviation:

$$I = W/\sigma_w \pm^{*} T/\sigma_t$$

where:

I = index value.

W = 5 week body weight (g).

T = 5 week testis weight (mg).

σ = within family phenotypic standard deviation.

* + for HH/LL lines, - for HL/LH lines.

σ_w and σ_t were estimated from measurements taken on all the male mice in generation zero: σ_w = 1.82 g, and σ_t = 8.9 mg. making the index: $I = 0.54W \pm 0.112T$, where W is measured in grammes and T in milligrammes. This same index was used throughout the 6 generations of selection.

3.4 Maintenance of the lines.

In each line 8 pair matings were arranged every generation, with an additional four "spare" matings in case any of the eight proved unsuccessful. The males for the matings were selected within families as outlined above and the females were picked randomly. The males to form the spare matings were the "second best" males from the appropriate litters. The mating system was the same as that used by Falconer (1973) and designed to minimise inbreeding. It is shown in figure 3.2.

Figure 3.2 Mating system used throughout the selection experiment.

	Family of origin			New mating number	
	Male	x	Female		
	1	x	2	1	
	3	x	4	2	
	5	x	6	3	
	7	x	8	4	
	2	x	1	5	
	4	x	3	6	
	6	x	5	7	
	8	x	7	8	
Second choice males	1 or 2	x	2 or 1	9	Four spare matings
	3 or 4	x	4 or 3	10	
	5 or 6	x	6 or 5	11	
	7 or 8	x	8 or 7	12	

Litters were numbered from 1 to 8. When the litter from a spare mating (numbered 9 to 12) was used to replace one of the 8 it was fitted into the mating scheme in place of the original.

The males remained with the females throughout pregnancy and until the litters were weaned. At birth litter size was adjusted to between 6 and 10 pups per litter by adding or removing pups. When pups were added to a litter they were identified by toe-clipping and discarded at weaning. The young mice were weaned at 3 weeks of age at which time the "spare" litters which were not needed were discarded (i.e. only 8 of the 12 litters were retained). At weaning a maximum of 6 male and 2 female progeny were kept per litter.The males and females were separated and they were raised in groups of up to 6 mice of the same sex per cage. Body weights of all the mice were recorded at 5 weeks of age, and all the males from the appropriate lines were hemicastrated and a single testis weight

recorded for each mouse. The parents of the subsequent generation were mated at approximately 9 weeks old, 12 weeks following the date on which their parents were mated.

The environmental conditions throughout the experiment were as follows:

Temperature: $70^{o} \pm 2^{o}F$.

Relative humidity: 30 - 40%

Feeding: B.P.'s Rat and Mouse No 1 Expanded Maintenance Diet ad libitum.

Tap water: ad libitum.

3.5 Data.

The following observations were made during the selection programme:

- Body weight at 5 weeks of all mice in every generation.
- Single testis weight at 5 weeks of males every generation in the lines selected on testis weight or on an index including testis weight.
- Testis weight at 5 weeks of all males in all other lines in generations 0, 3 and 6 only.
- Body weight at 10 weeks of age of all males (all of which were hemicastrated at 5 weeks) in generation 3.
- Body weight at 3, 5, 7 and 9 weeks of age of all males (hemicastrated at 5 weeks) and females in generation 6.
- Litter size at birth in all lines every generation.

3.6 Statistical analysis.

The main aim of analyses was to test the responses to selection. The design of the experiment as shown in figure 3.1 is basically two 2 x 5 cross-classified experiments (replicate x line) nested within a main effect, "type of selection", and data which were collected during the experiment were analysed according to this design.

Responses to selection in quantitative traits are subject to variability due to random genetic drift: the "response" seen in a selected line may be partly "real" in that a repetition of the same selection procedure would produce the same effect, and partly an expression of random drift or genetic sampling. Replication of selected lines provides the means of estimating the amount of random genetic drift (Hill, 1971) and so the proportion of an observed response which is "real" can also be estimated. The significance of the size of the "real" effects of selection can be calculated by testing the variability of responses amongst selected lines against the variance due to drift which is expressed between replicates of lines. In this experiment there were only two replicates of each line, but it was possible to estimate the error due to random drift with greater accuracy (with 8 degrees of freedom). This was done by making a combined estimate from the drift variances which were observed between the replicates of each of the 10 lines (counting control lines for the single trait selection separately from the controls for the double trait selection). The validity of such a combined estimate involved the assumption that the drift error was the same no matter what was the object of selection, i.e. the

variance between replicates of the same line in the response in any trait was homogeneous for all lines. From preliminary tests it would appear that this assumption was true, and so in all analyses the effects of selection were tested against a combined estimate of the error due to random drift which was expressed by the interaction between replicate and line in the analyses of variance described below.

Harvey's mixed model least-squares and maximum likelihood computer program (Harvey, 1977) was used to perform analyses of variance in which the following basic model was fitted to each set of observations:

Equation 3.1:

$$X_{ghijk} = M + T_g + R_{1h} + R_{2h} + L_{1i} + L_{2i} + (RL)_{g(h.i)} + F_{ghij} + e_{ghijk}$$

X_{ghijk} is an observation on the kth individual of the jth litter in the hth replicate of the ith line within the gth type of selection.

M is the overall mean

T_g is the effect of the gth type of selection (g = single trait, 1, or double trait, 2).

R_{1h} is the effect of the hth replicate nested within the 1st type of selection (single trait), h = 1 or 2.

R_{2h} is the effect of the hth replicate nested within the 2nd type of selection (double trait), h = 1 or 2.

L_{1i} is the effect of the ith line nested within the 1st type of selection, i = 1 to 5.

L_{2i} is the effect of the ith line nested within the 2nd type of selection, i = 1 to 5.

$(RL)_{g(h.i)}$ is the effect of the interaction of the hth replicate with the ith line within the gth type of selection.

F_{ghij} is the jth litter randomly nested within the hth replicate of the ith line of the gth type of selection. (Note: F effects were not fitted to observations of litter size.)

e_{ghijk} is the error.

The model was changed according to the data which were being analysed -

1) When observations were on mice from more than one generation (analyses of litter size, section 4.5) the effects of generation (G) and interactions with generation were included:

Equation 3.2:

$$X_{ghijkn} = \text{Equation 3.1} + G_n + (GR)_{1(h.n)} + (GR)_{2(h.n)} + (GL)_{1(i.n)} + (GL)_{2(i.n)} + (GRL)_{g(h.i.n)}$$

n = 4 to 6

2) When observations were on more than one sex (analyses of growth data, sections 4.6, 5.5.1 and 5.5.2), the effects of sex (S) and interactions with sex were included:

Equation 3.3:

$$X_{ghijkp} = \text{Equation 3.1} + S_p + (SR)_{1(h.p)} + (SR)_{2(h.p)} + (SL(_{1(i.p)} + (SL)_{2(i.p)} + (SRL)_{g(h.i.p)}$$

p = 1 or 2 in generation 6

p = 1 to 3 in generation 7

3) Litter size at birth (NO), and adjusted litter size between birth and weaning (NA), were accounted for where appropriate by fitting them as regressions: $b_{X.NO}$ and $b_{X.NA}$.

The degrees of freedom attributed to each effect were as in table 3.1. The replicate by line interaction nested within type of selection ($(RL)_{g(h.i)}$), assumed to be an expression of the variation caused by random drift (see above), was used as the error line for testing the effects of selection. Based on the same argument, the effects of sex on responses were observed by testing the sex by line interactions ($(SL)_{1(i.p)}$ and $(SL)_{2(i.p)}$) against the sex by replicate by line interaction within type ($(SRL)_{g(h.i.p)}$).

Table 3.1 Degrees of freedom attributed to each effect in the statistical models fitted to the experimental data.

Effect	Degrees of freedom	
	Generation 6	Generation 7
M	1	1
T_g	1	1
R_{1h}	1	1
R_{2h}	1	1
L_{1i}	4	4
L_{2i}	4	4
$(RL)_{g(h.i)}$	8	8
G_n		2 (data from
$(GR)_{1(h,n)}$		2 generations
$(GR)_{2(h.n)}$		2 4, 5 and 6)
$(GL)_{1(i.n)}$		8
$(GL)_{2(i.n)}$		8
$(GRL)_{g(h.i.n)}$		18
S_p	1	2
$(SR)_{1(h.p)}$	1	2
$(SR)_{2(h.p)}$	1	2
$(SL)_{1(i.p)}$	4	8
$(SL)_{2(i.p)}$	4	8
$(SRL)_{g(h.i.p)}$	9	18
NO	1	2
NA	1	1

IV RESULTS OF SELECTION

4.1 Selection differentials.

The selection differentials of 5 week body weight, testis weight and both indexes were calculated for all lines in each generation except for those lines in which testis weight was not measured every generation. The selection differential in a line in any generation was the mean deviation in the line between a selected male and the corresponding family (male) mean. Cumulated selection differentials for the six generations of selection are presented in table 4.1. Selection differentials for each generation separately are given in appendix 1.

The magnitude of the selection differential was of roughly the same order in both replicates of each line. It was also much the same but in opposite directions in divergent lines. Selection on the HH/LL index ($I = 0.54W + 0.112T$) achieved the desired degree and direction of selection pressure: the selection differential on body weight effected by selecting on the index was about the same as that which was achieved by selecting on body weight alone, and the pressure on testis weight was about the same as that in the lines selected only on testis weight. Selection on the HL/LH index ($I = 0.54W - 0.112T$) achieved the desired direction of pressure on the two traits but the selection differential for each was less than that in the single trait selection lines. This was expected since selection on this index is against the positive correlation between body weight and testis weight. The amount by which the

Table 4.1 Selection differentials cumulated over 6 generations.

Line	Replicate	Body weight (g)	Testis weight (mg) *	Index 1 *	Index 2 *
Control	1 (grp 1)	-0.9			
	2 (grp 3)	-0.7			
HX	1	11.5			
	2	8.0			
LX	1	-9.4			
	2	-11.6			
XH	1	6.7	62.7	9.4	-3.0
	2	5.4	46.3	7.4	-2.0
XL	1	-6.1	-59.0	-9.0	2.9
	2	-3.0	-33.1	-4.8	1.7
Control	1 (grp 2)	-1.8			
	2 (grp 4)	-0.7			
HH	1	9.4	59.1	10.6	-1.2
	2	11.7	51.8	11.2	0.8
LL	1	-8.3	-45.0	-8.6	0.4
	2	-10.0	-47.4	-9.7	-0.3
HL	1	6.3	-15.1	1.7	4.7
	2	4.3	-31.3	-0.9	5.2
LH	1	-7.5	20.4	-1.7	-5.9
	2	-7.3	22.7	-1.4	-6.0

* Testis weight was not measured in every line every generation, therefore cumulated selection differentials are not available for the lines not selected on testis weight.

selection pressure was reduced was less than a half for body weight and just over a half for testis weight, so an equal balance between the weighting placed on each trait was attained.

4.2 Responses at five weeks of age.

Line means of 5 week body weight, testis weight, and the indexes are given for each generation in tables in appendix 2. Graphs of these values against generation are shown in figures 4.1 to 4.9. Line means given are the averages of the litter means in a line because selection was within family, and so that both the responses and selection differentials are expressed in "within family" terms. Regression coefficients of responses in body weight and testis weight on generation were estimated (table 4.2). Responses were expressed as deviations between selected line means and control line means. In the HX and LX lines the regression of response in testis weight on generation was estimated from observations in generation 3 and 6 only. All other regressions included measurements taken in all 6 generations. The control lines did not always lie between the high and low lines throughout the 6 generations as can be seen in the graphs in figures 4.1 to 4.9. Hence, for example, the value of the regression of LX-control body weight divergence on generation was unexpectedly positive in the second replicate of the LX line. To give a better summary of responses to selection, regression coefficients of responses on generation of body weight, testis weight and the indexes were estimated with response expressed as the deviation between the means of divergent lines (table 4.3). These coefficients were converted to " within family phenotypic standard

FIGURE 4.1 RESPONSES IN BODY WEIGHT
IN THE HX AND LX LINES.

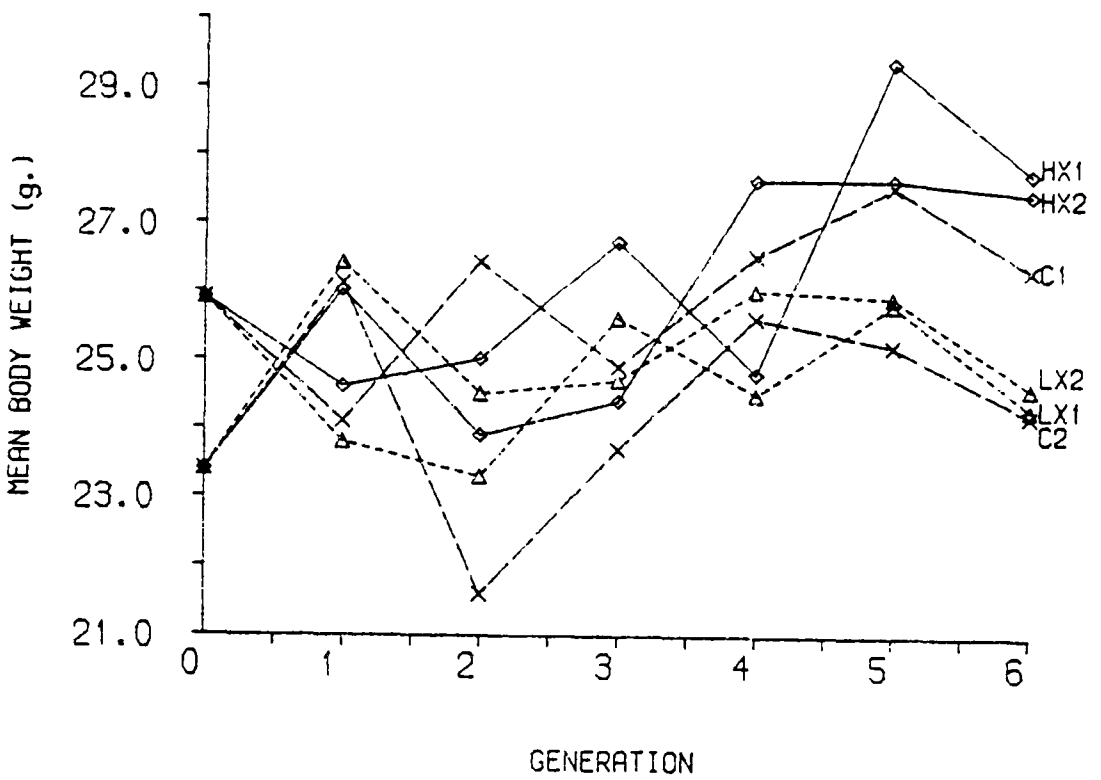


FIGURE 4.2 RESPONSES IN TESTIS WEIGHT
IN THE SINGLE TRAIT LINES.

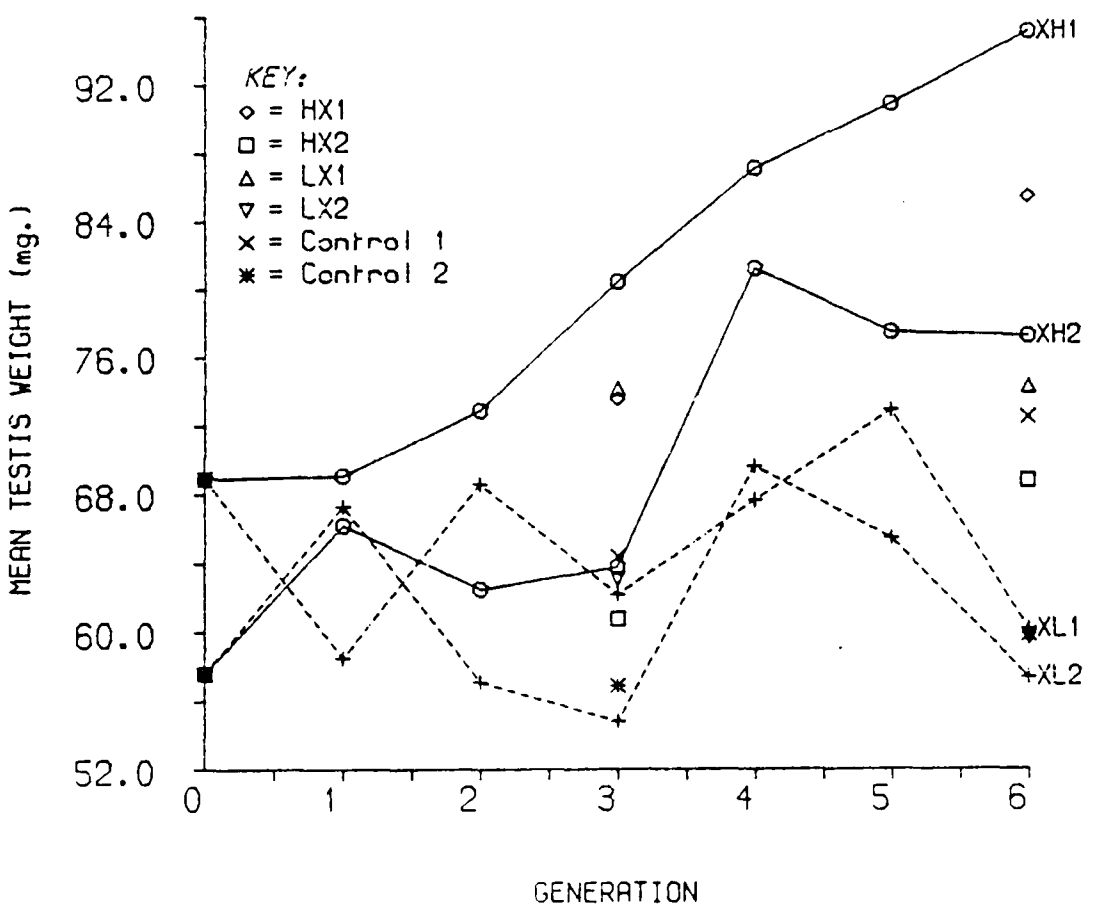


FIGURE 4.3 RESPONSES IN BODY WEIGHT IN THE XH AND XL LINES.

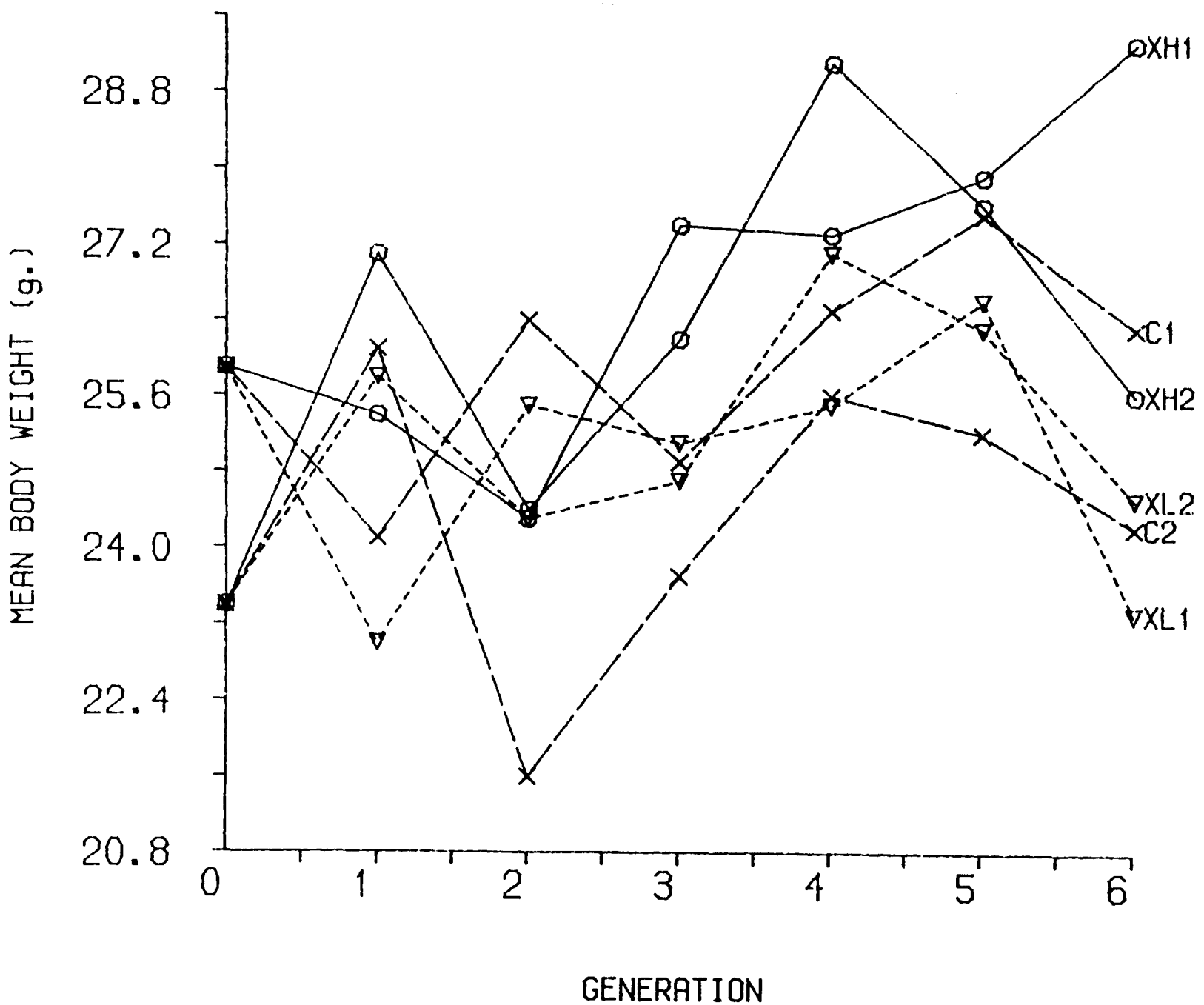


FIGURE 4.4 RESPONSES IN THE INDEX ($I = 0.54\hat{W} + 0.112T$) IN THE HH AND LL LINES.

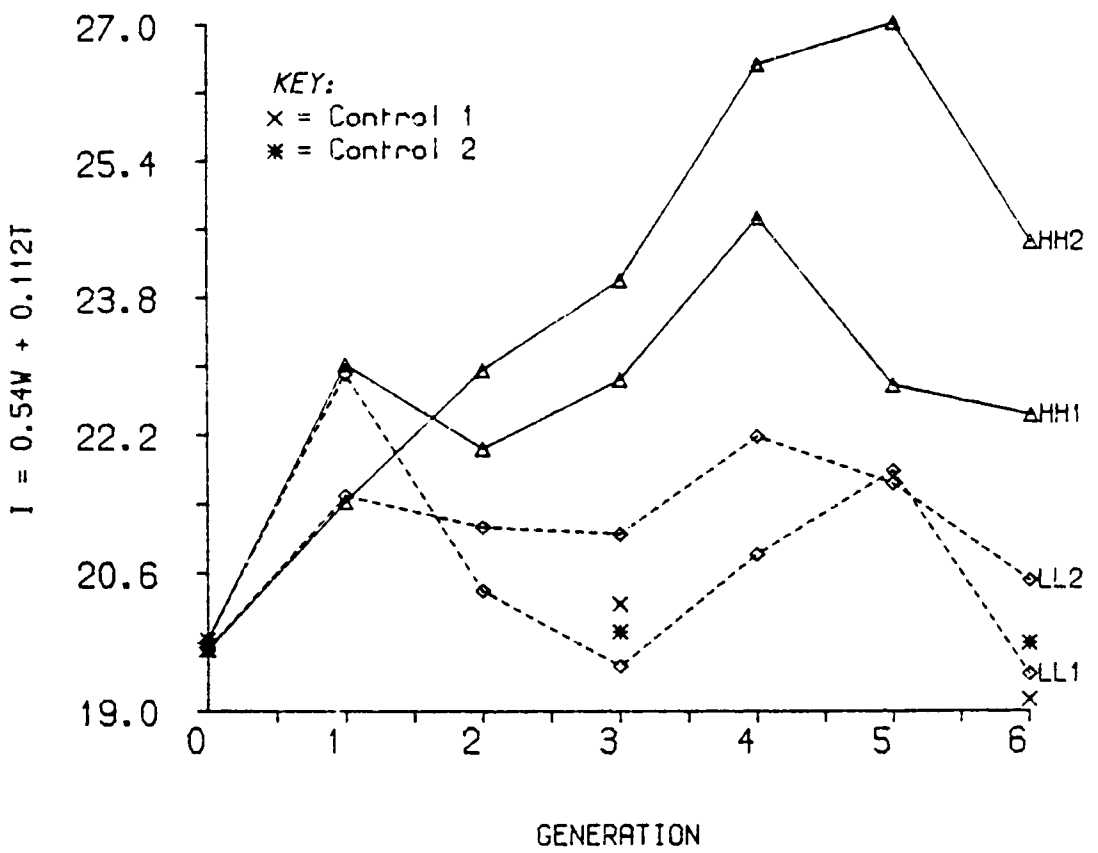


FIGURE 4.5 RESPONSES IN THE INDEX ($I = 0.54\hat{W} - 0.112T$) IN THE HL AND LH LINES.

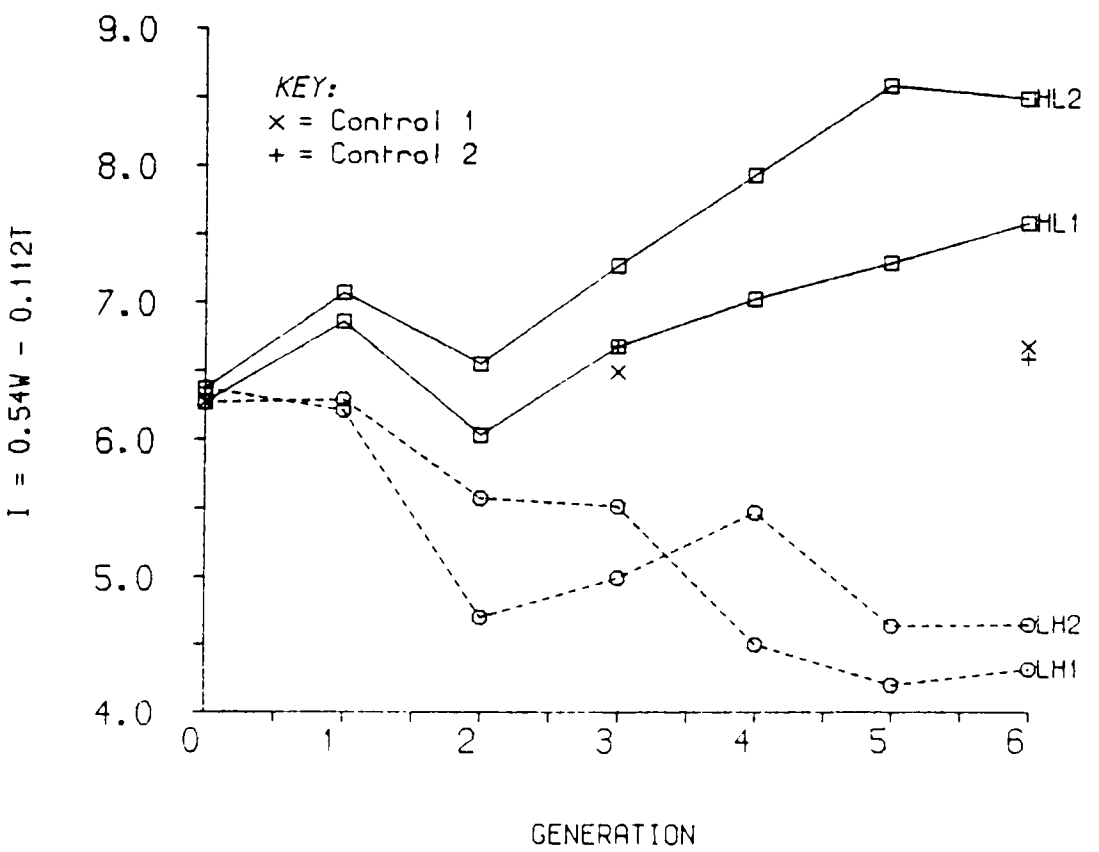


FIGURE 4.6 RESPONSES IN BODY WEIGHT IN THE HH AND LL LINES.

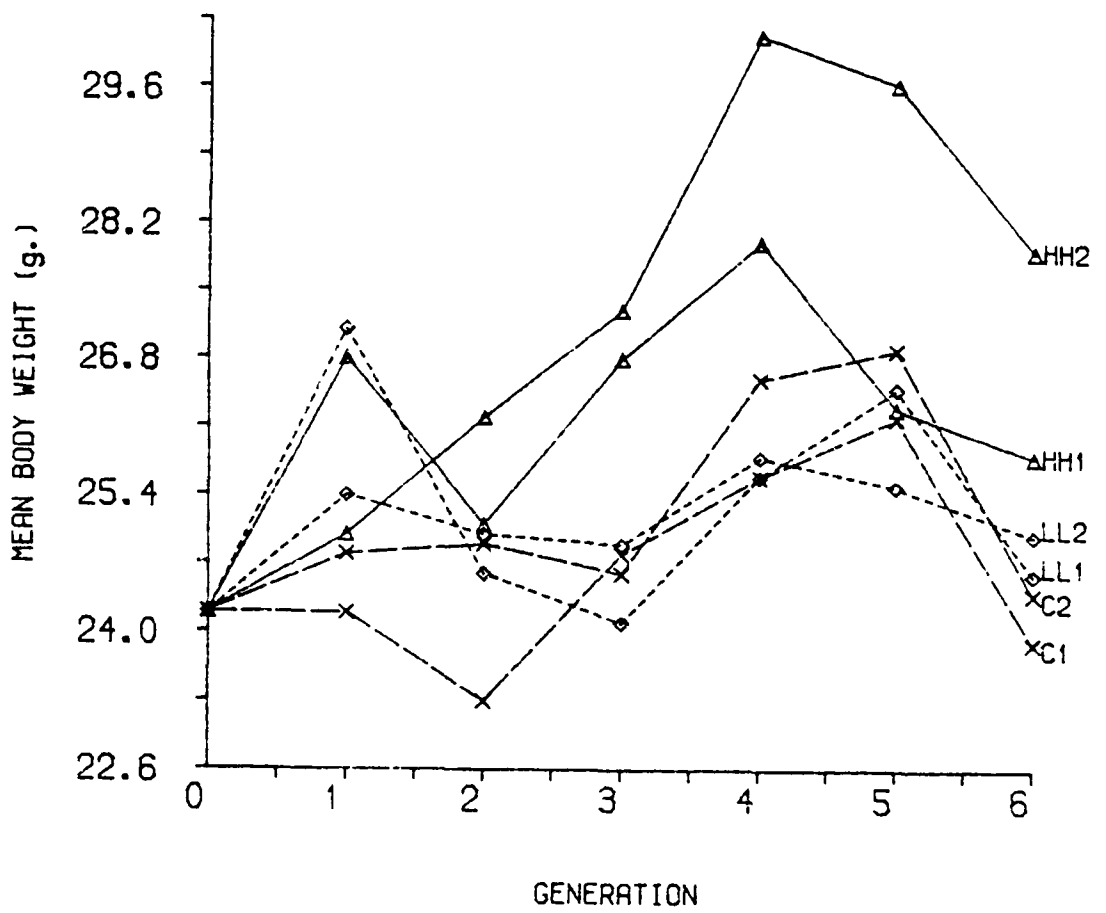


FIGURE 4.7 RESPONSES IN TESTIS WEIGHT IN THE HH AND LL LINES.

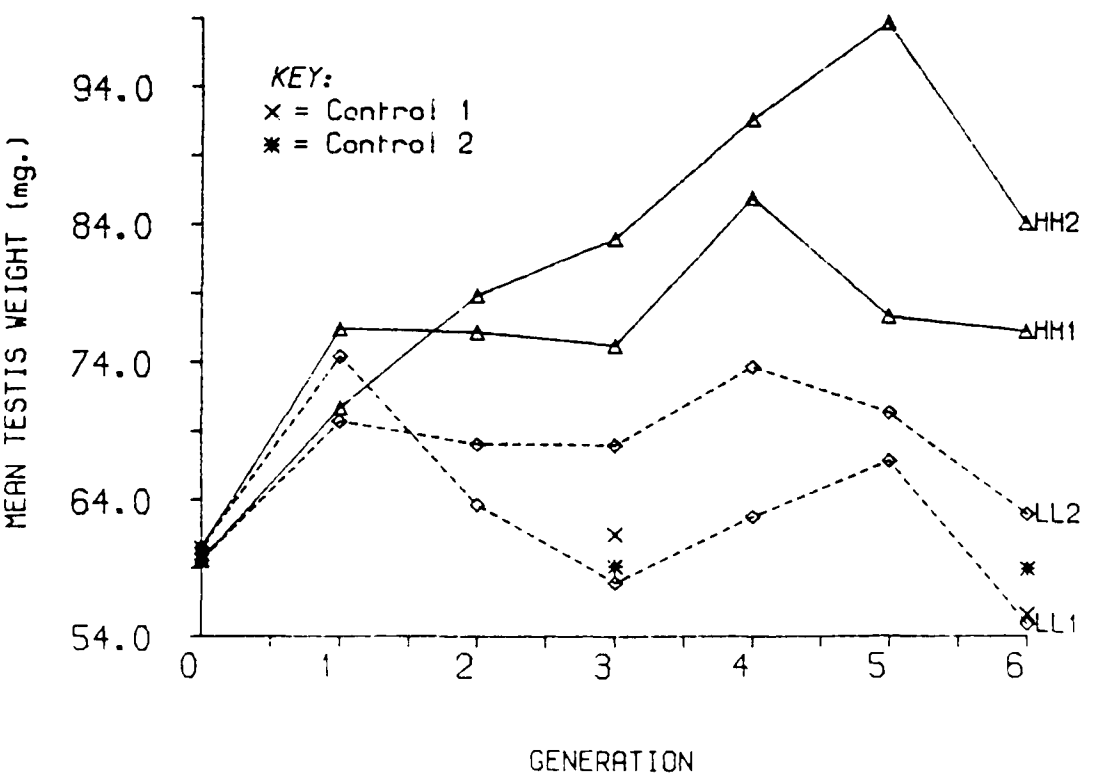


FIGURE 4.8 RESPONSES IN BODY WEIGHT IN THE HL AND LH LINES.

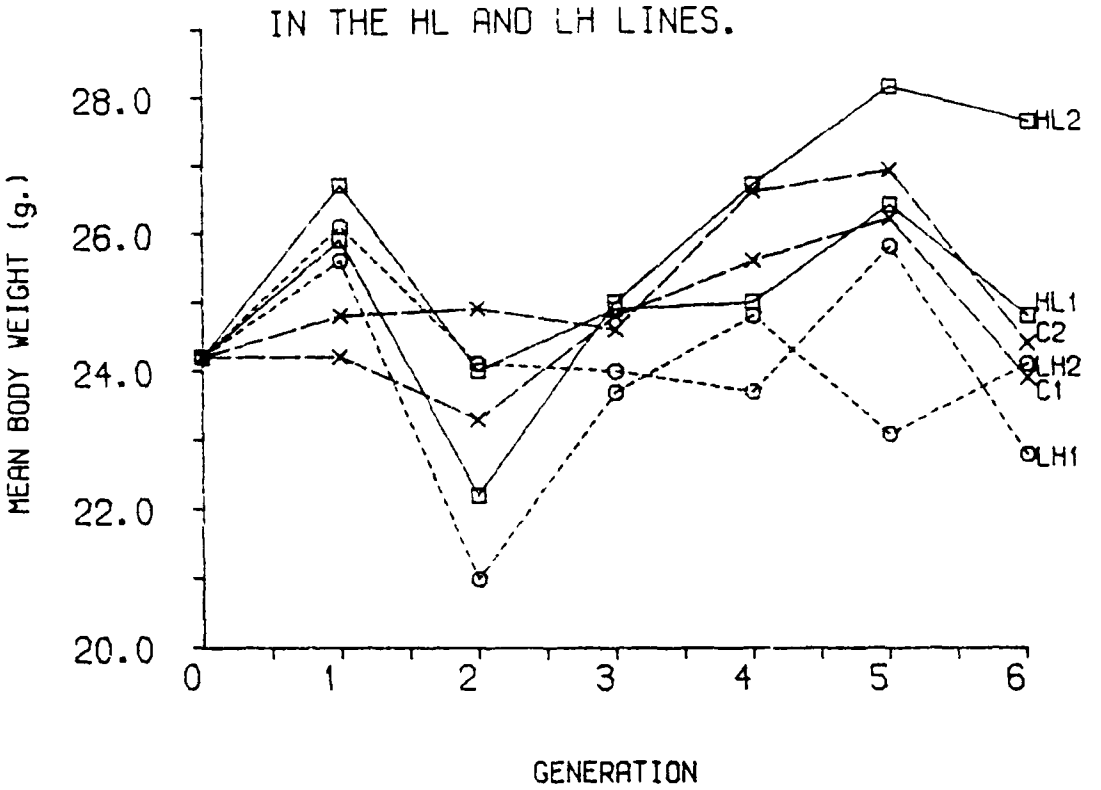


FIGURE 4.9 RESPONSES IN TESTIS WEIGHT IN THE HL AND LH LINES.

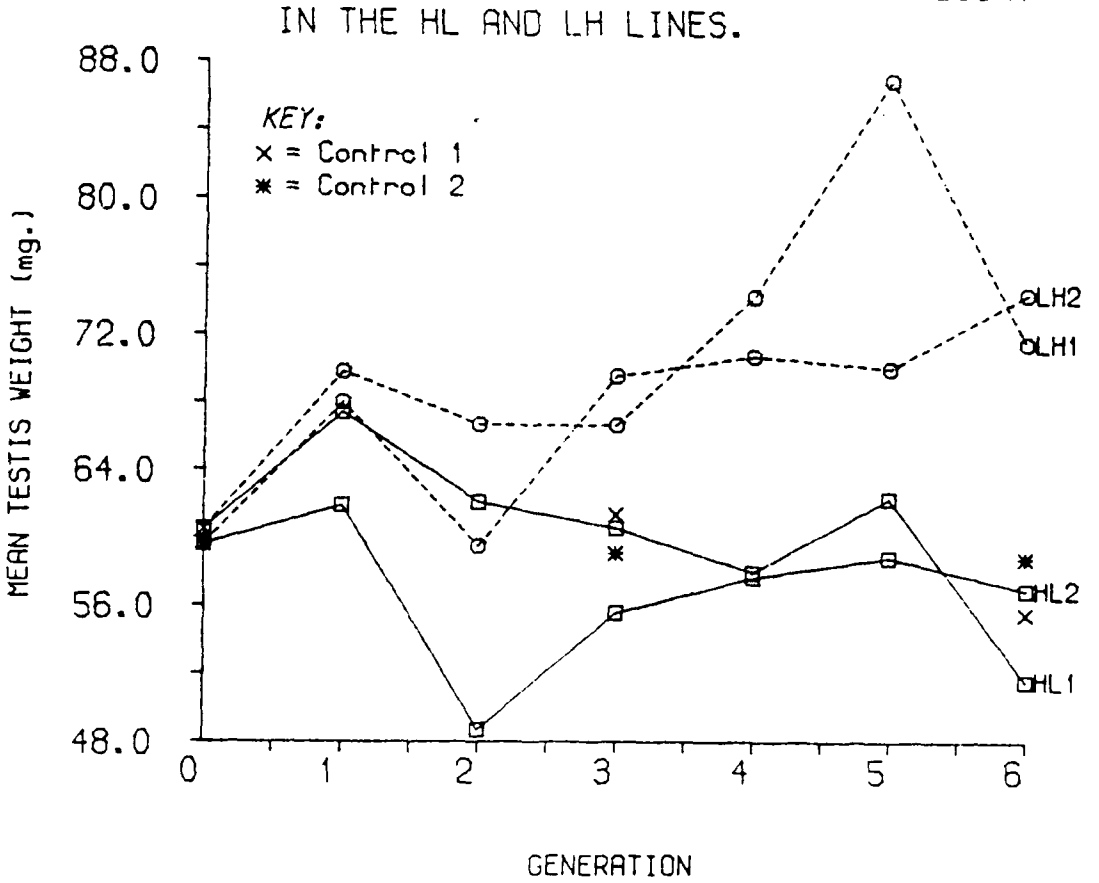


Table 4.2 Regression coefficients of response on generation - responses as deviations from control lines.

Lines	Replicate	Response in body weight g		Response in testis weight mg	
		High	Low	High	Low
HX/LX	1	0.09	-0.43	2.45	1.00
	2	0.48	0.22	1.44	0.26
XH/XL	1	0.27	-0.43	4.21	-1.59
	2	0.64	0.25	3.06	-0.24
HH/LL	1	0.35	0.13	3.81	-0.05
	2	0.75	-0.03	5.20	1.35
HL/LH	1	0.01	-0.14	2.70	-0.44
	2	0.24	-0.42	2.82	-0.35

Table 4.3 Regression coefficients of response on generation - responses as deviations between divergent lines.

Lines	Replicate	Response in body weight g	σ*	Response in testis weight mg	σ*	Response in index 1 units	σ*	Response in index 2 units	σ*
HX/LX	1	0.52	0.29	1.45	0.16	0.41	0.24	0.13	0.12
	2	0.27	0.15	1.18	0.13	0.22	0.13	-0.03	-0.03
XH/XL	1	0.64	0.35	4.87	0.55	0.78	0.46	-0.16	-0.15
	2	0.41	0.23	3.20	0.36	0.53	0.32	-0.13	-0.12
HH/LL	1	0.23	0.13	2.76	0.31	0.45	0.27	-0.23	-0.21
	2	0.66	0.36	4.31	0.48	0.77	0.46	-0.10	-0.09
HL/LH	1	0.19	0.10	-3.95	-0.44	-0.32	-0.19	0.48	0.45
	2	0.66	0.36	-2.93	-0.33	0.03	0.02	0.62	0.58

* Response in terms of within-family phenotypic standard deviation.

deviations per generation" in table 4.3 so that the rates of response in different traits could be compared.

By the sixth generation of selection all the lines had changed in the desired directions. The rate of response in body weight was fairly slow (mean divergence = 0.23 σ per generation). It took until generation 3 before any of the selected lines began to show any degree of divergence in 5 week weight. The rate of body weight response appeared especially slow when compared with the responses achieved in Falconer's (1973) lines which were the same size as the lines here and were also selected within family but on 6 week weight. However, Falconer selected on both sexes. The slow response observed here was probably due to the fact that selection was only on males and so the potential intensity of selection was halved. The lines changed more rapidly in testis weight: mean divergence between lines was 0.35 σ per generation; but there was a greater response upwards (mean high line - control divergence = 3.20 mg/generation) than downwards (mean low line - control divergence = -0.34 mg/generation).

The mean rate of divergence in the index, I = 0.54W + 0.112T, between HH and LL lines was 0.37 σ per generation.Responses in body weight and testis weight in these lines (0.25 σ /generation and 0.40 σ /generation respectively) were of the same order as those produced by direct selection on each trait alone (mean divergence in body weight between HX and LX = o.22 σ /generation, and mean divergence in testis weight between XH and XL =

0.46 σ /generation).The response in body weight in the single trait

testis weight lines (XH and XL) (mean divergence = 0·29 σ /generation) was also of the same order as that in the HX and LX lines so that the response in the HH/LL index in the lines selected on testis weight alone (0.39 σ /generation) was much the same as that produced by direct selection on this index.

The mean rate of divergence in the index, I = 0.54W - 0.112T, between HL and LH lines was 0.52 σ per generation and faster than the rate of the response in the other index in the HH/LL lines when selection was <u>with</u> the positive correlation between body weight and testis weight. The magnitudes of the responses in body weight and testis weight in the HL and LH lines were similar to those achieved by selecting on each trait separately, but the directions of responses were as directed by the index: the HL lines became heavier than the LH lines in body weight by an average of 0·23 σ /generation, and lighter in testis weight by an average of 0.40 σ/generation.

Comparisons amongst single and double trait lines when responses are expressed as deviations between divergent lines may be affected by the difference in timing of lines of the two types of selection. (see figure 3.1). For this reason it might be suggested that some of the comparisons made above are not reliable. However it is expected that any time effect on these comparisons would be small. Further, if responses are expressed as deviations from the corresponding control lines as in table 4.2, the time effect is removed and responses are directly comparable amongst all the lines. If the same comparisons as above are made using the rates of

response in table 4.2 and taking the slightly aberrant behaviour of the control lines into account, it is still possible to draw the same conclusions, namely:

1) Selection on I = 0.54W + 0.112T produced the same rates of response in 5 week body weight and testis weight as single trait selection for each trait respectively.
2) Selection on I = 0.54W - 0.112T produced the same rates of response as in (1) and in the desired direction, i.e. against the positive correlation between body weight and testis weight.
3) Selection on testis weight alone achieved the same responses in 5 week body weight and testis weight as selection on I = 0.54W + 0.112T.

4.3 Realised heritabilities.

Realised heritabilities were calculated from regressions of response on cumulative selection differential. The regressions were forced through the origin because the lines came from the same base population. The regression coefficients estimated half the heritability since selection was on only one sex. Response was taken as the difference in mean litter mean between two divergent lines selected for the trait in question. Cumulative selection differential was the mean deviation of a selected male from the family mean summed over six generations and over the two divergent lines. Since responses and selection differentials were expressed within family, the value given by twice the regression of response on cumulative selection differential was the realised within family heritability. Overall realised heritability was calculated using

the formula given by Falconer (1981):

$$h^2 = h^2_w(1 - t)/(1 - r)$$

where: h^2_w = within family heritability

t = intraclass correlation

r = 1/2 for full sib families

Intraclass correlations were calculated for body weight, testis weight and both indexes every generation (appendix III). There was some variation between lines and generations but generally the intraclass correlations remained at about the same level as those in the base population throughout selection. The values of the intraclass correlations in the base population are shown in table 4.4.

Table 4.4 Intraclass correlations in the base population - pooled over the four base population groups.

Trait	Intraclass correlation
5 week body weight	0.60
5 week testis weight	0.54
I = 0.54W + 0.112T	0.78
I = 0.54W - 0.112T	0.70

All the values are high: if a trait is not influenced by common environmental effects the intraclass correlation calculated from full sib families estimates half the heritability of the trait (Falconer, 1981) and, therefore, would be expected to be less

than 0.5. The fact that all the estimates of intraclass correlation obtained here are greater than 0.5 implies that body weight, testis weight and both the indexes were subject to non-additive or common environmental variation, namely maternal effects.

All estimates of realised heritability are given with their standard errors in table 4.5. Standard errors were calculated so as to include the error due to random drift. Based on the assumption that the drift error was the same under any type of selection (see section 3.6), the standard error of heritability was estimated as:

$$SE = ((V_{pool}(b_{R.g}))/S^2) \times 2(1 - t)/(1 - r)$$

where: V_{pool} = pooled variance between replicates of the same line.

$b_{R.g}$ = regression coefficient of response on generation.

S = mean selection differential per generation for the trait, in the lines from which the heritability is calculated.

Three estimates of each type of realised heritability are given in table 4.5 for each trait: one calculated from each replicate, and one from the two replicates pooled together. The last value was taken as the best estimate of realised heritability. This being so, it was concluded that the realised within family heritabilities of the traits were: 5 week body weight, 0.24 ± 0.10, 5 week testis weight, 0.48 ± 0.07, $I = 0.54W + 0.112T$, 0.36 ± 0.09, and $I = 0.54W - 0.112T$, 0.60 ± 0.07. The overall realised heritabilities were: body weight, 0.19 ± 0.08, testis weight, 0.44 ± 0.07, $I = 0.54W + 0.112T$, 0.16 ± 0.04, and $I = 0.54W - 0.112T$, 0.36 ± 0.04.

Table 4.5 Realised heritabilities.

Trait	Replicate	Within family heritability h^2	S.E.	Overall heritability h^2	S.E.
Body weight (HX/LX)	1	0.28	0.14	0.22	0.11
	2	0.16	0.15	0.13	0.12
	*Pooled	0.24	0.10	0.19	0.08
Testis weight (XH/XL)	1	0.46	0.09	0.42	0.08
	2	0.48	0.13	0.44	0.12
	*Pooled	0.48	0.07	0.44	0.07
I = 0.54W + 0.112T (HH/LL)	1	0.28	0.13	0.12	0.06
	2	0.40	0.11	0.18	0.05
	*Pooled	0.36	0.09	0.16	0.04
I = 0.54W - 0.112T (HL/LH)	1	0.54	0.11	0.32	0.07
	2	0.66	0.11	0.40	0.06
	*Pooled	0.60	0.07	0.36	0.04

* Pooled estimates calculated by regressing mean responses on mean selection differentials.

4.4 Realised genetic correlation.

The realised genetic correlation between 5 week body weight and 5 week testis weight was calculated from their direct and correlated responses in the single trait selection lines:

$$r_A^2 = CR_w.CR_t/R_w.R_t$$

where: r_A = realised genetic correlation.

CR_w = correlated response in body weight under selection on testis weight.

CR_t = correlated response in testis weight under selection on body weight.

R_w = direct response in body weight under selection on body weight.

R_t = direct response in testis weight under selection on testis weight.

To incorporate information from more than one generation the correlation was calculated with regression coefficients of responses on generation:

$$r_A^2 = b_{CRw.G}.b_{CRt.G}/b_{Rw.G}.b_{Rt.G}$$

where: $b_{CRw.G}$ = regression coefficient of correlated response in body weight on generation.

etc.

The correlated response in testis weight in the body weight selected lines was only measured in generations 3 and 6. Therefore $b_{CRt.G}$ was calculated from two measurements whereas the other regressions were calculated from six. Responses were expressed as deviations of line means (mean litter means) between divergent lines. The regressions were forced through the origin. The standard error of

the realised genetic correlation was calculated from the formula given by Hill (1971) which gives an approximation of the variance of r_A:

$$V(r_A) = ((1 - r_A^2)/(4.h_w^2.h_t^2)) \times (V(h_w^2 + V(h_t^2))$$

Within family estimates of heritability were used in the formula because the value of r_A was itself an estimate of the realised within family correlation.

The estimates of the realised within family genetic correlation between body weight and testis weight at five weeks obtained from the single trait selected lines are given in table 4.6.

Table 4.6 Realised genetic correlations.

Replicate	Genetic correlation	Standard error
1	0.60	0.28
2	0.70	0.25
Pooled*	0.70	0.25

* Pooled estimate calculated with regressions of mean responses on generation.

The estimates are high suggesting that testis weight and body weight are strongly correlated genetically in 5 week old mice.

4.5 Litter size and mating success.

A table of generation mean litter sizes is given in appendix IV. The values were averaged over replicates and plotted against generation in figures 4.10 and 4.11. From these graphs it can be seen that there were no large obvious responses in litter size. An analysis of variance was performed on the newborn litter sizes of generations 4, 5 and 6, fitting the model described by equation 3.2, section 3.6. Least squares estimates of litter size over these 3 generations and over both replicates are presented in table 4.7. The differences amongst lines were small and not significant. However, the general trends agreed with the responses to selection on body weight or testis weight obtained by some previous workers (see section 1.3). The mean litter size in the line selected for high testis weight (XH) was larger than that in the low testis weight line (XL) by an average of 0.6 pups, and the mean litter size in the high body weight line (HX) was larger by 0.8 pups than that in the low line (LX). Litter sizes in the HL and LH lines followed the direction of selection on testis weight rather than body weight: LH mean litter size was larger than that of the HL line by 0.5 pups. Litter sizes in the HH and LL lines were the same as in the control.

"Mating success" was observed by counting the number of matings which failed in each line every generation. The ratios of unsuccessful to total matings for the last three generations (4, 5 and 6) are presented in table 4.8. The numbers from both replicates of each line were combined. An "unsuccessful" mating was one in which both parents survived throughout the potential mating and

FIGURE 4.10 RESPONSES IN LITTER SIZE IN THE SINGLE TRAIT LINES (MEAN OF TWO REPLICATES).

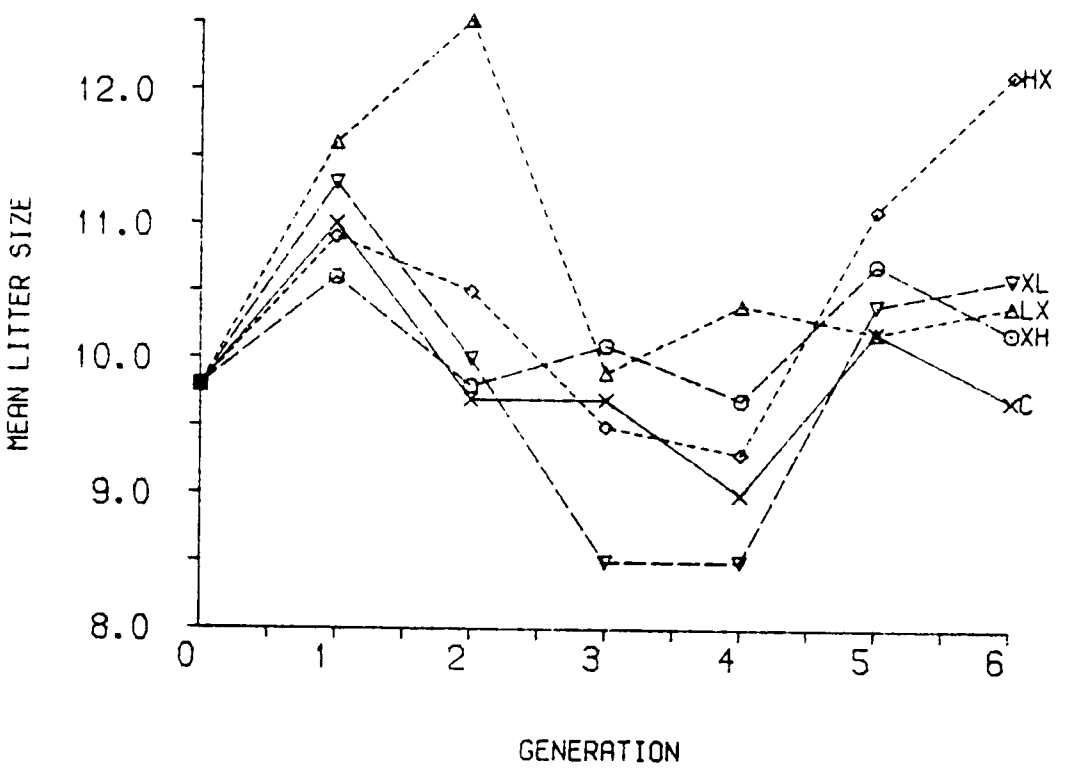


FIGURE 4.11 RESPONSES IN LITTER SIZE IN THE INDEX LINES (MEAN OF TWO REPLICATES).

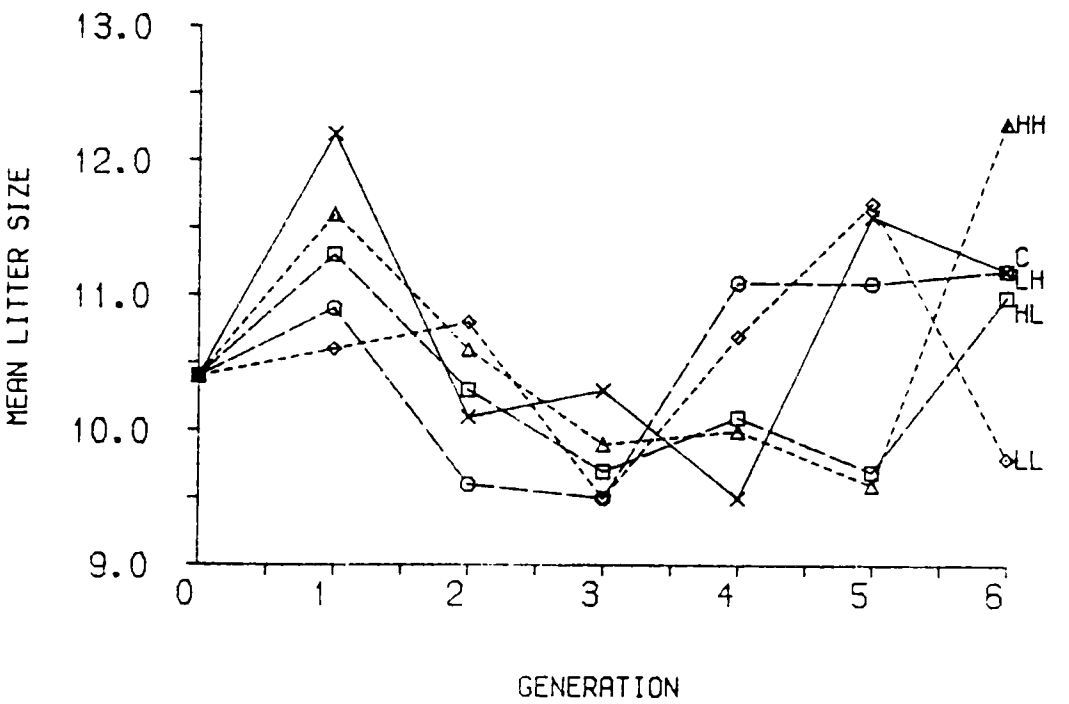


Table 4.7 Mean litter sizes for generations 4 to 6, averaged over two replicates.

Line	*Mean litter size in generations 4, 5 and 6
Control (groups 1 and 3)	9.7
HX	10.8
LX	10.0
XH	10.3
XL	9.7
Control (groups 2 and 4)	10.7
HH	10.6
LL	10.7
HL	10.5
LH	11.0
Standard error	0.3

* Least squares estimates from analysis of variance.

Table 4.8 Proportion of total matings which were unsuccessful in each line in generations 4, 5 and 6 - both replicates combined.

	Unsuccessful matings/total matings			
Line	Gen.4	Gen.5	Gen.6	Total over 3 gen's.
Control (groups 1 and 3)	0/24	1/23	2/22	3/69
HX	0/24	0/24	1/24	1/72
LX	0/24	1/24	0/22	1/70
XH	1/24	1/24	0/22	2/70
XL	3/23	1/22	2/24	6/69
Control (groups 2 and 4)	2/23	0/24	2/24	4/71
HH	1/24	2/24	2/23	5/71
LL	0/24	1/24	0/24	1/72
HL	2/24	1/24	2/23	5/71
LH	2/24	0/24	1/24	3/72

gestation period, but failed to produce a litter. A chi-squared test performed on the data for the 3 generations in table 4.8 was not significant, perhaps not surprisingly since the differences amongst lines were all small. It was concluded that if selection on body weight and/or testis weight did influence fertility, the effects in six generations of selection were small.)

4.6 Responses in the shape of the growth curve.

In generations 3 and 6 weights were taken at ages above 5 weeks so that the effects of selection on the pattern of growth could be monitored. Body weight at 5 weeks taken as a ratio of weight at age "5 + p" was called the "relative degree of maturity" in weight at 5 weeks of age. Age "5 + p" was equivalent to 10 weeks in generation 3 and 9 weeks in generation 6. The relative degree of maturity (RDM) of each 5 week old male mouse was calculated and an analysis of variance was performed on the values in each generation separately, fitting the model described by equation 3.1 and including the regression of RDM on NA. Least squares estimates produced by the analysis are given in table 4.9. The effects of selection were not significant, but in both generations 3 and 6 each of the XH and HH lines was more mature in weight at 5 weeks of age than its opposite line selected for low testis weight (XL and LL). There was hardly any difference between the HL and LH lines in relative maturity at 5 weeks. Although the selection had not produced significant changes in the relative degree of maturity by generation 6, differences which were present among lines were slightly more pronounced and they remained in the directions

Table 4.9 Relative maturity in body weight of hemicastrated mice at 5 weeks of age in generation 6.

Line	Relative degree of maturity in body weight (%)#	
	*Generation 3	$Generation 6
HH	75.9	76.5
LL	72.7	74.9
HL	71.7	76.6
LH	72.1	76.4
Control (groups 2 and 4)	73.8	74.9
HX	72.8	75.4
LX	73.4	77.6
XH	72.9	77.5
XL	71.9	74.2
Control (groups 1 and 3)	72.0	77.5
Standard error&	0.7	0.7

Least squares etimates from analysis of variance.
* 100 x 5 week weight/10 week weight.
$ 100 x 5 week weight/ 9 week weight.
& Within line error.

predicted at the beginning of the experiment. Comparisons between the high, high (HH) line and the high, low (HL) line, and between the low, low (LL) and low, high (LH) lines should reveal effects of selection on testis weight on degree of maturity in body weight. The ratio of 5 week weight to 9 week weight was the same in the former two lines, but in the latter comparison the lines selected for low body weight and high testis weight were more mature at 5 weeks than the ones selected for low body weight and low testis weight, which suggests that the inclusion of selection for high testis weight along with low body weight produced a somewhat earlier maturing strain of mice.

A second analysis of variance was performed on the log-transformed weights of hemicastrated males and females in generation 6 at 3, 5, 7 and 9 weeks of age. The model fitted to the data included the effect of sex: equation 3.3 + b^{*}_{NA}. The weights were log-transformed to reduce the heterogeneity of the variance of weight within sex, and so that differences between two lines at different ages were on the same scale. Least squares estimates from the analysis are presented in table 4.10. Line effects on body weight were significant ($p = 0.05$) at 7 and 9 weeks but not at the two younger ages. Contrasts between divergent lines are given in table 4.11. There seemed to be definite trends in the differences with age from the selection age of 5 weeks up to 9 weeks: the HX-LX and HL-LH divergences became larger with age, and the XH-XL and HH-LL divergences became smaller. Selection on W and T had apparently produced lines with differing patterns of growth which conformed to the predictions made at the beginning of the experiment

* Regression of trait on adjusted litter size between birth and weaning

in section 1.3: selection for high body weight produced faster growing mice than did selection for low body weight, but the inclusion of selection for high testis weight reduced later growth rate while selection for low testis weight increased it. Further investigations into the effects of selection on the growth patterns of the lines were made in a seventh generation (section V).

Table 4.10 Line mean body weights with age in generation 6 - both sexes (hemicastrated males and females).

Line	100 x Mean log body weight*			
	3 weeks	5 weeks	7 weeks	9 weeks
HH	106.42	139.39	146.31	150.05
LL	102.83	135.28	142.47	146.39
HL	102.33	137.81	144.40	148.83
LH	99.52	133.82	140.01	144.22
Control (groups 2 and 4)	99.95	134.49	141.64	145.83
HX	106.40	139.51	146.29	150.39
LX	103.18	134.73	141.12	145.02
XH	106.94	140.11	146.37	149.93
XL	100.98	133.99	141.52	145.71
Control (groups 1 and 3)	102.12	135.06	141.89	146.11
Standard error&	0.53	0.45	0.36	0.36

* Least squares estimates from analysis of variance.
& Within line error.

Table 4.11 Contrasts between the mean body weights of divergent lines - both sexes (hemicastrated males and females).

Contrast	100 x log body weight			
	3 weeks	5 weeks	7 weeks	9 weeks
HH - LL	3.59	4.11	3.84	3.66
HL - LH	2.81	3.99	4.39a	4.61a
HX - LX	3.22	4.78	5.17b	5.37b
XH - XL	5.96	6.12a	4.85a	4.22
Standard error&	2.62	2.30	1.85	1.81

& Error including random drift.
Significance levels: a: $p<0.050$, b: $p<0.025$

V MEASURING THE EFFECTS OF SELECTION ON THE PATTERN OF GROWTH

5.1 Introduction.

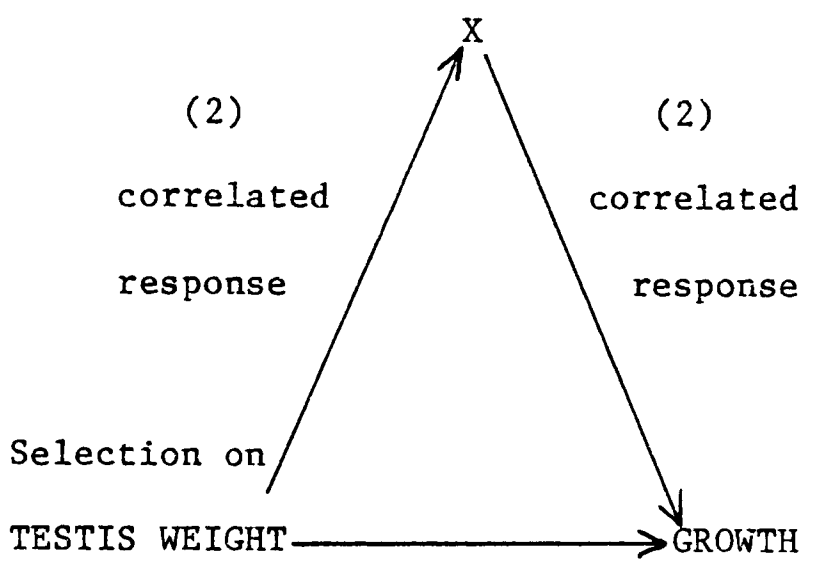
The growth of hemicastrated male and of female mice in generation 6 suggested that selection may have produced changes in the pattern of growth. Responses in the shape of the growth curve and the directions of any changes were investigated more thoroughly in generation 7 by measuring the growth of entire mice up to 15 weeks of age and looking for differences amongst lines in the pattern of growth.

Tail growth was also measured to try to determine if the selection altered the growth pattern of overall body size. Tail length is positively correlated to femur length ($r = 0.54$) and femur weight ($r = 0.40$) (Rutledge, Eisen and Legates, 1973) so it may be expected to give some indication of skeletal size. A response in weight not mirrored by a corresponding response in tail length could indicate that the weight change was due to an alteration in body composition rather than a change in overall size.However, it should be noted that tail length was probably only a rough indicator in this respect.

If the predictions set out in section 1.3 proved to be true and selection on combinations of testis weight and body weight did result in altered growth patterns, then it was also of interest to look at the mechanisms producing the responses. Figure 5.1 illustrates two ways in which selection on testis weight may

influence growth. Any responses in growth may be directly related to changes in testis weight (route 1), or they may be mediated by another factor(s), X, which is associated with both testis weight and growth (route 2).

Figure 5.1 Possible routes of response in growth resulting from selection on testis weight.



The growth of castrate males, and females was monitored to determine if it was necessary for the testes to be present for the expression of responses in growth. If not, then the possibility of the response being mediated via connection "1" in figure 5.1 could be ruled out. The growth of the females was an indirect response since selection was only on males and although the testes were absent from female mice, the female gonads, the ovaries, were still present and perhaps capable of fulfilling the same role as the testes in the control of growth. Growth of castrate males provided a more direct

test of the role of the testis in mediating responses in growth. The males were castrated at the earliest practicable date which was the weaning age of 3 weeks. Castration earlier than weaning would have involved the risk of differential maternal effects on castrated and non-castrated mice.

Since selection on combinations of body weight and testis weight was expected to alter the shape of the curve of growth in body weight, it may also be expected to affect the pattern of testicular growth. In generation 7 measurement of testis weight was possible at two ages: at 3 weeks when half of the males were castrated, and at 19 weeks when surplus entire males were killed. A measurement at the intermediate age of 5 weeks was also available from hemicastrated mice in generation 6. There was one generation of selection difference between mice of generation 6 and generation 7, and obviously, the testes measurements at 19 weeks in generation 7 were not from the same mice as those weighed at 3 weeks. Therefore the observations on testes weights gave a composite measurement of testis growth.

To analyse the tail and body weight growth data it was proposed to describe the growth of each mouse in the terms of a fitted function and to use the estimated parameters as metric traits in statistical analyses. The practical advantages in doing this are: 1) the data for each individual can be summarised in the form of a few parameters, and 2) if the model fitted to the data is based on observed growth phenomena, it can be used to extrapolate and interpolate from the data. Bakker (1974) reviewed the most common

types of mathematical functions fitted to growth curves. There are two types of function: theoretical and non-theoretical. Theoretical functions are based on fundamental postulates about the growth process, include parameters which have a clear biological interpretation, and can be used to interpolate and extrapolate from the observed data. Non-theoretical functions are often third or fourth degree polynomials, the parameters of which have no biological significance, are used to obtain the maximum fit, and can be used for interpolation but not for extrapolation. Non-theoretical functions were not considered here.

The theoretical function which best describes the growth curve is the four parameter Richards function fitted by means of an iterative procedure (Bakker and Koops, 1978). The Richards formulae are:

$$W^{(1-m)} = A^{(1-m)}(1 - be^{-kt}) \quad \text{for } m < 1$$

$$W^{(1-m)} = A^{(1-m)}(1 + be^{-kt}) \quad \text{for } m > 1$$

where: W = weight at age t

A = asymptotic weight (estimate of mature weight)

b = integration constant (estimates the starting position of the growth curve along the time axis)

k = rate constant (determines the spread of the curve along the time axis)

m = determines the position of the point of inflexion

By substituting different values for m it is possible to deduce the four best known theoretical functions:

m = 0 is the monomolecular function, $W_t = A(1 - be^{-kt})$.

m = 2/3 is the Bertalanffy function, $W_t = A(1 - be^{-kt})^3$.

m→1 is the Gompertz function (m = 1 gives no solution),

$$W_t = Ae^{-be^{-kt}}.$$

m = 2 is the logistic function, $W = A/(1 + be^{-kt})$.

In practice, fitting the Richards function is complicated by the number of parameters in the iteration, the fact that the parameter m cannot equal 1, and the occurrence of wrong estimates of m when local minima in the residual variance are met during the iteration (McCarthy and Bakker, 1979). An alternative method described by Bakker and Koops (1978), and used by McCarthy and Bakker (1979), is to fit the Richards function to each individual in a sample of the total data set using a number of alternative values of m. The best function to use on the whole data set can then be selected by picking the value of m giving the smallest residual variance. An attempt was made to fit the Richards function to the growth data measured in the seventh generation of this experiment by this method.

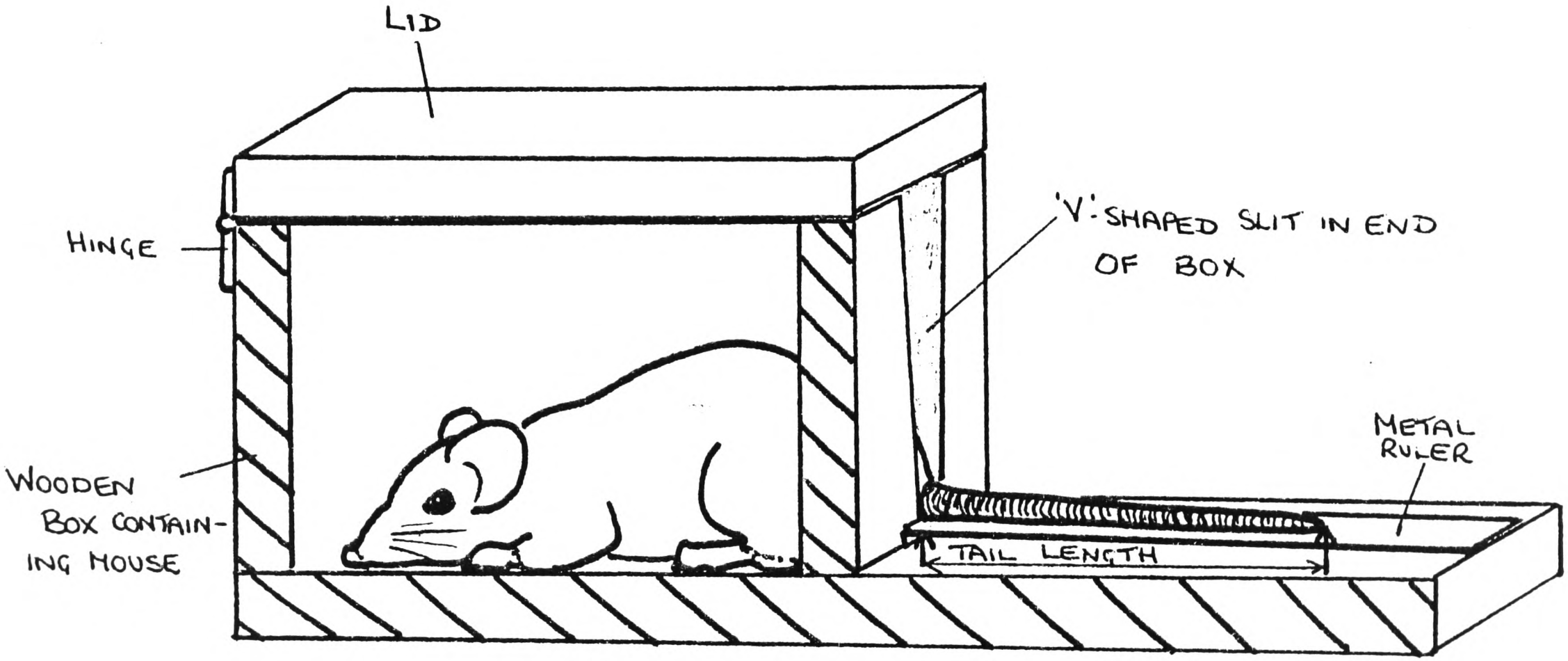
5.2 Materials and methods.

Male mice were selected in generation 6 as in the previous generations. Each male was mated to two females from the appropriate litter so that there were twice the usual number of mice born into the seventh generation. The males were removed from the breeding cages one week before the births were due, and the females were put into single cages. At birth the size of each litter was

restricted to 9 or 10 pups. The ideal was 6 male and 3 female pups born into a litter. Where pups were added to make up numbers, they were identified by toe-clipping and discarded at weaning as in previous generations. The litters were weaned at 3 weeks of age. If possible a maximum of 2 female and 4 male offspring per litter were kept at weaning and the remainder of the litter was discarded. All the mice of the same sex from one litter were put into one stock cage. On the day following weaning, on average half of the males from each litter were fully castrated and their testes weighed. The remaining males were "dummy castrated", i.e. a small incision was made in the scrotum under anaesthesia but the mice were kept entire.

Between 3 and 16 weeks of age the liveweight and tail length of every mouse were recorded at regular intervals. Tail length was measured using a device made to the same design as that used by Falconer (1953) and illustrated in figure 5.2. The mouse was placed in the box and its tail was drawn out along the graduated rule. As Falconer stated "with some practice it was possible to make the tension fairly constant and so to eliminate serious errors of measurement". However, although the majority of tail measurements were taken by one person, a second person took over during one period in the experiment and it was clear that there was an "operator difference". A small trial was carried out in which both operators measured the tails of the same mice. The differences between measurements taken by the two operators were nearly constant within ages.Therefore all measurements taken by the relief operator were corrected by the appropriate within age mean difference.

FIGURE 5·2 DEVICE TO MEASURE THE TAIL LENGTH OF A LIVE MOUSE.



Unselected pair matings were made between mice within lines at approximately 18 weeks of age to maintain the lines for further generations of selection. The unmated entire males were weighed and killed at 19 weeks of age, and their testes removed and weighed.

In generation 7 the following observations were made:

- Total litter weight and litter size at birth (the birth weight of each mouse was calculated as the mean individual weight in the litter into which it was born).
- Liveweights of 496 entire males, 460 castrated males, and 524 females, at 3, 6, 9, 12 and 15 weeks of age (the 3 week weights of castrated males were taken before castration).
- Tail lengths of the same mice at 4, 7, 10, 13 and 16 weeks of age.
- Total testes weights and body weights of 465 males at 3 weeks of age, and of 166 males at 19 weeks.

The single testis weights and body weights of 683 males measured at 5 weeks in generation 6 were also included in the analysis of testis growth.

Environmental conditions were the same as those maintained throughout selection as listed in section 3.4.

5.3 Fitting growth curves.

5.3.1 Method.

An attempt was made to fit the Richards function to a sample of the data using the method of Bakker and Koops (1978) outlined in section 5.1. A sample of 30 mice was selected from the whole data set. The sample included the body weights at 0, 3, 6, 9, 12 and 15 weeks of age of one mouse of each sex (male, castrate male, and female) from the first replicate of each line. The parameter m in the Richards function was fixed at 2.00, 1.33, 0.89, 0.75, 0.67, 0.50, 0.25, 0, and -0.25 and a Richards curve was fitted for each of the nine m values to the log transformed data of each mouse in the sample. To do this a computerised iterative "hill-climbing" routine was used. This minimised the sums of squared deviations between the logs of the fitted weights and the logged observed weights by altering the values of A, b and k in the function. The data were log transformed to take account of the fact that weights at younger ages were less variable than those at older ages. The residual variance remaining after fitting the function for each value of m was recorded for each mouse. The whole process was repeated with the tail lengths of a similar sample of mice at 0, 4, 7, 10, 13 and 16 weeks of age. Tail length was not measured at birth but the mean value of tail length at birth estimated in the preliminary experiment described in section II was taken as the measurement for every mouse at 0 weeks.

5.3.2 Results.

The results were similar for body weight and tail length. A plot of residual variance against m value had two minima for 50% of the mice in each sample. For the remaining 50%, the "best" value of m (i.e. the one which gave the least residual variance) varied between individuals. Therefore it was impossible to choose one value of m to use for fitting curves to the whole data set.

The fit of the curves to the data was fairly close. However, the direction of error between the observed and fitted values of measurements was consistently the same. For example, in general, the fitted body weights were too high at 3, 9 and 12 weeks of age, and too low at 6 and 15 weeks. It was suggested that the consistency of this error could cause a bias in conclusions drawn from an analysis using parameters of the fitted curves as metric traits.

5.3.3 Conclusion.

Bakker and Koops (1978) and McCarthy and Bakker (1979) successfully used this method of curve fitting for dairy cattle and mice respectively. However, their data included observations taken more frequently and over longer periods than those used here. Bakker and Koops (1978) had 27 weights for each cow from birth up to 100 days following her fourth calving, and McCarthy and Bakker (1979) used the data from mice which were individually weighed at weekly intervals from 3 to 11 weeks of age and at intervals of two

weeks from 11 to 21 weeks.

It was concluded that the observations taken in this study were too few per individual and/or that they were made over too short a time period for growth curves to be fitted to the data with the required efficiency. Analysis was therefore carried out directly on the observed data.

5.4 Analysis.

The aim of the analysis was to look for differences amongst the selected lines in the shapes of the growth curves of body weight and tail length. This was done in two ways which were similar to the methods used to analyse the growth data from generation 6 (section 4.6).

One method was to observe the difference between divergent selected lines in body weight or tail length over ages. A trend in the size of the difference with age was taken as evidence for a response in the shape of the corresponding growth curve. Before looking at age trends, the data were scaled by either log- (to the base 10) transformation or by expressing the average value of the mice in a line as a percentage of the appropriate control line mean. This made the line differences directly comparable across ages. Expressing the data as percentages of control lines also meant that it was possible to make direct comparisons between double trait and single trait selected lines and so avoid any effects of the difference in timing of these two types of lines. Line mean body weights and tail lengths were calculated across replicates for each

sex separately, expressed as percentages of the appropriate control line means, and plotted against age to obtain visual pictures of the growth curves. Statistical analysis of the tail and body weight data was carried out by fitting the model described by equation 3.3 in section 3.6 to:

1) log body weight at age p (p = 0, 3, 6, 9, 12, 15 weeks)

2) log tail length at age q (q = 4, 7, 10, 13, 16 weeks).

Litter size at birth (NO) and adjusted litter size between birth and weaning (NA) were also fitted in the model as linear regressions. As well as putting all the data on the same scale, the log transformation reduced the heterogeneity of the within-sex variation making it feasible to include the data from all three sexes in the one analysis. Contrasts were made over all sexes between the following lines for each trait:

- High body weight and low body weight (HX - LX)
- High testis weight and low testis weight (XH - XL)
- High body weight, high testis weight and low body weight, low testis weight (HH - LL)
- High body weight, low testis weight and low body weight, high testis weight (HL - LH)

and also between the divergence of the HH and LL lines and the divergence of the HL and LH lines ((HH - LL) - (HL - LH)).

The second method of checking the responses in growth patterns was to look for differences amongst lines in "relative degree of maturity". The relative degree of maturity in weight of each mouse at a particular age, "X", was defined as the body weight at age X expressed as a percentage of weight at 15 weeks. "Maturity curves"

were drawn by plotting line mean relative maturity in body weight against age for each sex separately. The maturity curves of the single trait lines and the double trait lines were plotted on separate graphs because of the difference in timing of the two types of line. The same statistical model as above was fitted to the relative maturity in weight at 6 weeks (6 week weight/15 week weight), and to the relative maturity in tail length at 7 weeks (7 week tail length/16 week tail length) of all the mice. Contrasts between divergent lines were also made as above.

To look for differences in the responses to selection shown by the three sexes, the growth curves and data were observed for each sex separately and compared. Contrasts between divergent lines in each of the traits analysed were made within each sex, and these divergences were contrasted between sexes. If the sizes of line divergences for males, females and castrates were similar at all ages it could be concluded that responses in growth were expressed equally in all three sexes. A trend in the sizes of differences in line divergences between sexes with age could indicate that there was a greater change in the pattern of growth of one sex compared to another.

An analysis of variance was performed on the measurements of testis weight taken in generations 6 and 7, fitting the model in equation 3.1 (section 3.6) plus NO and NA fitted as regressions to each of the following:

1) Testis weight (both testes) at 3 weeks of age in generation 7.

2) Testis weight (single testis) at 5 weeks of age in generation 6.

3) Testis weight (both testes) at 19 weeks of age in generation 7.

4) Testis weight (both testes) (mg)/body weight (g) at 3 weeks of age in generation 7.

5) Testis weight (single testis) (mg)/body weight (g) at 5 weeks of age in generation 6.

6) Testis weight (both testes) (mg)/body weight (g) at 19 weeks of age in generation 7.

The model was fitted to log- (to the base 10) transformed and untransformed data of the first 3 variables. The latter 3 were untransformed. Contrasts between divergent lines in log transformed testis weight and in testis weight/body weight ratio were made as for body weight and tail length (above).

5.5 Results.

5.5.1 Pattern of total growth.

Untransformed growth curves of mean line male body weight against age are shown in figures 5.3 and 5.4. These same curves with line means expressed as percentages of control lines are plotted in figure 5.5. The control lines lie at 100% at all ages on the graph. Therefore vertical fluctuation in one of the selected lines represents a change with age in the size of the mean difference in body weight between the line and the control. Least squares estimates produced from an analysis of variance on the log-transformed body weights of all three sexes are presented in table 5.1, and values and significance levels of the contrasts between the log weights of divergent lines are given in table 5.2.

FIGURE 5.3 MALE GROWTH CURVES IN THE SINGLE TRAIT LINES.

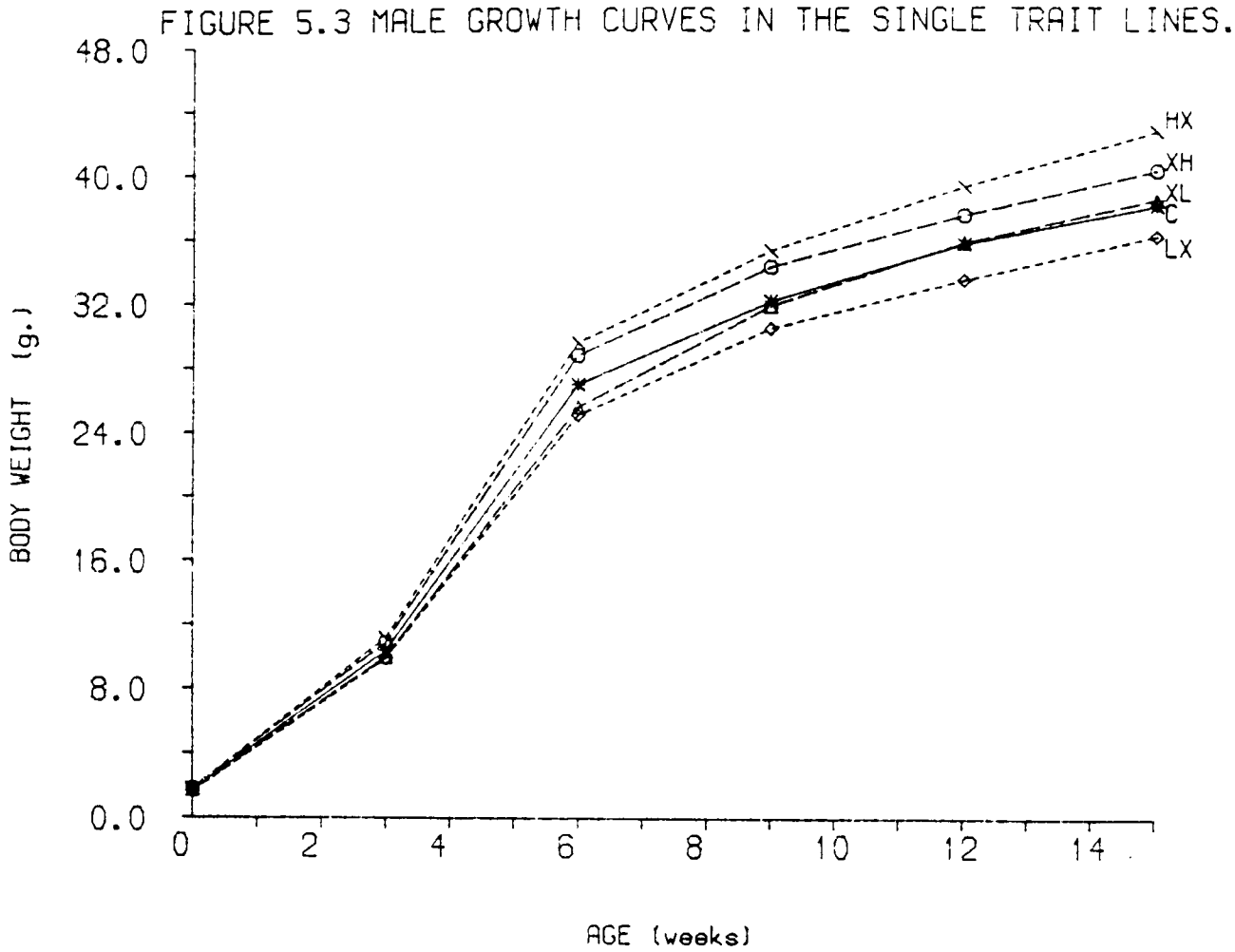


FIGURE 5.4 MALE GROWTH CURVES IN THE DOUBLE TRAIT LINES.

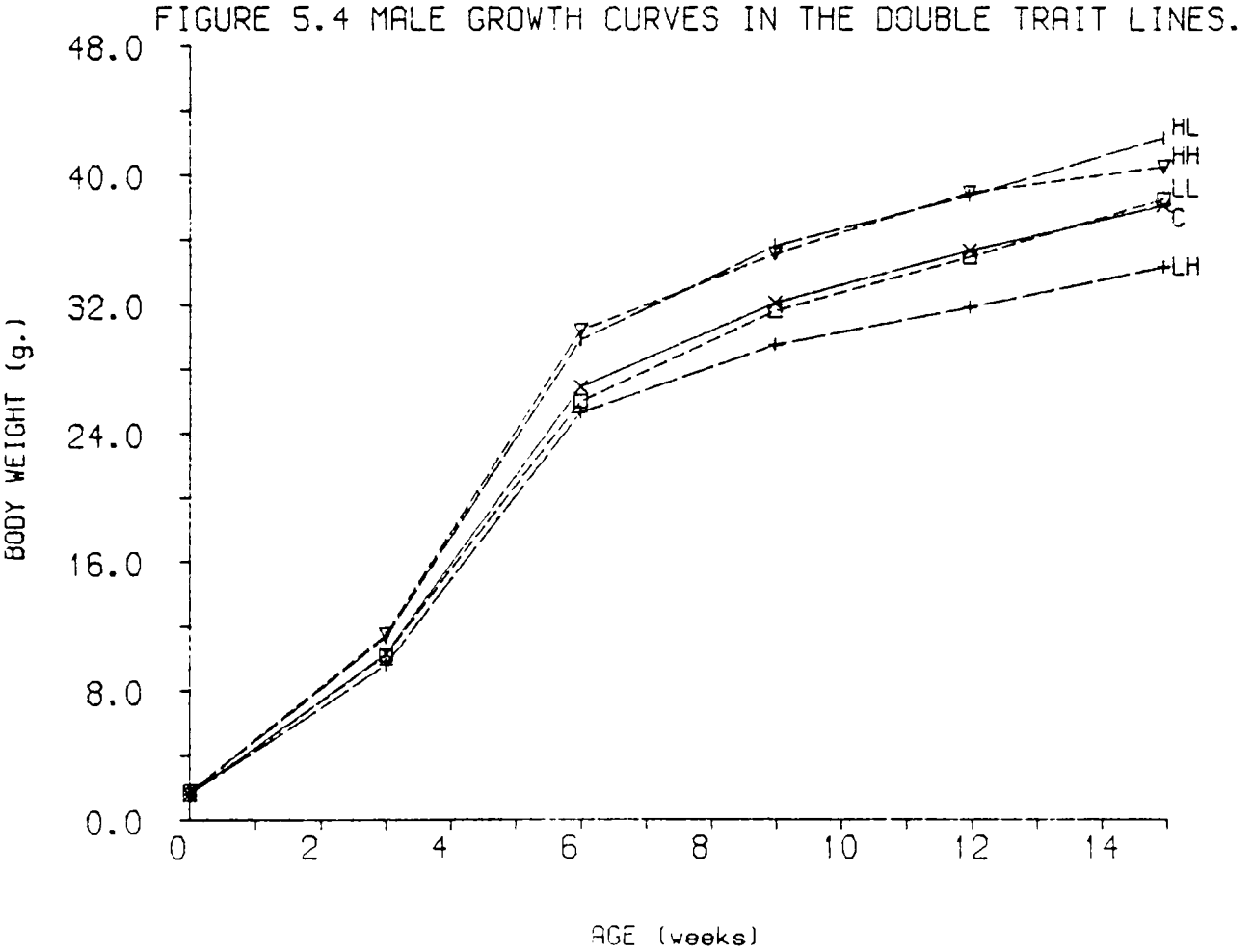
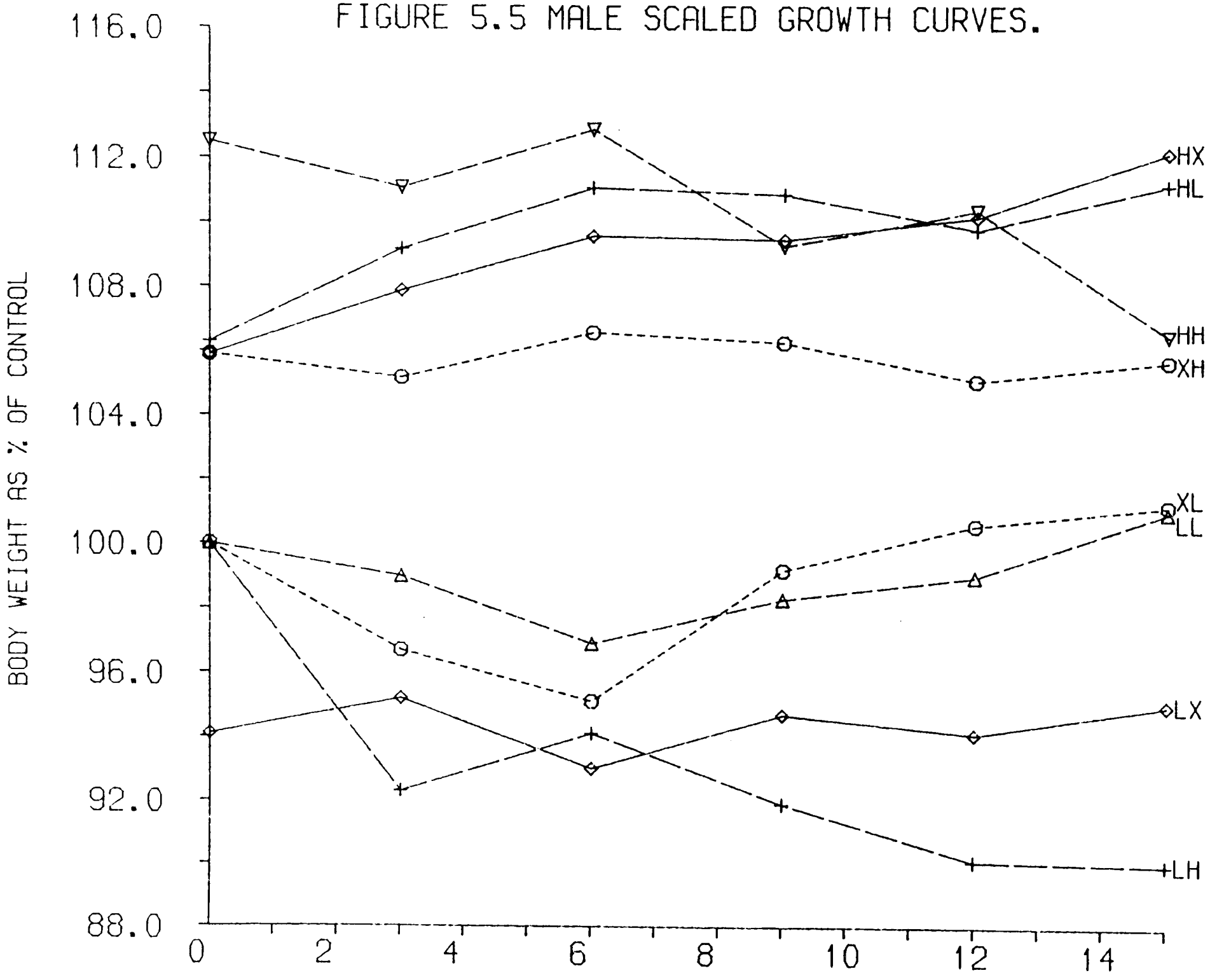


FIGURE 5.5 MALE* SCALED GROWTH CURVES.



* Bodyweight expressed as a percentage of appropriate control

Table 5.2 Contrasts in body weight between divergent lines - all sexes.

Contrast	100 x log body weight					
	0 weeks	3 weeks	6 weeks	9 weeks	12 weeks	15 weeks
HH - LL	5.84c	6.07c	6.91d	5.53c	5.21b	3.86
HL - LH	0.28	6.73d	5.97c	7.05d	8.01d	8.87e
HX - LX	2.91	3.95a	6.12c	5.71c	6.65d	7.38d
XH - XL	3.56	3.72	4.11a	2.64	1.61	1.90
Standard error	1.21	1.68	1.75	1.50	1.67	1.75
(HH - LL) - (HL - LH)	5.56	-0.66	0.94	-1.52	-2.80	-5.01
Standard error&	2.07	2.36	2.45	2.10	2.34	2.45

Significance levels: a: $p<0.050$, b: 0.025, c: 0.010, d: 0.005, e: 0.001
& Error including random drift.

Apart from those between the XH and XL lines, most of the contrasts were significant at least at the 5% probability level.

The numbers presented in tables 5.1 and 5.2 confirm the visual evidence of figure 5.5, that the pattern of responses in body weight growth were very much as predicted at the beginning of the experiment in section 1.3. In general, selection for high testis weight at 5 weeks of age restricted the rate of growth after selection age and selection for low testis weight enhanced it. In the lines selected on testis weight alone this effect was only seen in the low line (XL) which grew faster than both the control and high (XH) lines from 6 weeks onwards causing the mean body weights of the two selected lines to converge. The difference in weight between these lines was significant at 6 weeks of age ($p = 0.05$) but not at later ages. Selection on both body weight and testis weight at once produced lines which diverged in weight up to 6 weeks of age by roughly the same amount as lines selected on body weight alone (HX and LX). Subsequently the growth rate of the lines in which selection was for high testis weight fell relative to the other lines. Growth rate in the lines selected for low testis weight did not, so that after 6 weeks the body weights of the HH and LL lines began to converge, and the HL and LH lines continued to diverge.

Table 5.3 includes the differences between divergent lines in log body weight at 3, 6 and 9 weeks of age in both generations 6 and 7. Six week weight contrasts in generation 6 were obtained by weighting the contrasts at 5 and 7 weeks of age by their standard errors and taking averages. The growth patterns seen in

Table 5.3 Contrasts in body weight between divergent lines - generations 6 and 7 combined.

Contrast	100 x log body weight 3 weeks	6 weeks*	9 weeks
Generation 6$			
HH - LL	3.59	3.95	3.66
HL - LH	2.81	4.23a	4.61
HX - LX	3.22	5.01b	5.37
XH - XL	5.96	5.36a	4.22
Standard error&	2.62	2.08	1.81
Generation 7#			
HH - LL	6.07c	6.91d	5.53c
HL - LH	6.73d	5.97c	7.05d
HX - LX	3.95a	6.12c	5.71c
XH - XL	3.72	4.11a	2.64
Standard error&	1.68	1.75	1.50
Mean of generations 6 and 7@			
HH - LL	5.88c	5.67d	4.78d
HL - LH	6.15d	5.24c	6.07e
HX - LX	4.11a	5.65d	5.57d
XH - XL	4.81b	4.64c	3.27a
Standard error&	1.52	1.34	1.15

* Mean of contrasts at 5 and 7 weeks of age in generation 6 - weighted by the standard errors.
$ Female and hemicastrated male mice.
# Female, entire and castrated male mice.
@ Mean of contrasts in generations 6 and 7 - weighted by the standard errors.
& Error including random drift.
Significance levels: a: $p<0.050$, b: 0.025, c: 0.010, d: 0.005, e: 0.001.

generation 7 and described above were the same as those observed for females and hemicastrated males in the previous generation. Pooling the contrasts from the two generations as in table 5.3 emphasises these patterns of responses. The differences between divergent lines were rather larger in the seventh generation. The divergence between HL and LH lines did become increasingly greater than that between HH and LL lines with age but the difference between the two divergences was not great enough to be significant at any age even in generation 7.

Selection on 5 week body weight alone (HX and LX) produced correlated responses in body weight at all ages. The HX line was consistently heavier, and the LX line consistently lighter than the control in figure 5.5, and the size of the difference between the two lines remained about the same from 6 weeks of age upwards. Thus the responses in the growth patterns of mice in the HH, LL, HL and LH lines suggested by the data measured in generation 6 and also shown by data measured in generation 7 were obviously dependent on the inclusion of selection for testis weight along with selection on body weight.

Maturity curves of all the lines for males only are shown in figures 5.6 and 5.7. The graphs are not very clear because the differences amongst lines were small. However both graphs show that the lines selected for high testis weight were consistently more mature than lines selected for low testis weight at all ages. Least squares estimates of relative degree of maturity in body weight at 6 weeks of age, produced from an analysis of variance on the data of

FIGURE 5.6 MALE MATURITY CURVES
- SINGLE TRAIT SELECTION.

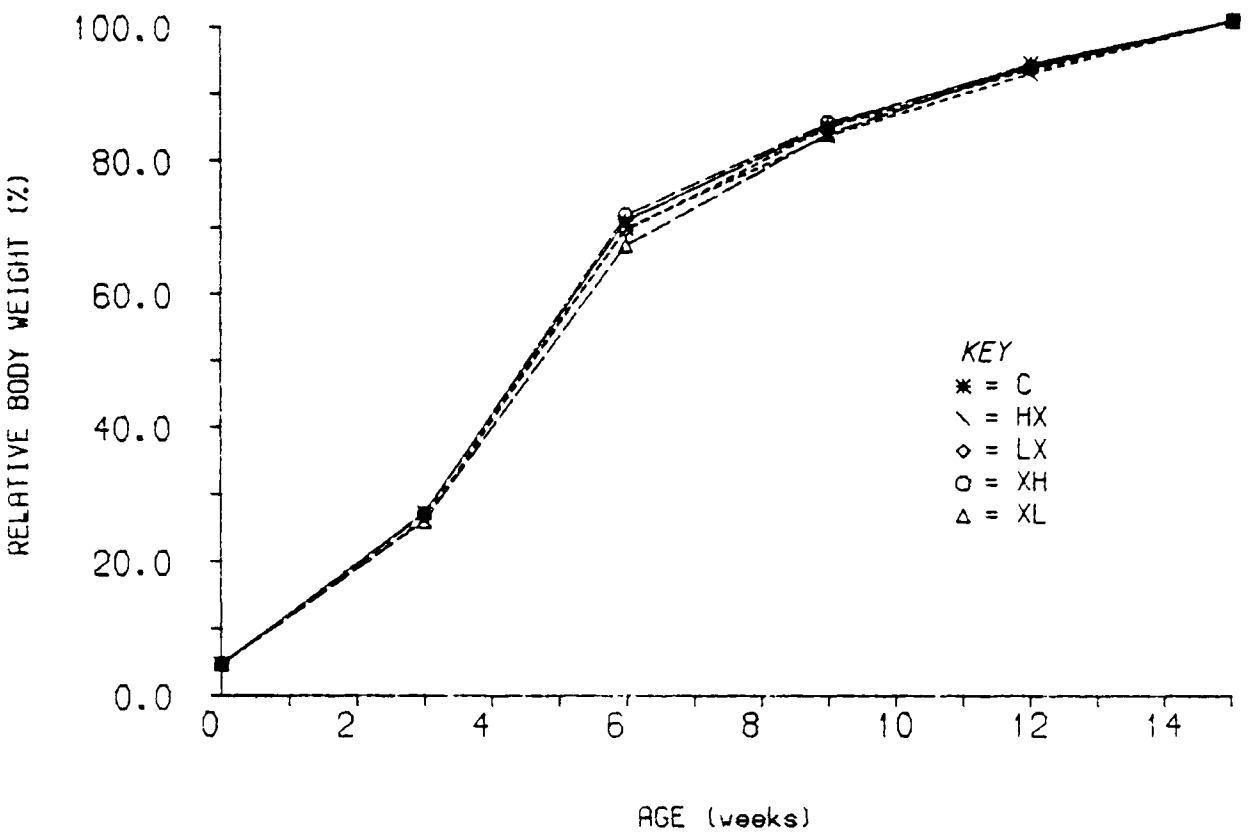
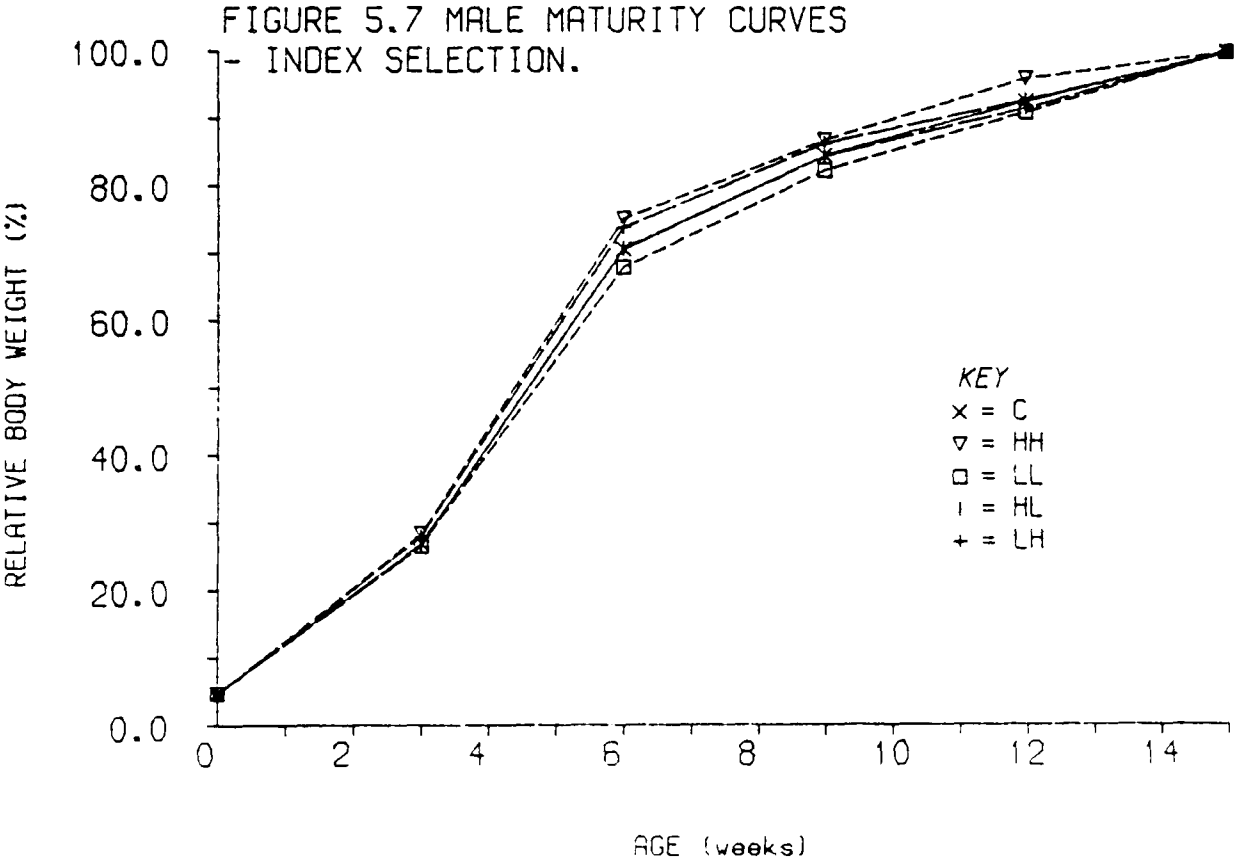


FIGURE 5.7 MALE MATURITY CURVES
- INDEX SELECTION.



all sexes, are given in table 5.4. Contrasts between lines are shown in table 5.5. These contrasts were larger than the corresponding differences between lines in generation 6 when relative degree of maturity was measured as the ratio of 5 week weight to 9 week weight, and the effects of selection on relative maturity were not significant. In the seventh generation the HH line was significantly ($p = 0.05$) more mature in body weight at 6 weeks of age than the LL line, and the LH line was significantly ($p = 0.05$) more mature than the HL line. The relative maturity of the high body weight line at 6 weeks was greater than that of the low line, and the high testis weight line was more mature than the low testis weight line, but these differences were not significant. The significant responses in relative maturity in the double trait lines provide further evidence to support the conclusion that selection on combinations of body weight and testis weight can alter the shape of the body weight growth curve.

To summarise the responses in the pattern of total growth:

- Including testis weight in selection on body weight modified the pattern of growth after selection age: in general selection for high testis weight restricted later growth and selection for low testis weight increased it.
- The result was that lines selected for high testis weight were relatively more mature in body weight at ages after selection age than lines selected for low testis weight.
- Selecting on 5 week body weight alone produced positive responses in weight up to that age and also at later ages.

Table 5.4 Body weight at 6 weeks of age as a percentage of 15 week weight (relative maturity) - all sexes.

Line	Relative maturity in body weight at 6 weeks (%)*
HH	73.04
LL	68.26
HL	67.32
LH	71.86
Control (groups 2 and 4)	68.17
HX	67.44
LX	69.48
XH	69.69
XL	66.25
Control (groups 1 and 3)	68.17
Standard error&	0.50

* Least squares estimate.
& Within line error.

Table 5.5 Contrasts of the relative degree of maturity in body weight at 6 weeks between divergent lines - all sexes.

Contrast	Relative maturity in body weight at 6 weeks (%)
HH - LL	4.78a
HL - LH	-4.54a
HX - LX	2.04
XH - XL	3.44
Standard error&	1.81

& Error due to random drift.
Significance level: a: $p < 0.05$

- These responses were observed in the data measured in generations 6 and 7.

5.5.2 Pattern of tail growth.

Graphs of line mean male tail length against age are shown in figures 5.8 and 5.9. The tail growth curves of males expressed as percentages of controls are shown in figure 5.10. Least squares estimates produced from an analysis of variance on the log transformed tail lengths of all sexes are presented in table 5.6. The contrasts between the mean values of divergent lines are given in table 5.7.

Generally the responses in tail length were small. The contrast between the single trait lines selected on body weight (HX and LX), was significant at 10 and 13 weeks of age ($p = 0.05$) but apart from this, none of the contrasts in tail length between divergent lines were significant. The sizes of differences in tail length between the single trait testis weight selected lines (XH and XL) were particularly small and the mean tail length in both lines was longer than the control. However, in general the mean tail lengths in each of the lines selected for high body weight were longer than those in the appropriate divergent lines at all ages, so that there was perhaps some small correlated response in tail length with selection on body weight. The changes in the sizes of divergences between lines with age were also very small suggesting that there had been little change in the pattern of tail growth.

FIGURE 5.8 MALE TAIL GROWTH CURVES
- SINGLE TRAIT SELECTION.

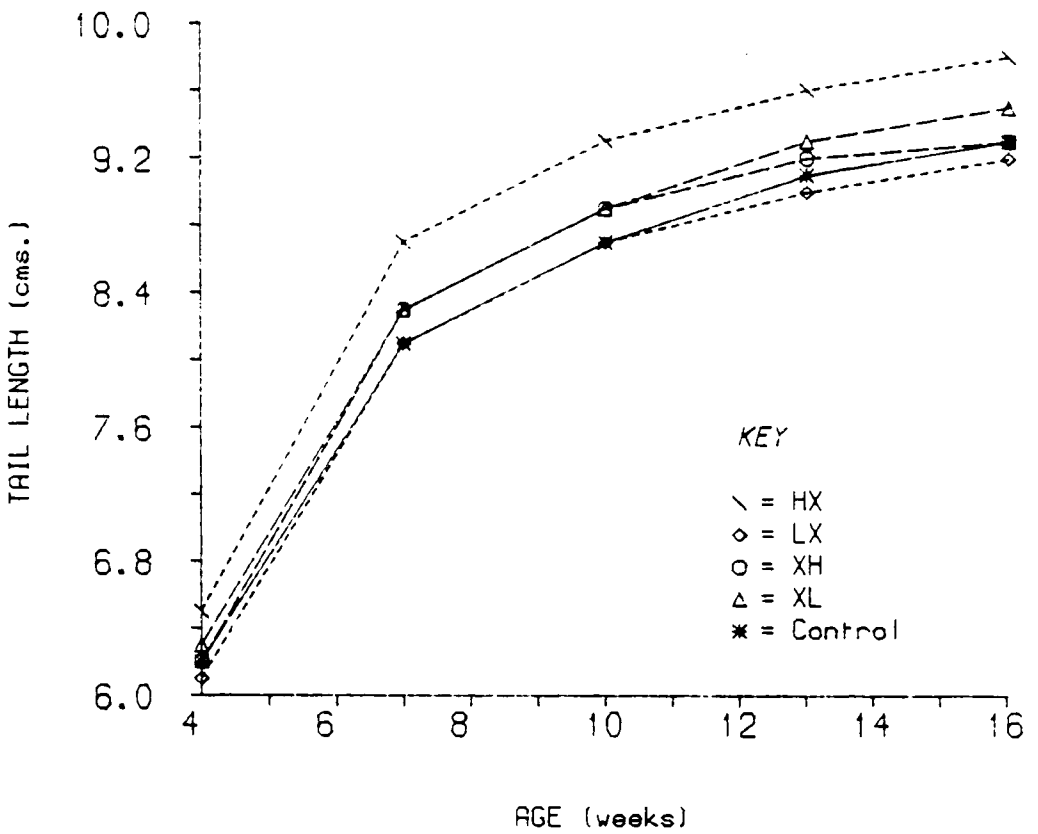


FIGURE 5.9 MALE TAIL GROWTH CURVES
- INDEX SELECTION.

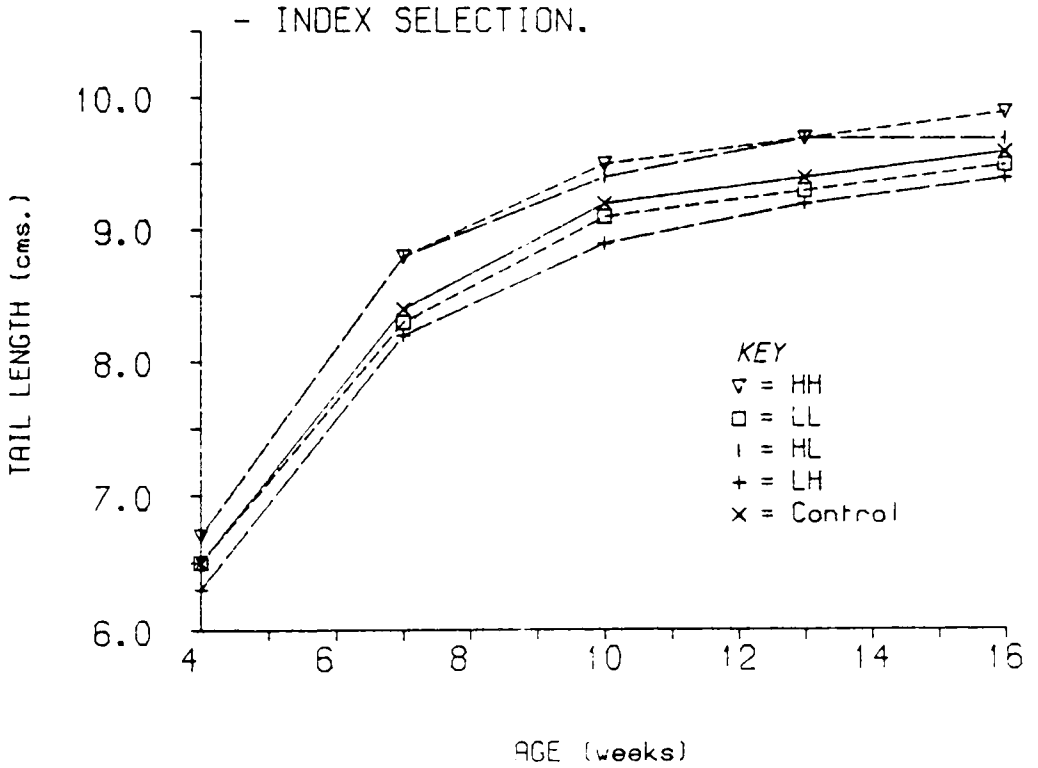
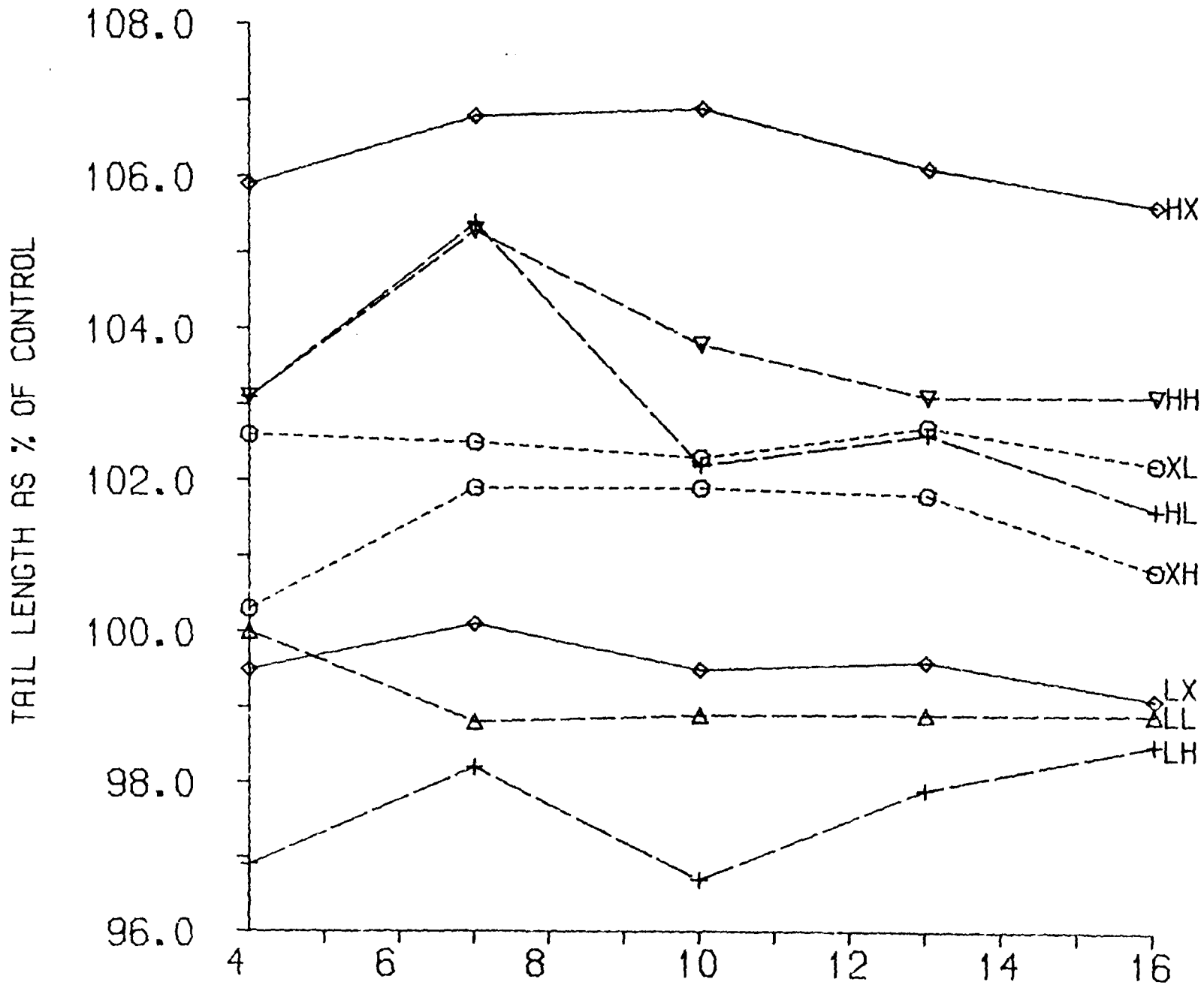


FIGURE 5.10 MALE SCALED* TAIL GROWTH CURVES.



* Tail length as a percentage of the appropriate control line

Table 5.6 Line mean tail lengths - all sexes.

Line	100 x Mean log tail length*				
	4 weeks	7 weeks	10 weeks	13 weeks	16 weeks
HH	82.93	94.32	97.69	99.00	99.69
LL	81.15	91.72	95.60	96.87	97.73
HL	82.38	93.51	96.47	97.90	98.50
LH	79.72	91.56	94.92	96.68	97.58
Control (groups 2 and 4)	81.40	92.35	96.15	97.41	98.18
HX	81.52	93.82	96.92	98.50	99.22
LX	78.88	90.65	93.78	95.55	96.51
XH	79.40	92.11	95.20	96.94	97.81
XL	79.98	92.22	95.49	97.33	98.22
Control (groups 1 and 3)	78.68	90.50	93.75	95.41	96.45
Standard error&	0.32	0.22	0.18	0.16	0.17

* Least squares estimate from analysis of variance.
& Within line error.

Table 5.7 Contrasts in tail length between divergent lines - all sexes.

Contrast	100 x log tail length				
	4 weeks	7 weeks	10 weeks	13 weeks	16 weeks
HH - LL	1.78	2.59	2.10	2.12	1.95
HL - LH	2.67	1.95	1.55	1.22	0.92
HX - LX	2.64	3.17	3.13a	2.95a	2.71
XH - XL	-0.58	-0.10	-0.29	-0.38	-0.40
Standard error&	1.55	1.17	1.16	1.19	1.22
(HH - LL) - (HL - LH)	-0.89	0.65	0.54	0.90	1.03
Standard error&	2.19	1.66	1.64	1.68	1.73

& Error including random drift.
Significance level: a: $p < 0.05$

The least squares estimates of relative degree of maturity in tail length at 7 weeks of age are given in table 5.8. Contrasts between the relative maturity of tail length of divergent lines are shown in table 5.9. None of these contrasts were significant. The differences between the HX and LX lines, and between the XH and XL lines were very small suggesting that the growth curves of tail length were nearly parallel in the divergent lines and from figure 5.4 it can be seen that they were parallel to the control. The tail length at 7 weeks of age in the HH line was slightly more mature than that in the LL line, and the relative maturity of 7 week tail length in the HL line was greater than that in the LH line. But since these differences were not significant, there was no strong evidence for any response in the shape of the tail growth curve.

To summarise:

- Responses in tail length were very small and nearly all non-significant.
- Selection on body weight may have produced positive correlated responses in tail length, but only the responses in the lines selected directly on body weight were of any magnitude.
- It was concluded that selection on body weight and/or testis weight had not produced any substantial responses in the shape of the tail growth curve.

Table 5.8 Tail length at 7 weeks as a percentage of 16 week tail length (relative maturity) - all sexes.

Line	Relative maturity in tail length at 7 weeks (%)*
HH	88.45
LL	87.14
HL	89.20
LH	87.16
Control (groups 2 and 4)	87.52
HX	88.37
LX	87.48
XH	87.82
XL	87.18
Control (groups 1 and 3)	87.25
Standard error&	0.27

* Least squares estimate.
& Within line error.

Table 5.9 Contrasts of the relative degree of maturity in tail length at 7 weeks of age between divergent lines - all sexes.

Contrast	Relative maturity in tail length at 7 weeks (%)
HH - LL	1.31
HL - LH	2.04
HX - LX	0.90
XH - XL	0.64
Standard error&	0.97

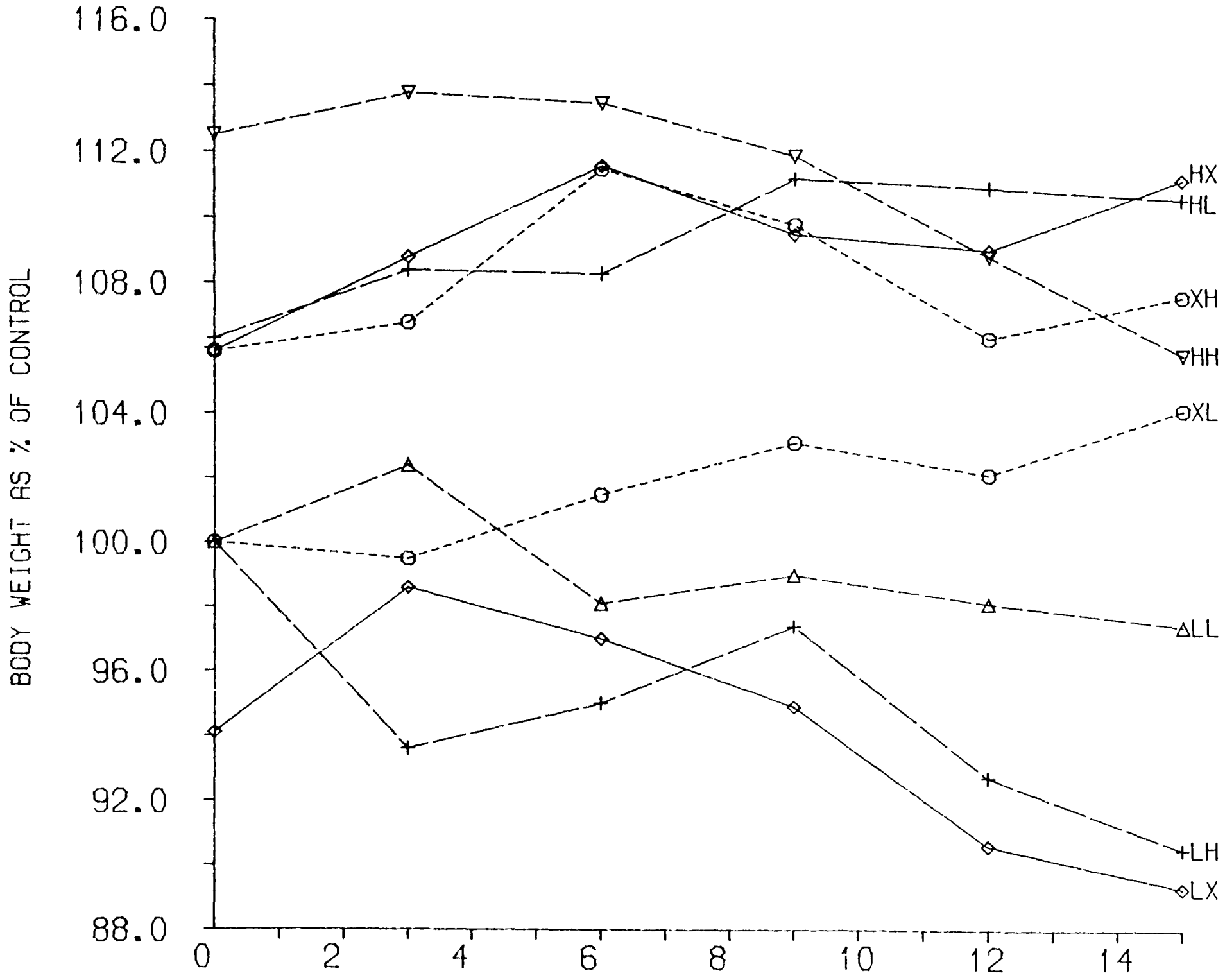
& Error including random drift.

5.5.3 Responses in males, castrate males, and females.

The corresponding graphs presented in sections 5.5.1 and 5.5.2 are shown separately for castrate males and females in figures 5.11 to 5.14. Line mean body weights, relative maturities, and contrasts, as given for all sexes combined in the previous two sections, are presented for males, castrates and females separately in tables 5.10 to 5.13, 5.15, 5.16, and 5.18 to 5.21.

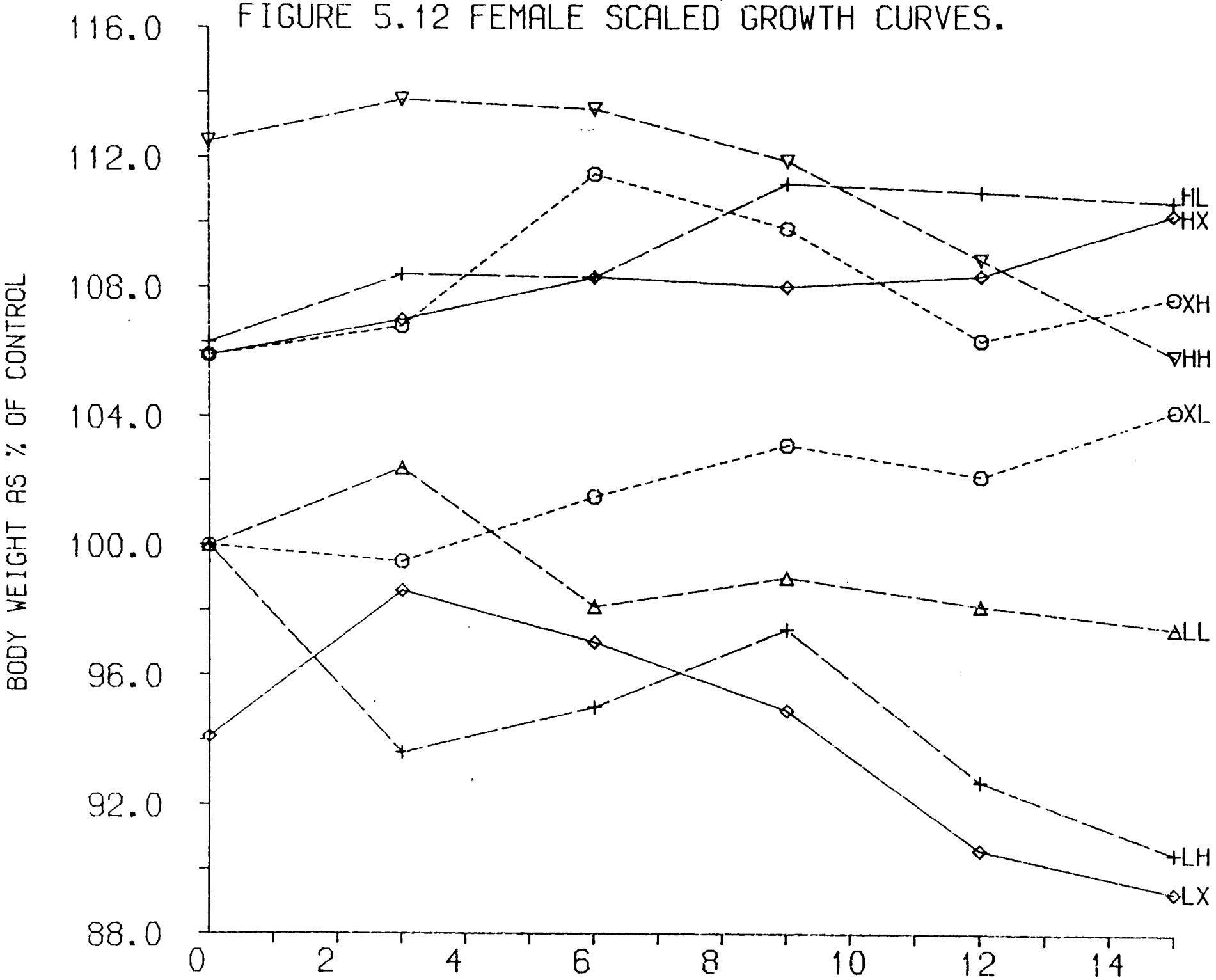
The patterns of responses in growth in body weight were similar for all three sexes as can be seen in figures 5.5, 5.11 and 5.12, and in table 5.13. Growth rate of all sexes in the lines selected for high testis weight apparently fell with respect to the lines selected for low testis weight from 6 weeks of age upwards, so that the sizes of the HH/LL and XH/XL divergences fell with age, and the HL/LH divergence increased. This age trend was most marked in the growth of entire males and least obvious in the females. Contrasts amongst the sexes in the sizes of line divergences in body weight are shown in table 5.14. It should be noted that the 3 week body weights of castrated males were measured before the mice were castrated so that "males" and "castrates" were equivalent at 3 weeks of age, and differences between the two groups of mice should be negligible at 3 weeks. Most of the contrasts in table 5.14 were no larger than the small differences between the male and castrate groups at 3 weeks and very few were significant. There was a slight trend for the size of difference in male body weight between the HH and LL lines to become increasingly less with age than the same difference for either castrate males or females. This could

FIGURE 5.11 CASTRATE SCALED* GROWTH CURVES.



* Body weight as a percentage of the appropriate control line

FIGURE 5.12 FEMALE SCALED* GROWTH CURVES.



*Bodyweight as a percentage of the appropriate control line

Table 5.10 Line mean body weights - males

Line	100 x Mean log body weight*				
	3 weeks	6 weeks	9 weeks	12 weeks	15 weeks
HH	105.71	148.16	154.72	158.92	161.05
LL	99.48	140.86	149.57	154.17	158.27
HL	104.64	147.39	155.25	159.07	162.85
LH	97.36	139.98	146.76	150.28	153.55
Control (groups 2 and 4)	100.13	142.56	150.61	154.86	158.30
HX	104.00	146.54	154.40	158.80	162.45
LX	99.20	139.40	148.26	152.22	155.70
XH	103.26	145.47	153.24	157.03	160.29
XL	99.12	140.35	150.12	154.90	158.06
Control (groups 1 and 3)	100.85	142.61	150.49	154.78	157.76
Standard error&	0.87	0.64	0.59	0.65	0.69

* Least squares estimates from analysis of variance.
& Within line error.

Table 5.11 Line mean body weights - castrate males

Line	100 x Mean log body weight*				
	3 weeks	6 weeks	9 weeks	12 weeks	15 weeks
HH	106.24	142.54	150.48	155.21	159.72
LL	100.67	135.82	144.72	150.23	155.55
HL	104.17	140.57	149.99	155.80	161.42
LH	97.60	134.81	144.42	148.26	152.93
Control (groups 2 and 4)	100.04	136.90	145.21	151.15	156.91
HX	103.90	140.12	149.30	155.20	160.81
LX	100.12	134.23	143.37	147.44	151.69
XH	103.37	140.29	149.58	154.39	159.79
XL	100.04	136.01	146.74	152.51	158.14
Control (groups 1 and 3)	100.37	135.43	145.43	151.56	156.32
Standard error&	0.90	0.67	0.61	0.67	0.72

* Least squares estimates from analysis of variance.
& Within line error.

Table 5.12 Line mean body weights - females

Line	100 x Mean log body weight*				
	3 weeks	6 weeks	9 weeks	12 weeks	15 weeks
HH	105.85	141.76	146.59	150.79	153.28
LL	99.43	135.07	140.91	144.89	148.66
HL	103.82	138.51	145.85	150.22	154.50
LH	97.47	133.79	138.77	142.53	145.68
Control (groups 2 and 4)	100.12	135.46	141.33	146.22	150.34
HX	102.81	137.88	144.56	149.26	153.26
LX	99.53	132.56	139.49	143.67	146.99
XH	103.51	139.06	144.86	148.60	152.58
XL	99.84	136.11	142.89	147.77	150.76
Control (groups 1 and 3)	100.01	134.42	141.25	145.81	149.09
Standard error&	0.87	0.64	0.59	0.65	0.69

* Least squares estimates from analysis of variance.
& Within line error.

Table 5.13 Contrasts in body weights between divergent lines - males, castrate males, and females separately.

Contrast	100 x log body weight				
	3 weeks	6 weeks	9 weeks	12 weeks	15 weeks
MALES:					
HH - LL	6.22	7.30a	5.15	4.76	2.78
HL - LH	7.28a	7.41a	8.49b	8.80b	9.30b
HX - LX	4.80	7.14a	6.14a	6.58	6.76
XH - XL	4.15	5.12	3.11	2.14	2.23
Standard error&	2.88	3.01	2.57	2.85	3.02
CASTRATE MALES:					
HH - LL	5.58	6.73	5.76	4.98	4.17
HL - LH	6.57	5.76	5.57	7.54b	8.50a
HX - LX	3.78	5.89	5.92	7.76a	9.12b
XH - XL	3.33	4.28	2.85	1.88	1.65
Standard error&	2.99	3.13	2.67	2.96	3.14
FEMALES:					
HH - LL	6.41a	6.69	5.68a	5.89	4.62
HL - LH	6.34a	4.72	7.08b	7.69b	8.82b
HX - LX	3.28	5.33	5.07	5.59	6.27
XH - XL	3.67	2.94	1.97	0.82	1.82
Standard error&	2.80	2.93	2.49	2.77	2.94

& Error including random drift.
Significance levels: a: $p<0.050$, b: 0.025

Table 5.14 Contrasts amongst the 3 sexes in the sizes of line divergences in body weight.

Contrast	100 x log body weight				
	3 weeks	6 weeks	9 weeks	12 weeks	15 weeks
HH - LL					
Male - Castrate	0.65	0.57	-0.61	-0.22	-1.39b
Male - Female	-0.19	0.60	-0.53	-1.14	-1.84d
Castrate - Female	-0.84	0.03	0.08	-0.91	-0.45
Standard error&	1.12	0.60	0.95	1.14	0.53
HL -LH					
Male - Castrate	0.71	1.65b	2.92c	1.25	0.80
Male - Female	0.94	2.69e	1.41	1.10	0.47
Castrate - Female	0.23	1.04	-1.50	-0.15	-0.33
Standard error&	1.15	0.61	0.98	1.17	0.54
HX - LX					
Male - Castrate	1.02	1.25	0.22	-1.18	-2.36e
Male - Female	1.51	1.81c	1.07	0.99	0.48
Castrate - Female	0.50	0.56	0.85	2.17	2.85e
Standard error&	1.14	0.61	0.99	1.17	0.54
XH - XL					
Male - Castrate	0.81	0.84	0.27	0.26	0.58
Male - Female	0.48	2.18d	1.15	1.31	0.41
Castrate - Female	-0.33	1.33a	0.88	1.06	-0.17
Standard error&	1.15	0.61	0.99	1.17	0.55

& Error including random drift.
Significance levels: a: $p<0.050$, b: 0.025, c: 0.010, d: 0.005, e: 0.001

suggest a small reduction in the size of response in the pattern of growth in mice lacking testes in these lines. However, the sizes of differences in the HL/LH divergence between the sexes remained fairly constant with age. Thus the enhanced later growth in the HL line and restricted growth in the LH line was expressed equally in male, castrate male, and female mice.

The values of relative maturity in body weight provide a similar picture. The lines selected for high testis weight were generally the most mature at all the observed ages whether maturity was measured in males, castrates or females. Table 5.16 shows that all sexes were more mature in the HH line than the LL line at 6 weeks of age, and less mature in the HL than in the LH line. The difference in relative maturity between the HH and LL lines was rather greater for males than for either of the other two sexes and this difference was significant ($p = 0.025$) between males and females (table 5.17). An unexpected result was that castrate males and females were more mature in weight in the low body weight line (LX) than in the high line (HX) at 6 weeks of age, but the relative maturity of 6 week old males was about the same in both lines. The explanation for this may lie in the observation that the weight of castrate and female mice showed a sharp rise in the HX relative to the LX line between 12 and 15 weeks of age (table 5.13, figures 5.11 and 5.12). Relative degree of maturity was calculated as the ratio of weight at 6 weeks to 15 week weight in percentage terms. Therefore the lower values of relative maturity of castrates and females seen in the HX line probably reflect the relatively large differences in 15 week weight.

Table 5.15 Relative maturity in body weight at 6 weeks of age - males, castrate males, and females separately.

Line	Relative maturity in body weight at 6 weeks (%)*		
	Males	Castrate males	Females
HH	74.63	67.70	76.78
LL	67.41	64.06	73.30
HL	70.25	62.19	69.52
LH	73.35	66.14	76.08
Control (groups 2 and 4)	69.88	63.34	71.30
HX	69.57	62.34	70.42
LX	69.16	67.15	72.13
XH	71.49	64.01	73.56
XL	66.92	60.21	71.61
Control (groups 1 and 3)	70.77	62.11	71.64
Standard error&	0.83	0.86	0.83

* Least squares estimates from analysis of variance.
& Within line error.

Table 5.16 Contrasts of the relative degree of maturity in body weight at 6 weeks between divergent lines - males, castrate males, and females separately.

Contrast	Relative maturity in body weight at 6 weeks (%)		
	Males	Castrate males	Females
HH - LL	7.21a	3.64	3.48
HL - LH	-3.10	-3.96	-6.57
HX - LX	0.41	-4.82	-1.71
XH - XL	4.56	3.80	1.94
Standard error&	3.09	3.20	3.00

& Error including random drift.
Significance level: a: $p<0.05$

Table 5.17 Contrasts amongst the 3 sexes in the sizes of line divergences in relative maturity in body weight at 6 weeks of age.

Divergence	Contrast in relative maturity in body weight at 6 weeks (%)		
	Male - castrate	Male - female	Castrate - female
HH - LL	3.57	3.73b	0.16
HL - LH	0.85	3.47	2.61
HX - LX	5.23c	-2.12	-3.11
XH - XL	0.76	2.62	1.86
Standard error&	1.79	1.73	1.77

Error including random drift.
Significance levels: a: $p<0.050$, b: 0.025, c: 0.010

There were greater responses in body weight in the single trait testis weight lines (XH and XL) in males and castrate males than in females, especially at 6 weeks of age (table 5.14). The divergence in relative maturity of the females between these lines was also less than that of either entire or castrate males. Thus the correlated response in female growth in body weight to selection on male testis weight alone was rather less than the correlated response in male growth in weight.

The responses in tail growth were small in all three sexes (table 5.21). The general patterns of tail growth were similar (figures 5.10, 5.13 and 5.14) and the contrasts in table 5.21 show that none of the sexes expressed a big response in the pattern of tail growth. One point to emerge from studying the tail length data was that castration at 3 weeks of age resulted in mice with longer tails than their entire contemporaries at all subsequent ages, and the tails of females were generally shorter than those of entire males.

In summary:

- In general the directions and sizes of responses in the pattern of growth in weight were very similar in entire males, castrate males and females.
- The size of the response in the growth patterns of females and castrates in the HH and LL lines was possibly less than that of entire males.
- The body weights of females and castrate males increased in the HX relative to the LX line at 15 weeks of age.

Table 5.18 Line mean tail lengths - males

Line	100 x Mean log tail length*				
	4 weeks	7 weeks	10 weeks	13 weeks	16 weeks
HH	82.35	94.18	97.35	98.47	99.14
LL	80.92	91.58	95.49	96.70	97.41
HL	82.33	94.07	96.77	98.10	98.52
LH	79.43	91.22	94.50	96.23	97.24
Control (groups 2 and 4)	81.01	92.18	96.04	97.17	97.85
HX	81.30	93.87	96.90	98.40	99.09
LX	78.43	90.67	93.83	95.47	96.36
XH	78.78	91.61	94.67	96.37	97.08
XL	79.81	92.08	95.03	96.75	97.60
Control (groups 1 and 3)	78.60	90.82	94.03	95.58	96.57
Standard error&	0.54	0.36	0.30	0.29	0.28

* Least squares estimate from analysis of variance.
& Within line error.

Table 5.19 Line mean tail lengths - castrate males.

Line	100 x Mean log tail length*				
	4 weeks	7 weeks	10 weeks	13 weeks	16 weeks
HH	83.24	95.61	99.55	101.20	102.02
LL	81.05	92.73	97.15	98.66	99.59
HL	82.34	94.84	98.11	99.66	100.39
LH	79.41	92.70	96.63	98.70	99.70
Control (groups 2 and 4)	81.24	93.44	97.76	99.20	100.04
HX	81.42	95.19	98.65	100.40	101.17
LX	78.88	91.42	94.98	97.01	98.19
XH	79.37	93.51	97.03	99.02	100.01
XL	79.76	93.10	97.09	99.29	100.22
Control (groups 1 and 3)	78.72	91.93	95.76	97.60	98.69
Standard error&	0.56	0.38	0.31	0.30	0.29

* Least squares estimates from analysis of variance.
& Within line error.

Table 5.20 Line mean tail lengths - females.

Line	100 x Mean log tail length*				
	4 weeks	7 weeks	10 weeks	13 weeks	16 weeks
HH	83.16	93.18	96.15	97.29	97.89
LL	81.45	90.87	94.14	95.24	96.21
HL	82.44	91.65	94.53	95.93	96.56
LH	80.32	90.76	93.64	95.11	95.80
Control (groups 2 and 4)	82.03	91.41	94.66	95.85	96.66
HX	81.84	92.40	95.20	96.70	97.40
LX	79.37	89.84	92.56	94.17	94.99
XH	80.00	91.25	93.88	95.44	96.35
XL	80.37	91.47	94.35	95.93	96.83
Control (groups 1 and 3)	78.70	88.74	91.46	93.05	94.09
Standard error&	0.52	0.35	0.29	0.28	0.27

* Least squares estimates from analysis of variance.
& Within line error.

Table 5.21 Contrasts in tail length between divergent lines - males, castrate males, and females separately.

Contrast	100 x log tail length				
	4 weeks	7 weeks	10 weeks	13 weeks	16 weeks
MALES:					
HH - LL	1.43	2.60	1.86	1.77	1.73
HL - LH	2.90	2.85	2.27	1.87	1.29
HX - LX	2.87	3.20	3.07	2.94	2.73
XH - XL	-1.04	-0.48	-0.36	-0.39	-0.52
Standard error&	2.68	2.00	2.00	2.08	2.08
CASTRATE MALES:					
HH - LL	2.19	2.88	2.40	2.54	2.43
HL - LH	2.93	2.13	1.48	0.96	0.70
HX - LX	2.54	3.77	3.67	3.40	2.98
XH - XL	-0.39	0.41	-0.06	-0.27	-0.21
Standard error&	2.77	2.09	2.08	2.15	2.15
FEMALES:					
HH - LL	1.71	2.31	2.02	2.05	1.68
HL - LH	2.11	0.89	0.89	0.82	0.76
HX - LX	2.47	2.56	2.64	2.52	2.41
XH - XL	-0.36	-0.23	-0.48	-0.49	-0.48
Standard error&	2.59	1.94	1.94	2.01	2.03

& Error including random drift.

FIGURE 5.13 CASTRATE SCALED TAIL GROWTH CURVES.

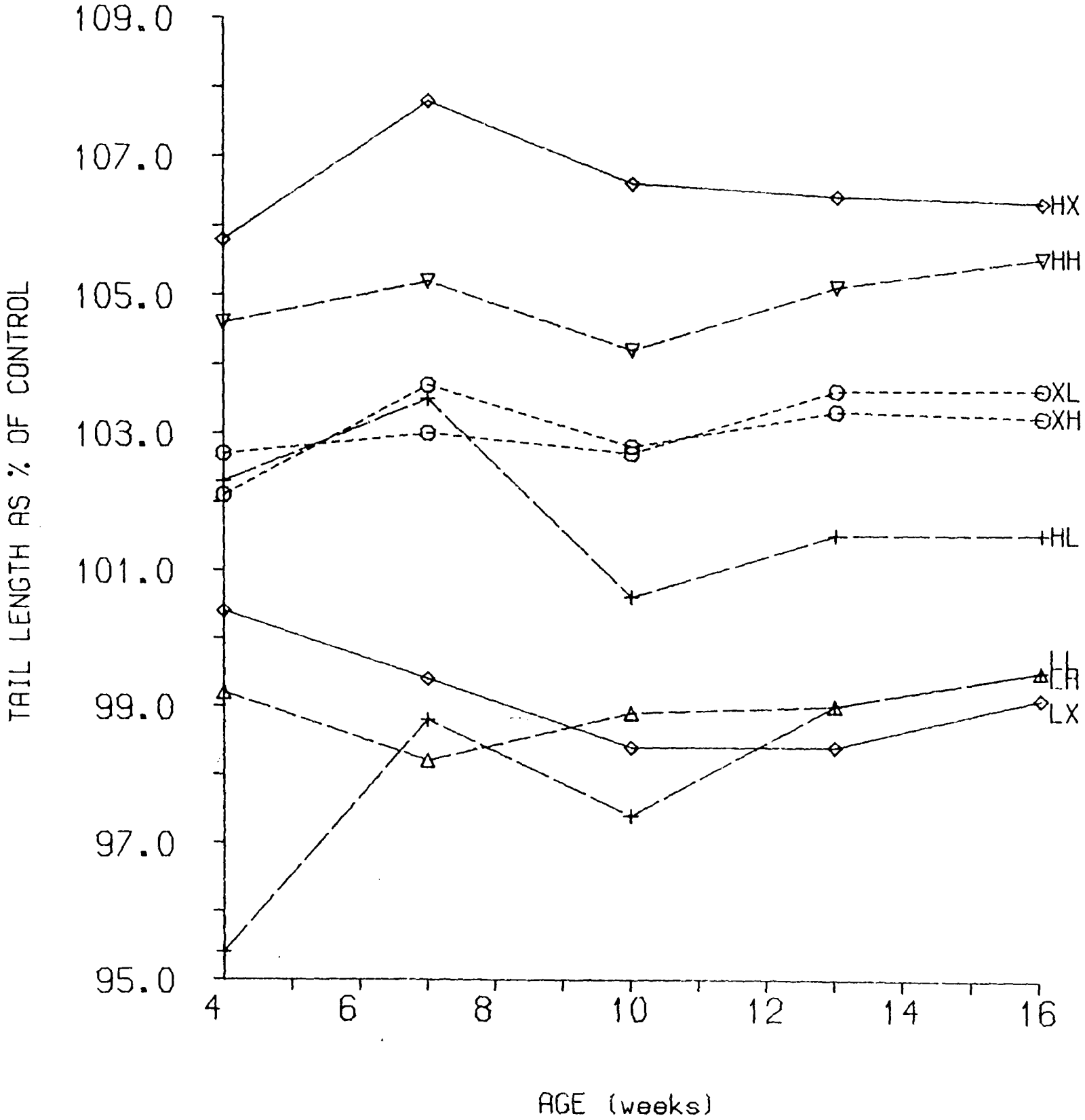
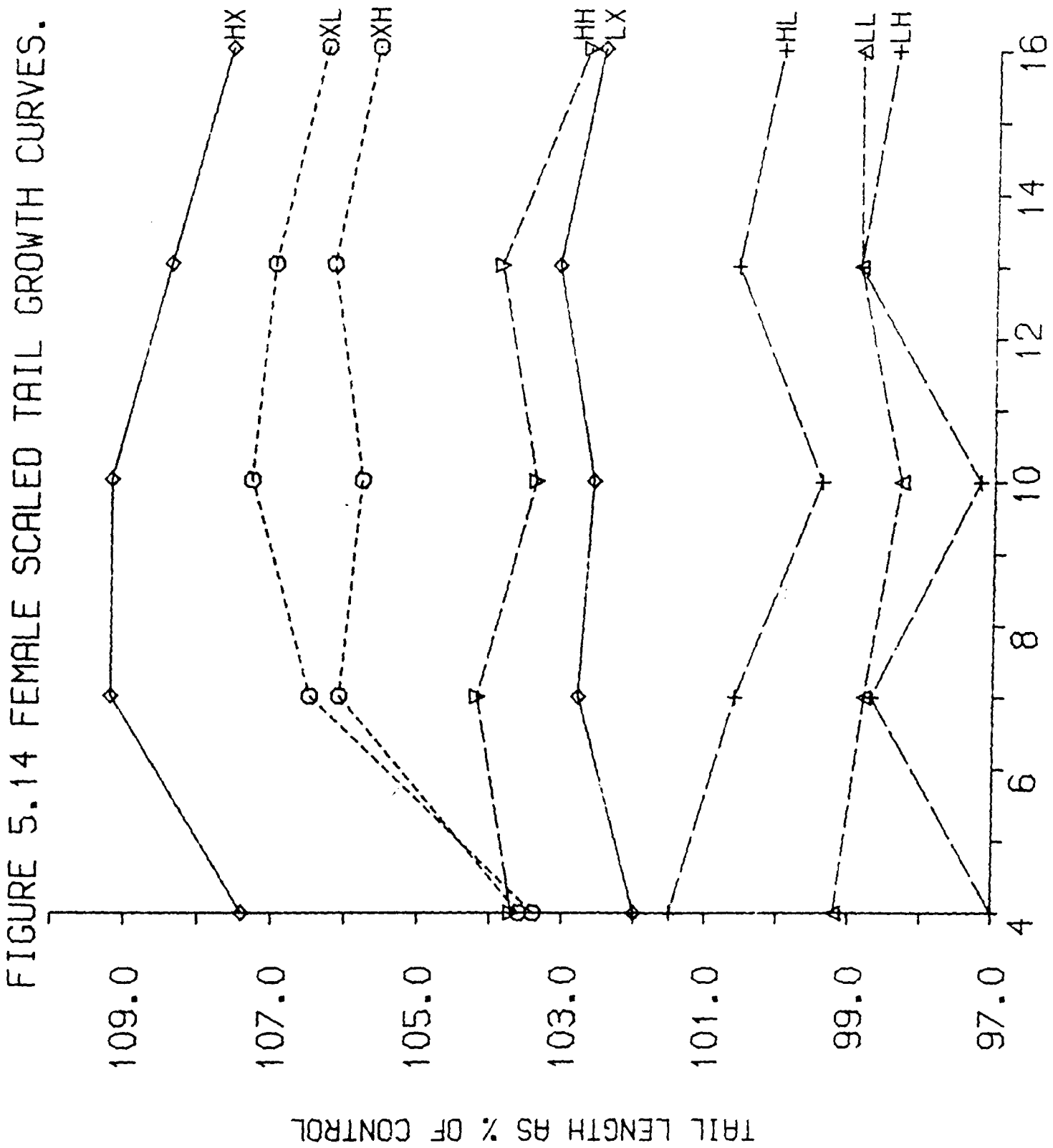


FIGURE 5.14 FEMALE SCALED TAIL GROWTH CURVES.



- The correlated responses in body weight in entire and castrated males in the XH and XL lines were greater than the same responses in females, especially at 6 weeks of age.
- There was very little response in tail growth in any of the three sexes.
- The tails of castrated mice were longer than entire males or females at all ages.

5.5.4 Growth of the testes.

The least squares estimates of untransformed testis weights measured at 3, 5 and 19 weeks of age are shown in table 5.22. Log transformed estimates are presented in table 5.23 and contrasts between divergent lines in the transformed values are given in table 5.24. The sizes of the line divergences in testes weights at 5 weeks of age in generation 7 would probably be larger than those presented here which were measured in generation 6.

Selection on testis weight and combinations of body weight and testis weight produced positive responses in testis weight in the desired directions at all three ages. The greatest responses in testis weight uncorrected for body weight were obtained by selecting directly on the trait in the XH and XL lines. Selection on body weight and testis weight in the same direction (HH and LL lines) produced responses in testis weight of a similar magnitude. Both types of selection apparently caused an overall shift in the testis weight growth curve. Testis weights responded at a young (3 weeks), intermediate (5 weeks) and a mature (19 weeks) age. Schinckel,

Table 5.22 Line mean testis weights - untransformed.

Line	Testis weight (mg)* 3 weeks$	5 weeks#	19 weeks$
HH	55.8	80.1	286.2
LL	39.0	59.4	188.6
HL	38.7	57.2	179.8
LH	45.6	72.8	227.9
Control (groups 2 and 4)	40.2	57.1	205.4
HX	45.4	75.7	249.2
LX	39.4	67.1	189.5
XH	49.1	85.2	269.3
XL	38.3	58.8	168.5
Control (groups 1 and 3)	42.8	67.2	210.0
Standard error&	1.7	1.8	10.0

* Least squares estimate from analysis of variance.
$ Two testes, generation 7.
# One testis, generation 6.
& Within line error.

Table 5.23 Line mean testis weights - log transformed.

Line	100 x mean log testis weight* 3 weeks$	5 weeks#	19 weeks$
HH	170.4	190.2	245.5
LL	157.7	175.6	226.2
HL	157.6	172.0	225.0
LH	164.2	186.2	235.0
Control (groups 2 and 4)	158.9	174.3	231.0
HX	164.7	186.4	238.5
LX	157.3	181.9	227.0
XH	166.8	192.5	240.9
XL	157.1	173.5	221.6
Control (groups 1 and 3)	161.9	181.5	230.3
Standard error&	1.9	1.7	2.3

* Least squares estimate from analysis of variance.
$ 100 x mean log of weight of 2 testes measured in in generation 7.
# 100 x mean log of weight of single testis measured in generation 6.
& Within line error.

Table 5.24 Contrasts of testis weights between divergent lines.

Contrast	100 x log testis weight 3 weeks$	5 weeks#	19 weeks$
HH - LL	12.6	14.6c	19.2b
HL - LH	-6.6	-14.2c	-10.0
HX - LX	7.3	4.5	11.5
XH - XL	9.7	19.0d	19.3b
Standard error&	5.8	4.1	6.6

$ Two testes, generation 7.
# One testis, generation 6.
& Error including random drift.
Significance levels: a: $p<0.050$, b: 0.025, c: 0.010, d:0.005, e: 0.001

Johnson and Kittok (1983) found that selection on testis weight in pigs also produced a shift in the testis growth curve rather than a change in its shape. Selection on body weight alone (HX and LX) produced correlated responses in testis weight at all 3 ages but the responses were relatively small and not significant. The divergence in testis weight between the HL and LH lines was negative as desired, and at 5 weeks the size of the response was the same as that between the HH and LL lines. However, at 3 and 19 weeks, the response in testis weight in the HL and LH lines was only as great as that in the HX and LX lines. This suggests that selection on body weight and testis weight in opposite directions altered the shape of the testis growth curve. Selection in the LH lines apparently produced mice in which the testes matured in weight earlier than those of mice in the HL lines.

The above refers to the growth of the testes uncorrected for body weight. The aim of selection in the HL and LH lines was to alter the balance between testis weight and body weight. Responses in the HL/LH index and in 5 week body weight and testis weight discussed so far (section 4.2), imply that this aim was achieved and body weight and testis weight were altered in opposite directions. Analyses of testis weight expressed per gramme body weight were carried out to test these responses further. Table 5.25 contains the least squares estimates of testis weight expressed per gramme body weight and the corresponding contrasts between divergent lines are given in table 5.26. The contrasts in testis weight/body weight ratio between the HL and LH lines were significant at 3 ($p<0.025$), 5 ($p<0.001$), and 19 ($p<0.005$) weeks of age - further evidence that selection against the

Table 5.25 Line mean ratio of testis weight to body weight.

Line	Testis weight (mg)/body weight (g)*		
	3 weeks$	5 weeks#	19 weeks$
HH	4.72	2.95	2.38
LL	3.79	2.41	2.36
HL	3.47	2.20	2.13
LH	4.73	3.08	2.72
Control (groups 2 and 4)	3.96	2.33	2.32
HX	4.08	2.88	2.12
LX	3.88	2.76	2.48
XH	4.40	3.10	2.22
XL	3.78	2.50	2.25
Control (groups 1 and 3)	4.17	2.67	2.39
Standard error&	0.12	0.06	0.06

* Least squares estimate from analysis of variance.
$ Two testes, generation 7.
# One testis, generation 6.
& Within line error.

Table 5.26 Contrasts of testis weight to body weight ratio between divergent lines.

Contrast	Testis weight/body weight		
	3 weeks$	5 weeks#	19 weeks$
HH - LL	0.92a	0.54d	0.02
HL - LH	-1.26b	-0.88e	-0.59d
HX - LX	0.21	0.12	-0.37
XH - XL	0.62	0.60d	-0.03
Standard error&	0.40	0.13	0.16

$ Two testes, generation 7.
# One testis, generation 6.
& Error including random drift.
Significance levels: a: $p<0.050$, b: 0.025, c: 0.010, d: 0.005, e: 0.001.

correlation between testis weight and body weight was successful. Responses were achieved not only at the selection age, but also at a younger and an older age. Selection with the correlation between the two traits in the HH and LL lines also significantly affected the balance between them at 3 ($p<0.05$) and 5 ($p<0.005$) weeks. There was a response in testis weight/body weight at 3 and 5 weeks of age in the XH and XL lines in which all the intended selection pressure was on testis weight, but only the response at 5 weeks was significant ($p<0.005$).

To conclude:

- Selection on testis weight alone or on testis weight and body weight in the same direction caused a shift in the testis growth curve when testis weight is uncorrected for body weight.
- Selection on body weight and testis weight in opposite directions influenced the pattern of testis growth (uncorrected for body weight).
- The ratio of body weight to testis weight was altered by selecting on combinations of the two traits, especially when they were selected in opposite directions.
- This balance was also affected by selection on testis weight alone.

VI DISCUSSION

The aim of this study was to investigate a method of altering the shape of the growth curve with the ultimate aim of applying the technique to the improvement of the efficiency of meat production. The method which involved selecting for testis weight and body weight at an immature age, was tested on the mouse.

Advantages and restrictions of research with laboratory animals for the benefit of livestock improvement have been discussed by Robertson (1959), Chapman (1961), Roberts (1965) and Falconer (1966). The use of the mouse in this study provided the advantages of large numbers and a short generation interval. If there is a relationship between testis size and growth, it will probably exist in most mammalian species, although the nature of such a relationship may not be the same for all species especially seasonal and non-seasonal breeders. Correlated responses to selection involving testis size and growth may also be species specific. Therefore, as the above mentioned authors have suggested, one must be careful in directly applying the results from mice to livestock improvement and the results obtained in this experiment should be regarded as preliminary information concerning the existence of a "useful" genetic connection between testis size and degree of maturity in body weight.

Estimates of genetic parameters realised in the single trait selected lines are comparable to those obtained in previous selection experiments on mice which were quoted in section 2.4. The

realised heritability of 5 week body weight (0.19 $\pm$ 0.08) lies just within the range of estimates for 3 week up to 10 week weight listed in table 2.3. These were all from selection experiments lasting for more than 6 generations and involving larger numbers of mice than in this study. The realised heritability of 5 week testis weight (0.44 $\pm$ 0.07) was lower than that of 0.52 $\pm$ 0.07 for 11 week testis weight estimated by Islam, Hill and Land (1976) following 5 generations of selection. The realised genetic correlation between 5 week body weight and testis weight calculated from responses in the HX/LX and XH/XL lines (r_A = 0.70 $\pm$ 0.25) was higher than that estimated at 6 weeks of age by Eisen and Johnson (1981) (r_A = 0.60 $\pm$ 0.03). It was also higher than the correlation at 11 weeks of age calculated in the experiment by Islam *et al* (1976) (r_A = 0.20).

In theory the responses to selection against a genetic correlation are expected to be low. Selection in the HL and LH lines which was against the correlation between body weight and testis weight produced significant responses which were less than the responses to single trait selection (see table 6.1 for summary) but not remarkably so. Eisen and Bandy (1977) selected against the positive genetic correlation between body weight and tail length and showed that this antagonistic index selection yielded smaller responses than did single trait selection. Eisen (1978) found that antagonistic index selection on litter size and body weight yielded even lower responses than those predicted from estimates of genetic parameters calculated in the base population. The divergence in litter size was about one half of that expected and the divergence

Table 6.1 Summary of line divergences in 5 week body weight and testis weight.

	SELECTION ON:							
	HX/LX		XH/XL		HH/LL		HL/LH	
OBSERVED RESULTS	SD	RESP	SD	RESP	SD	RESP	SD	RESP
Body weight (g)	20.3	3.1	10.6	3.6	19.7	2.1	12.7	2.8
Testis weight (mg)	10.2	100.6	27.6	101.7	21.3	-44.8	-18.8	
I = 0.54W + 0.112T	2.34	15.3	5.03	20.1	3.48	2.0	-0.64	
I = 0.54W - 0.112T	0.26	-4.8	-1.14	-0.3	-1.27	10.9	3.57	

SD = Selection differential.
RESP = Response.

in 6 week body weight was slightly less than expected. The responses in body weight and testis weight expected in the index lines selected here were calculated using realised genetic parameter estimates from the single trait lines. The procedure to do this is set out below:

Response, R_X, in trait X, to selection on an index, I, is the product of the genetic regression of X on I, and the selection differential on I:

$$R_X = b_{XI} \cdot S_I$$

$$= S_I \cdot COV_A(X,I)/V_p(I)$$

where COV_A = genetic covariance.

V_p = phenotypic variance.

The genetic covariance of X with I when I includes two traits ($I = b_1X + b_2Y$) is:

$$COV_A(X,I) = b_1V_A(X) + b_2COV_A(X,Y)$$

where V_A = genetic variance.

Therefore:

$$R_X = (S_I/V_p(I)).(b_1V_A(X) + b_2COV_A(X,Y))$$

Selection was only on males and so the selection differential is halved:

$$R_X = (S_I/2V_p(I)).(b_1V_A(X) + b_2COV_A(X,Y))$$

With selection on two indexes, each including two traits as in this experiment, there are four such equations, one for the response in each trait under selection on each index:

Equation 6.1:

$$R_{W.I1} = (S_{I1}/2V_p(I1)).(0.54V_A(W) + 0.112COV_A(W,T))$$

Equation 6.2:

$$R_{T.I1} = (S_{I1}/2V_p(I1)).(0.54COV_A(W,T) + 0.112V_A(T))$$

Equation 6.3:

$$R_{W.I2} = (S_{I2}/2V_p(I2)).(0.54V_A(W) - 0.112COV_A(W,T))$$

Equation 6.4:

$$R_{T.I2} = (S_{I2}/2V_p(I2)).(0.54COV_A(W,T) - 0.112V_A(T))$$

Where: $I1 = 0.54W + 0.112T$

$I2 = 0.54W - 0.112T$

The genetic variances and covariances may be calculated from estimates of realised within family heritability and genetic correlation obtained in the single trait lines, and within family phenotypic variance estimated in the base population:

Equation 6.5: $h^2 = V_A/V_p$

Equation 6.6: $r_A = COV_A(W,T)/((V_A(W).V_A(T))^{1/2})$

Expected responses in body weight and testis weight in the index lines were calculated by substituting the appropriate values into equations 6.1 to 6.4. Responses were taken as differences between divergent lines. Both responses and selection differentials were averaged over replicates.

The predicted responses to index selection are shown in table 6.2 alongside those which were actually observed. The sizes of observed responses in body weight and testis weight when selection for the two traits was in the same direction (HH and LL lines) were slightly lower than predicted. However, unlike the results of Eisen (1978) the responses to antagonistic selection in the HL and LH lines were larger than those predicted.

An alternative way to compare observed responses with those expected in theory is to predict the responses in HX/LX and XH/XL lines basing the predictions on parameters estimated in the index lines. Solving equations 6.1 and 6.3, and 6.2 and 6.4 as two pairs of simultaneous equations gives two estimates of the genetic covariance and one each for $V_A(W)$ and $V_A(T)$:

From responses in body weight to selection on the indexes:

$$V_A(W) = 1.1g^2,\ COV_A(W,T) = 0.0.$$

From responses in testis weight to selection on the indexes:

$$V_A(T) = 44.2mg^2,\ COV_A(W,T) = 1.90.$$

This procedure to estimate genetic variances and covariance from populations selected simultaneously for two traits is a specific example of a technique described and used by Berger and Harvey (1975). Realised heritabilities of body weight and testis weight, and the genetic correlation between the two were calculated from equations 6.5 and 6.6.

The two estimates of genetic covariance calculated from responses to index selection were averaged. The genetic correlation was calculated using this average value.

Under single trait selection:

$$R_X = h_X^2.S_X$$

and the correlated response in Y to selection on X, CR_Y is:

$$CR_Y = i_X.h_X.h_Y.r_A(X,Y).(V_p(W))^{1/2}$$

Where $i_X = S_X/(V_p(X))^{1/2}$ (selection intensity).

By substituting the appropriate values into these equations the responses to single trait selection predicted by parameter estimates from the index lines were calculated. The results of these calculations are also shown in table 6.2. Observed direct responses

were close to those predicted. The sizes of correlated responses were larger than predicted. A general conclusion to be drawn from table 6.2 is that the "trait" described by the HL/LH index is not a simple combination of high body weight and low testis weight or vice-versa in genetic terms. For an unknown reason body weight and testis weight did not respond to antagonistic selection in the way expected.

Selection is continuing in these lines of mice and in the latest generation (the 9th of the experiment but actually the result of 8 generations of selection because mice were not selected in generation 7) reponses in the HL/LH lines are still of the same magnitude as responses in the single trait lines (table 6.3).

The selection pressures imposed by antagonistic selection on body weight and testis weight may be the same or equivalent to those which operate during the evolution of "large" and "small" breeds. In cattle, breeds of large mature size grow for longer and reach puberty later than smaller breeds whereas, within breed, puberty is reached first by the fastest growing individuals (Beverly, 1979). In the index lines selected here testis weight may be acting as a measure of degree of sexual maturity as well as a measure of degree of maturity in body weight. In which case the aim of selection in the HL line will be the mouse-equivalent of a "large" breed of cattle, and the aim in the LH line will be the equivalent of a "small" cattle breed. Price, Aherne, Elliot and Lodge (1981) observed a similar phenomenon in an experiment to assess the effects of age at puberty on growth of pigs. A group of crossbred gilts

Table 6.2 Observed and predicted responses in 5 week body weight and testis weight.

	RESPONSE IN:			
	Body weight (g)		Testis weight (mg)	
SELECTION ON:	Expected	Observed	Expected	Observed
I = 0.54W + 0.112T*	3.2	2.1	23.5	21.3
I = 0.54W - 0.112T*	-0.1	2.8	-10.3	-18.8
Body weight$	3.3	3.1	3.0	10.2
Testis weight$	0.6	3.6	28.2	27.6

* Predicted responses based on parameters estimated in the single trait lines.
$ Predicted responses based on parameters estimated in the index lines.

Table 6.3 Mean replicate 5 week body weight and testis weight in generation 9.

	Body weight		Testis weight*	
Line	g.	S.E.	mg.	S.E.
HH#	28.2	0.5	90.4	2.7
LL#	25.6	0.7	55.8	2.2
HL#	28.5	1.2	64.0	3.5
LH#	25.5	0.8	89.2	3.7
Control (groups 2 and 4)#	24.0	0.8		
HX	27.5	0.7		
LX	23.5	0.6		
XH	28.6	0.9	96.7	3.6
XL	25.6	0.9	57.4	2.6
Control (groups 1 and 3)	25.6	0.9		

* Testis weight was not measured in the lines not selected on testis weight.
# Mean in replicate 1 only.

were observed for date at first oestrus between 100 days of age and slaughter at a constant weight (109kg). Thirty-six per cent of the gilts reached puberty before slaughter and this group grew significantly more slowly than the other 64%. Paradoxically within the early maturing group the gilts which reached puberty first grew significantly faster than those which reached puberty later. In terms of growth patterns the group of early maturing gilts may be equivalent to the mice selected here for low body weight and high testis weight and the late maturing gilts the same as mice in the line selected for high body weight and low testis weight. To investigate this theory more thoroughly the age at puberty of the mice in the selected lines should be measured.

It was suggested in section 1.3 that selection on body weight would produce correlated responses in litter size, but responses in litter size in the lines selected on 5 week weight were small after 6 generations of selection. Eisen (1978) practised mass selection for 6 week weight on females only for 12 generations. The correlated response in litter size (as deviation from a control line) was 0.24 ± 0.07 pups/generation and significant at the 1% level. However, responses only became apparent after generation 5 and the direct response in 6 week weight (0.6g difference from the control per generation) was larger than the response in 5 week weight obtained in this study. Litter sizes are now available in the ninth generation of mice selected in this experiment (table 6.4). Mean litter size in the HX lines is still greater than that in the LX lines and it is also slightly greater in the HH than in the LL lines. The difference between the HL and the LH lines has

Table 6.4 Mean replicate litter sizes born into generation 9.

Line	Mean litter size			
	At birth		At day 17 of gestation*	
	Mean	S.E.	Mean	S.E.
Control (groups 1 and 3)	11.0	0.5	11.3	0.1
HX	10.8	0.6	11.0	0.2
LX	10.2	0.8	7.4	0.2
XH	12.4	0.9	12.4	0.2
XL	9.1	1.0	10.4	0.2
Control (groups 2 and 4)	11.2	0.6	11.6	0.2
HH	9.6	0.7	11.5	0.2
LL	9.0	0.7	10.2	0.3
HL	11.5	0.9	10.1	0.8
LH	10.8	0.8	10.8	0.2

* P. J. Cook, personal communication.

reverted and responses in litter size are in the directions of selection on body weight rather than of testis weight. The difference in litter size between the XH and XL lines has increased. When Islam, Hill and Land (1976) selected on 11 week testis weight in mice female ovulation rate responded in the same direction as testis weight, but litter size did not. Ovulation rate in each of the lines is currently being examined in more detail. The number of embryos alive at day 17 of gestation has also been counted and a summary of the records is included in table 6.4.

The results of the experiment show that selection on combinations of body weight and testis weight has altered the pattern of growth in body weight, and that the responses in the growth pattern were dependent on the inclusion of selection on testis weight along with selection on body weight. However, changes in the pattern of growth were fairly small. If the lines respond as desired the most sensitive way to detect responses in the pattern of growth is to test the size of the difference between the HL/LH divergence and the HH/LL divergence in body weight at older ages. This difference did become greater with age but it was not significant even at 15 weeks of age after 6 generations of selection. Only some of the previous attempts to change the growth curve of mice genetically have been successful (see section 1.1.2), and, in those which were, the rates of response were generally slow. These experiments generally involved selection for more than 6 consecutive generations. Selection is continuing in all of the lines in this study for a further 5 generations to try and enlarge the responses in the pattern of growth. If the lines continue to diverge during this

time, it should be possible to display clearer differences between them and also to observe larger correlated responses to selection. If it does prove possible to obtain large changes in the shape of the growth curve by this method of selection, then the technique has a potential application to livestock improvement. However, further research is necessary before it can be put into practice.

It has already been noted that the sizes of responses in 5 week body weight and testis weight in the index lines were of the same magnitude as the responses to direct selection on these traits. Thus the size of response in 5 week weight was not affected by the inclusion of selection on testis weight along with selection on body weight.

The method used here may be a way of avoiding this particular problem, but because testis size can only be measured on males, it is only possible to exert half of the potential selection intensity. An alternative could be to select males on testis size and body weight, and females only on body weight. Thus selection on early growth could be maintained in both sexes but some response in the pattern of growth could be achieved through selection on males. Additionally, information from relatives could be used to allow selection on the pattern of growth in females.

If this experimental technique to bend the growth curve is to be put to a practical use, it is important to know the effects of selection on carcass composition. The responses in tail length were small and did not follow the same pattern as responses in body

weight. If we can assume that tail length gives some indication of body size, then the lack of corresponding changes in tail length suggests that the responses in the pattern of growth were at least partly due to changes in body composition rather than in overall body size. Eisen and Bandy (1977) measured correlated responses in body composition in lines of mice selected for high body weight and low tail length at 6 weeks of age. They failed to find any significant responses in percentage fat, protein, ash or moisture even though the mice had responded in both body weight and tail length in the desired directions. Therefore, the grounds for making the suggestion that changes in the pattern of growth were due to some alterations in body composition, may not be valid. A more conclusive test of the effects of selection on body composition is currently in progress. This involves a preliminary survey of fatness in the lines by dissecting out and weighing two fat depots from male mice at 11 weeks of age. Results so far suggest that selection has produced some differences amongst the lines in body fat percentage. (P.J.Cook, personal communication).

Responses in the pattern of growth were similar in males, females and castrated males and differences amongst the sexes in the sizes of responses were not large. R.B.Land (personal communication) observed that in a line of sheep selected for testis size (corrected for body weight) both entire and castrated males showed correlated responses in body weight. Therefore, the responses in growth were probably not directly dependent on changes in testis weight, but were mediated by other factors associated with both testis size and growth. These factors could be hormones. Future work on the lines

of mice studied here could involve the measurement of the levels of hormones such as thyroxine, testosterone and luteinising hormone.

To conclude - the results of this experiment show that by selecting on combinations of body weight and testis weight measured at an immature age it is possible to produce lines of mice with:

a) increased early growth, but restricted mature weight (HH),

b) increased early growth and increased mature weight (HL),

c) reduced early growth and low mature weight (LH),

d) reduced early growth and delayed maturity (LL).

The responses have been relatively small so far, but selection is proceeding within the lines. If it proves possible to make large changes in the pattern of growth by selecting on combinations of body weight and testis weight, then the technique may have an application in agricultural practice. The next step should be to carry out investigations into the effects of selection on carcass composition, age at puberty, and ovulation rate and/or litter size. Antagonistic index selection on immature body weight and testis weight has apparently mimicked the evolution of large and small breeds of cattle. Consequently selection on combinations of the two traits may not only be an effective method to breed strains of animals with growth patterns modified to fit more efficient production systems, but also a method to investigate the process of breed evolution.

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APPENDIX I - SELECTION DIFFERENTIALS BY GENERATION

Appendix 1.1 Selection differentials of 5 week body weight (g).

Line	Generation					
	0	1	2	3	4	5
Control 1	0.5	-0.6	0.3	-0.2	-0.1	-0.8
HX	1.5	2.2	1.9	2.1	1.7	2.1
LX	-1.8	-1.9	-2.1	-1.6	-1.2	-0.8
XH	0.7	0.9	1.6	0.8	1.2	1.5
XL	-1.5	-1.7	0.0	-0.4	-1.5	-1.0
Control 2	0.2	0.1	-0.4	0.2	-1.0	-0.9
HH	1.4	1.7	1.8	1.1	1.7	1.7
LL	-0.9	-1.9	-1.2	-1.4	-1.3	-1.6
HL	1.0	0.9	0.7	1.1	1.2	1.4
LH	-1.5	-2.5	-1.0	-0.2	-0.4	-1.9
Control 3	-0.8	0.1	0.0	0.1	0.2	-0.3
HX	1.2	1.4	1.5	1.2	0.9	1.8
LX	-1.3	-1.7	-1.9	-1.7	-3.3	-1.7
XH	1.6	0.5	1.5	0.3	1.0	0.5
XL	-0.8	-0.5	-0.8	-0.1	-0.3	-0.5
Control 4	-0.2	-0.3	-0.3	0.2	-0.4	0.3
HH	2.1	2.8	1.9	2.2	1.4	1.3
LL	-1.5	-2.2	-1.8	-1.9	-1.3	-1.3
HL	1.0	0.0	0.8	0.5	1.0	1.0
LH	-1.0	-2.2	-1.8	-0.8	-0.9	-0.6

Appendix 1.2 Selection differentials of 5 week testis weight (mg).

Line	Generation 0	1	2	3	4	5
Control 1	-0.6			-1.6		
HX	0.2			7.6		
LX	0.4			-3.8		
XH	12.9	9.8	9.4	10.1	10.5	10.0
XL	-9.9	-14.5	-11.8	-6.5	-8.5	-7.8
Control 2	-0.6			2.2		
HH	10.9	7.8	11.7	11.1	9.1	8.5
LL	-6.7	-8.4	-5.2	-5.6	-10.6	-8.5
HL	-5.0	-1.0	-4.2	-3.0	-0.6	-1.3
LH	2.2	-0.8	3.7	8.0	5.9	1.4
Control 3	-1.0			5.1		
HX	2.3			2.5		
LX	-2.3			-4.4		
XH	8.7	5.4	6.4	7.6	13.0	5.2
XL	-6.9	-6.9	-5.4	-4.2	-4.5	-5.2
Control 4	-1.0			1.4		
HH	5.4	14.1	9.5	7.4	5.5	9.9
LL	-5.1	-10.8	-9.9	-7.6	-7.1	-6.9
HL	-5.8	-8.2	-4.3	-4.6	-3.3	-5.1
LH	4.3	4.7	-1.4	3.7	5.0	6.4

Appendix 1.3 Selection differentials of Index, I = 0.54W + 0.112T

	Generation					
Line	0	1	2	3	4	5
Control 1	0.2			-0.3		
HX	0.8			1.8		
LX	-0.9			-1.2		
XH	1.6	1.4	1.7	1.4	1.6	1.7
XL	-1.7	-2.3	-1.2	-0.9	-1.6	-1.3
Control 2	0.0			0.3		
HH	1.8	1.6	2.1	1.6	1.8	1.7
LL	-1.1	-1.8	-1.1	-1.3	-1.7	-1.6
HL	0.0	0.4	0.0	0.2	0.5	0.6
LH	-0.5	-1.3	-0.2	0.7	0.4	-0.8
Control 3	-0.5			0.5		
HX	0.8			0.9		
LX	-0.9			-1.3		
XH	1.7	0.8	1.4	0.9	1.8	0.8
XL	-1.1	-0.9	-0.9	-0.5	-0.6	-0.8
Control 4	-0.2			0.2		
HH	1.6	2.8	1.9	1.9	1.3	1.7
LL	-1.2	-2.2	-1.9	-1.7	-1.4	-1.3
HL	-0.1	-0.8	0.0	-0.2	0.2	0.0
LH	-0.1	-0.6	-1.0	0.0	0.0	0.3

Appendix 1.4 Selection differentials of Index, I = 0.54W - 0.112T

Line	Generation 0	1	2	3	4	5
Control 1	0.3			0.0		
HX	0.7			0.3		
LX	-0.9			-0.4		
XH	-0.9	-0.5	-0.2	-0.6	-0.5	-0.3
XL	0.3	0.6	1.2	0.4	0.1	0.3
Control 2	0.1			-0.1		
HH	-0.4	0.1	-0.3	-0.6	0.0	0.0
LL	0.2	-0.1	-0.1	-0.1	0.4	0.1
HL	1.0	0.6	0.8	0.8	0.7	0.8
LH	-1.0	-1.2	-0.9	-0.9	-0.8	-1.1
Control 3	-0.3			-0.5		
HX	0.4			0.4		
LX	-0.4			-0.4		
XH	-0.1	-0.3	0.1	-0.6	-0.8	-0.3
XL	0.3	0.4	0.1	0.4	0.3	0.2
Control 4	0.0			0.0		
HH	0.5	0.0	0.0	0.4	0.2	-0.3
LL	-0.2	0.0	0.1	-0.2	0.0	0.0
HL	1.1	0.8	0.8	0.7	0.8	1.0
LH	-0.9	-1.6	-0.8	-0.8	-1.0	-0.9

APPENDIX II - LINE MEAN LITTER MEANS BY GENERATION

Appendix 2.1 Mean litter mean body weight (g).

Line	Generation 0	1	2	3	4	5	6
Control 1	25.9	24.1	26.4	24.9	26.5	27.5	26.3
HX	25.9	24.6	25.0	26.7	24.8	29.3	27.7
LX	25.9	23.8	23.3	25.6	24.5	25.8	24.3
XH	25.9	25.4	24.3	27.4	27.3	27.9	29.3
XL	25.9	23.0	25.5	25.1	25.5	26.6	23.3
Control 2	24.2	24.2	23.3	24.8	25.6	26.2	23.9
HH	24.2	26.8	25.1	26.8	28.0	26.3	25.8
LL	24.2	27.1	24.6	24.1	25.6	26.5	24.6
HL	24.2	26.7	24.0	24.9	25.0	26.4	24.8
LH	24.2	26.1	24.1	24.0	23.7	25.8	22.8
Control 3	23.4	26.1	21.6	23.7	25.6	25.2	24.2
HX	23.4	26.0	23.9	24.4	27.6	27.6	27.4
LX	23.4	26.4	24.5	24.7	26.0	25.9	24.6
XH	23.4	27.1	24.4	26.2	29.1	27.6	25.6
XL	23.4	25.8	24.3	24.7	27.1	26.3	24.5
Control 4	24.2	24.8	24.9	24.6	26.6	26.9	24.4
HH	24.2	25.0	26.2	27.3	30.1	29.6	27.9
LL	24.2	25.4	25.0	24.9	25.8	25.5	25.0
HL	24.2	25.9	22.2	25.0	26.7	28.1	27.6
LH	24.2	25.6	21.0	23.7	24.8	23.1	24.1

Appendix 2.2 Mean litter mean testis weight (mg).

Line	Generation 0	1	2	3	4	5	6
Control 1	68.9			64.4			72.6
HX	68.9			73.6			85.6
LX	68.9			74.2			74.4
XH	68.9	69.1	72.9	80.5	87.2	91.0	95.3
XL	68.9	58.5	68.6	62.2	67.7	73.0	60.2
Control 2	60.5			61.4			55.6
HH	60.5	76.4	76.1	75.1	85.9	77.3	76.2
LL	60.5	74.4	63.6	57.9	62.7	66.8	54.9
HL	60.5	67.4	62.1	60.6	58.0	62.4	51.6
LH	60.5	69.8	66.7	66.7	74.3	87.0	71.6
Control 3	57.6			56.9			59.9
HX	57.6			60.8			68.9
LX	57.6			63.1			59.7
XH	57.6	66.2	62.5	63.8	81.3	77.6	77.4
XL	57.6	67.3	57.1	54.8	69.7	65.5	57.4
Control 4	59.6			59.1			58.9
HH	59.6	70.7	78.8	82.9	91.6	98.7	84.1
LL	59.6	69.7	68.0	67.9	73.6	70.3	62.9
HL	59.6	61.9	48.7	55.6	57.7	58.9	57.0
LH	59.6	68.0	59.5	69.6	70.8	70.1	74.5

Appendix 2.3 Mean litter mean index, I = 0.54W + 0.112T

Line	Generation						
	0	1	2	3	4	5	6
Control 1	21.69			20.68			22.32
HX	21.69			22.65			24.54
LX	21.69			22.15			21.46
XH	21.69	21.43	21.26	23.84	24.52	25.27	26.50
XL	21.69	18.97	21.45	20.55	21.33	22.54	19.32
Control 2	19.83			20.25			19.14
HH	19.83	23.03	22.05	22.86	24.75	22.80	22.46
LL	19.83	22.92	20.40	19.53	20.83	21.80	19.44
HL	19.83	21.96	19.95	20.26	20.03	21.26	19.16
LH	19.83	21.92	20.50	20.45	21.14	23.69	20.36
Control 3	19.10			19.20			19.78
HX	19.10			19.97			21.58
LX	19.10			19.64			19.98
XH	19.10	22.06	20.20	21.30	24.79	23.58	22.51
XL	19.10	21.45	19.50	19.47	22.46	21.54	19.63
Control 4	19.72			19.93			19.80
HH	19.72	21.43	22.97	24.02	26.53	27.01	24.47
LL	19.72	21.50	21.14	21.06	22.20	21.65	20.53
HL	19.72	20.93	17.45	19.73	20.85	21.80	21.28
LH	19.72	21.43	18.03	20.58	21.33	20.34	21.35

Appendix 2.4 Mean litter mean index, I = 0.54W - 0.112T

Line	Generation 0	1	2	3	4	5	6
Control 1	6.26			6.26			6.06
HX	6.26			6.16			5.38
LX	6.26			5.53			4.80
XH	6.26	5.96	4.93	5.80	5.00	4.88	5.15
XL	6.26	5.87	6.07	6.61	6.17	6.18	5.83
Control 2	6.27			6.49			6.69
HH	6.27	5.91	5.01	6.05	5.50	5.51	5.40
LL	6.27	6.29	6.16	6.55	6.80	6.85	7.13
HL	6.27	6.86	6.03	6.68	7.03	7.30	7.60
LH	6.27	6.29	5.57	5.51	4.50	4.20	4.32
Control 3	6.21			6.44			6.36
HX	6.21			6.34			6.54
LX	6.21			6.27			6.61
XH	6.21	7.23	6.19	7.00	6.59	6.21	5.17
XL	6.21	6.37	6.70	7.19	6.85	6.87	6.77
Control 4	6.37			6.68			6.60
HH	6.37	5.59	5.32	5.46	6.02	4.91	5.63
LL	6.37	5.89	6.55	7.27	5.71	5.92	6.44
HL	6.37	7.07	6.55	7.27	7.94	8.60	8.51
LH	6.37	6.21	4.70	4.99	5.47	4.64	4.65

APPENDIX III - INTRA CLASS CORRELATIONS BY GENERATION

Appendix 3.1 Intraclass correlations of 5 week body weight.

Line	Generation						
	0	1	2	3	4	5	6
Control 1	0.66	0.66	0.49	0.47	0.65	0.55	0.64
HX	0.66	0.48	0.54	0.70	0.73	0.59	0.60
LX	0.66	0.70	0.52	0.39	0.77	0.35	0.57
XH	0.66	0.64	0.55	0.61	0.62	0.31	0.54
XL	0.61	0.39	0.68	0.75	0.11	0.76	0.67
Control 2	0.54	0.59	0.60	0.69	0.30	0.36	0.71
HH	0.54	0.72	0.06	0.74	0.30	0.37	0.58
LL	0.54	0.55	0.69	0.25	0.12	0.38	0.53
HL	0.54	0.34	0.32	0.13	0.47	0.71	0.65
LH	0.54	0.63	0.39	0.66	0.58	0.56	0.53
Control 3	0.61	0.66	0.58	0.45	0.66	0.34	0.69
HX	0.61	0.58	0.70	0.51	0.68	0.26	0.88
LX	0.61	0.47	0.45	0.75	0.41	0.37	0.43
XH	0.61	0.60	0.46	0.65	0.58	0.89	0.29
XL	0.61	0.39	0.68	0.75	0.11	0.76	0.67
Control 4	0.61	0.66	0.33	0.55	0.65	0.56	0.83
HH	0.61	0.63	0.61	0.36	0.20	0.35	0.56
LL	0.61	0.67	0.23	0.50	0.30	0.82	0.43
HL	0.61	0.55	0.19	0.39	0.47	0.46	0.49
LH	0.61	0.35	0.53	0.62	0.65	0.65	0.69

Appendix 3.2 Intraclass correlations of 5 week testis weight.

Line	Generation						
	0	1	2	3	4	5	6
Control 1	0.47			0.42			0.58
HX	0.47			0.64			0.66
LX	0.47			0.63			0.72
XH	0.47	0.37	0.48	0.33	0.36	0.26	0.48
XL	0.47	0.60	0.50	0.50	0.55	0.61	0.75
Control 2	0.53			0.65			0.63
HH	0.53	0.77	0.23	0.37	0.46	0.32	0.64
LL	0.53	0.54	0.75	0.55	0.62	0.61	0.34
HL	0.53	0.50	0.11	0.51	0.64	0.57	0.60
LH	0.53	0.24	0.52	0.34	0.69	0.63	0.42
Control 3	0.65			0.45			0.19
HX	0.65			0.84			0.69
LX	0.65			0.67			0.20
XH	0.65	0.72	0.60	0.61	0.49	0.78	0.13
XL	0.65	0.49	0.53	0.49	0.67	0.65	0.63
Control 4	0.54			0.59			0.74
HH	0.54	0.22	0.64	0.53	0.41	0.42	0.23
LL	0.54	0.22	0.65	0.55	0.76	0.80	0.60
HL	0.54	0.58	0.48	0.47	0.32	0.29	0.63
LH	0.54	0.47	0.58	0.21	0.39	0.23	0.60

Appendix 3.3 Intraclass correlations of index, I = 0.54W + 0.112T

Line	Generation						
	0	1	2	3	4	5	6
Control 1	0.79			0.81			0.74
HX	0.79			0.79			0.74
LX	0.79			0.81			0.79
XH	0.79	0.73	0.75	0.72	0.74	0.65	0.69
XL	0.79	0.70	0.75	0.65	0.77	0.67	0.83
Control 2	0.74			0.87			0.85
HH	0.74	0.84	0.56	0.78	0.61	0.63	0.73
LL	0.74	0.67	0.86	0.65	0.65	0.71	0.71
HL	0.74	0.68	0.65	0.70	0.79	0.73	0.84
LH	0.74	0.78	0.81	0.71	0.83	0.76	0.86
Control 3	0.82			0.68			0.85
HX	0.82			0.86			0.88
LX	0.82			0.81			0.77
XH	0.82	0.82	0.74	0.74	0.70	0.94	0.57
XL	0.82	0.68	0.79	0.82	0.77	0.86	0.80
Control 4	0.78			0.77			0.88
HH	0.78	0.63	0.74	0.64	0.73	0.69	0.67
LL	0.78	0.69	0.69	0.71	0.85	0.88	0.76
HL	0.78	0.82	0.74	0.81	0.66	0.79	0.79
LH	0.78	0.77	0.75	0.75	0.88	0.75	0.85

Appendix 3.4 Intraclass correlations of index, I = 0.54W - 0.112T

Line	Generation 0	1	2	3	4	5	6
Control 1	0.59			0.73			0.72
HX	0.59			0.75			0.71
LX	0.59			0.71			0.71
XH	0.59	0.65	0.69	0.68	0.61	0.72	0.67
XL	0.59	0.59	0.42	0.71	0.72	0.75	0.63
Control 2	0.75			0.78			0.82
HH	0.75	0.63	0.63	0.66	0.76	0.68	0.79
LL	0.75	0.69	0.63	0.74	0.84	0.75	0.76
HL	0.75	0.77	0.74	0.74	0.82	0.77	0.76
LH	0.75	0.72	0.69	0.82	0.73	0.66	0.67
Control 3	0.76			0.73			0.67
HX	0.76			0.85			0.95
LX	0.76			0.78			0.55
XH	0.76	0.74	0.70	0.83	0.65	0.82	0.72
XL	0.76	0.75	0.83	0.79	0.70	0.76	0.85
Control 4	0.67			0.79			0.79
HH	0.67	0.72	0.72	0.59	0.78	0.70	0.77
LL	0.67	0.64	0.76	0.78	0.76	0.65	0.55
HL	0.67	0.65	0.42	0.70	0.65	0.62	0.74
LH	0.67	0.57	0.81	0.68	0.65	0.70	0.75

APPENDIX IV - MEAN LITTER SIZE BY GENERATION

Line	Generation 0	1	2	3	4	5	6
Control 1	9.4	11.8	11.5	9.8	8.5	9.9	10.1
HX	9.4	11.0	11.8	10.1	9.8	11.3	12.7
LX	9.4	12.2	12.6	8.8	9.3	9.3	9.2
XH	9.4	10.7	10.7	10.3	10.9	11.8	11.0
XL	9.4	11.7	11.1	7.4	9.3	11.5	10.8
Control 2	10.0	12.3	10.9	9.8	10.4	10.2	11.8
HH	10.0	11.9	10.0	9.5	9.1	9.2	12.0
LL	10.0	9.5	11.0	9.6	9.4	11.1	9.0
HL	10.0	12.1	10.5	10.4	10.6	9.4	11.3
LH	10.0	11.1	10.4	9.9	10.7	10.9	11.9
Control 3	10.1	10.2	7.8	9.5	9.5	10.5	9.3
HX	10.1	10.7	9.1	8.8	8.8	10.8	11.5
LX	10.1	10.9	12.4	11.0	11.4	11.0	11.6
XH	10.1	10.5	9.5	9.8	8.5	9.6	9.4
XL	10.1	10.8	8.8	9.5	7.7	9.3	10.4
Control 4	10.8	12.0	9.3	10.7	8.6	12.9	10.6
HH	10.8	11.2	11.2	10.2	10.8	10.0	12.5
LL	10.8	11.7	10.5	9.3	11.9	12.2	10.6
HL	10.8	10.4	10.1	8.9	9.6	10.0	10.7
LH	10.8	10.7	8.7	9.0	11.4	11.2	10.5