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Weight and age at puberty in female and male mice of strains selected for large and small body size

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SUMMARY

Puberty was studied in mice of the ninth selected generation of the Q-strain. There were 6 replicate lines selected for large body size (6-week weight), 6 replicates selected for small size and 6 replicate unselected controls. Female puberty was assessed by the opening of the vagina and male puberty by the first copulation plug. The sexes differed in the mean age at puberty, males being older by 13 days in the large, 4 days in the control and 8 days in the small lines. The sexes differed also in the way size affected puberty. In males the large and small lines reached puberty at the same age and both were older than the controls. In females the large lines on average were heavier and younger at puberty than the controls, and the small lines were lighter and older than the controls, though not significantly older. The replicates within each size-group, however, reached puberty at about the same weight, irrespective of their differences in growth rate. Thus, the differences of growth between the large, control and small groups affected both the weight and the age of females at puberty, but the differences of growth between the replicate lines within each size affected only the age at puberty. No explanation was found for this inconsistency between size-groups and replicates. Several lines of evidence led to the conclusion that in females puberty is partly or mainly weight-dependent, whereas in males it is almost wholly age-dependent.

1. INTRODUCTION

The work described here was done in order to find out how puberty, or the attainment of sexual maturity, was affected by genetic differences in growth rate and body size that had been produced by selection. Puberty is an event that occurs during development. It can be depicted as a point on an individual's growth curve. The position of the point on the growth curve can be expressed either as the body weight or as the age at which puberty occurred. A question of interest is whether puberty is mainly weight-dependent or age-dependent. Individuals vary in their growth rates. Do they tend to reach puberty when they have attained a particular weight (weight-dependence) or when they have reached a particular age (age-dependence)? Earlier work on an unselected random-bred strain suggested that puberty in female mice was mainly weight-dependent (Monteiro & Falconer, 1966). The basis for this conclusion was that the variance of weight at puberty was less than the variance of weight at a fixed age. The main purposes of the present work were to see if this conclusion would be borne out when the growth rate of this strain was altered by selection, and to investigate puberty in males in relation to their weight and age. The weights and ages at puberty were recorded when the strain had been subjected to nine generations of two-way selection for large and for small size with an unselected control.

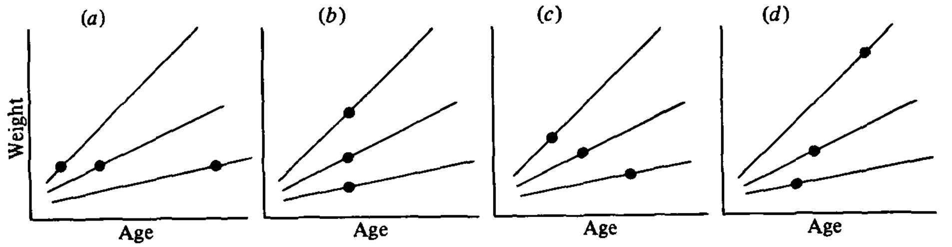

Fig. 1. Diagrams of weight-dependence and age-dependence of puberty. Three growth curves with the event of puberty marked on each. (*a*) Pure weight-dependence. (*b*) Pure age-dependence. (*c*) Dependence on both weight and age, negative association. (*d*) Positive association of weight and age.

There are two ways by which weight-dependence and age-dependence may be distinguished. Fig. 1 shows three growth curves which might represent three individuals in one strain or the means of the large, control and small strains. (The growth is shown as being linear, which is not far from the truth over the range of ages at which puberty occurs.) The event of puberty is marked on each curve. With pure weight-dependence (Fig. 1 *a*) the variance of weight at puberty is zero, and the regression of weight at puberty on age at puberty is zero. With pure age-dependence (Fig. 1 *b*) the variance of age at puberty is zero and the variance of weight at puberty is equal to the variance of weight at a fixed age, i.e. at the age of puberty; the regression of age on weight at puberty is zero and the regression of weight on age at puberty is infinite. Fig. 1 (*c*) shows a relationship intermediate between (*a*) and (*b*); puberty is partly weight- and partly age-dependent. Here the variance of weight at puberty is less than the variance of weight at a fixed age (the mean age at puberty), and the regression of weight on age at puberty is negative. If puberty is determined partly by weight and partly by age as depicted in Fig. 1 (*c*), it is of interest to quantify the relative importance of weight and age as determinants of the point on the growth curve at which puberty occurs. The means by which this may be done will be explained after the first of the results have been presented. A fourth possible relationship between weight and age at puberty is shown in Fig. 1 (*d*). Here the individuals or groups that are heavier at puberty are also older; the regression of weight on age at puberty is positive and the variance of weight at puberty is greater than the variance of weight at fixed age. This is the relationship found when species of different body sizes are compared. Larger species have, in general, a longer life-span and are slower in developing. At puberty, therefore, the larger species are heavier and older.

There has, of course, been much work done previously on the relation of female puberty to weight and age, though little on male puberty. Some of the previous work will be considered in conjunction with the results and in the discussion.

2. MATERIALS AND METHODS

(i) *Strains*

The mice that provided the data were the Q-strains described by Falconer (1973). Two-way selection for 6-week weight had been applied for 9 generations, and the Large strains were then on average 52 % heavier at 6 weeks than the Small strains. There were also some data on female puberty obtained by Mills (1973) after 18 generations of selection. The structure of the Q-strain was as follows. There were three 'size-groups', namely the selected Large, the selected Small, and the unselected Control. Each size-group consisted of six replicate lines which had been selected independently from the base population, or random bred in the case of the Controls. A question of importance for the present study is whether there was any inadvertent selection against late sexual maturity. Mated pairs that failed to produce litters were not discarded until well beyond the latest observed age of puberty, so only at most a trivial amount of selection against late sexual maturity can have occurred.

(ii) *Data*

The mice for use were weaned at 3 weeks of age. For the recording of female puberty 8 mice were taken from each replicate, as far as possible 2 from each of 4 litters. These litters were the first litters of Q-strain parents contemporaneous with generation 9 of the selected strains. The 8 females were housed in 2 cages, 4 per cage, from weaning. They were examined daily for the opening of the vagina, which was taken to be the indicator of puberty. On the day the vagina was found to be open the mice were weighed and their age was recorded, thus giving the weight and age at puberty, which will be symbolized by W_P and A_P respectively. They were also weighed at 3 weeks and at 6 weeks of age. To see if there was any evidence of synchrony among mice housed together in the same cage, an analysis of variance was carried out for both weight and age at puberty. No significant variance between cages was found. The records of female puberty were obtained during a period of about one month in August 1966, the mice being maintained under natural lighting. Vaginal opening does not necessarily coincide with functional puberty because the first oestrus occurs some days after the opening of the vagina. Furthermore, the interval between the two may vary with the age at which they occur or with the rate of growth. Thus Drickamer (1981) reported an interval of about 9 days in an unselected control strain, but intervals of 4 and 18 days respectively in strains selected for early and for late first oestrus. Working with rats fed two different diets, Frisch *et al.* (1975) found an interval of 1 day in the fast-growing group and 3 days in the slow-growing group. For these reasons the conclusions drawn here about vaginal opening may not be true of first oestrus.

For male puberty, mice from the second litters of the same parents were used.

There were again 8 mice from each replicate. Each male was housed in a separate cage at weaning. Each was given 2 females from the first litters which were at least 6 weeks old. These females were examined daily for vaginal plugs, which were taken to indicate puberty of the male. The weight and age of the male were recorded on the day when his first plug was found. The males were also weighed at 3 and 6 weeks of age. The records of female puberty showed that all the females used to test the males would have been sexually mature well before the males were ready to mate. The assessment of male puberty was, however, subject to some error due to the females because a male cannot mate if neither of his females is in oestrus. If the two females were cycling synchronously with a cycle of 4 days the observation of male puberty cannot have been more than about 2 days late on average. After the recording of the vaginal plug the females were left to give birth to a litter and the date of birth was recorded. This showed whether the first plug represented a fertile mating. The percentage of first plugs that proved to have been fertile was 47 % in the Large and the Small size-groups but only 21 % in the Control. It is, of course, not known whether the failure to produce a litter was due to lack of fertility in the male or to failure of the female to bring the litter to term. There was only one case in which the first litter born showed that the first plug had not been observed.

There were a few losses of animals between weaning and puberty. The number of animals in each size-group from which data on puberty were obtained are given in Table 1. The distributions of weights and ages at puberty did not depart from normality enough to require the use of any scale transformation before analysis.

The mice that gave records of puberty were not weighed at any ages other than 3 weeks, 6 weeks and puberty. However, data on life-time growth were obtained from mice of the next generation. The uses of these generation-10 data will be explained with the results.

3. RESULTS

(i) *Size-groups*

The size-groups will be examined first, then the replicates within the size-groups, and finally the individuals. To give an impression of the differences of growth between the size-groups the growth of the generation-10 mice up to 18 weeks, and their final weights, are given in Fig. 2. The means of the size-groups for all measurements on the generation-9 mice in which puberty was recorded are given in Table 1. We may first note that the males were older at puberty than the females in all three size-groups, the mean difference being 8 days. It is possible, however, that if female puberty had been assessed by the first oestrus there might have been little difference in age between the sexes.

Fig. 3 shows the size-group means of weight at puberty (W_P) plotted against age at puberty (A_P). Consider first the females in Fig. 3(a), where the data from generation 18 obtained by Mills (1973) are also shown, marked by the smaller symbols. Compared with the Controls, the Large mice are heavier at puberty and also younger, both differences being significant in the generation-9 data. The Small mice are less heavy than the Controls and older, but only the differences in W_P are significant in the generation-9 data. The generation-18 data are fully consistent with those of generation 9, reflecting the changes in growth resulting from the continued selection. Clearly puberty in females occurs neither at a fixed weight nor at a fixed age when strains differing genetically in body size and growth rate are compared. The regression of W_P on A_P is like Fig. 1 (*c*). The weight-dependence found by Monteiro & Falconer (1966) in the strain before selection does not apply when the strain becomes genetically differentiated in body size.

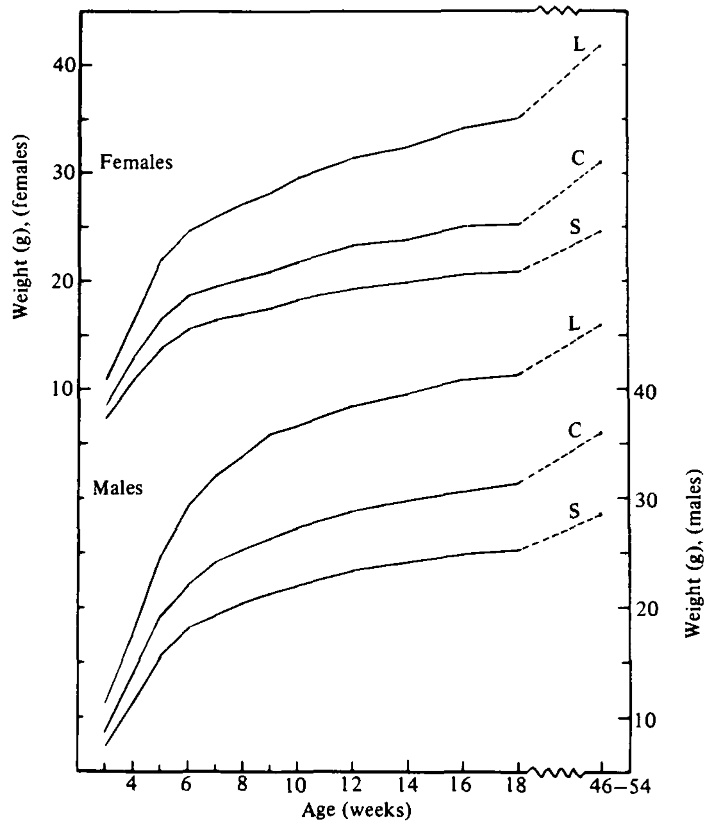

Fig. 2. Mean growth curves of generation-10 mice from 3 to 18 weeks, and final weights at 46–54 weeks.

Fig. 3 (*a*) suggests that the changes in female puberty have been asymmetrical in the Large and Small selected groups; when compared with the Controls, puberty in the Small mice seems to be less weight- and more age-dependent that it is in the Large mice; in other words, it looks as if two regression lines with different slopes are needed to fit the points in the figure. When two linear regressions are fitted, however, one to the four points for Large and Control and the other to the four points for Small and Control, the slopes are not significantly different ($P = 0{\cdot}08$). Furthermore, it will be obvious from the variation of the replicate means in Fig. 5 that a single regression line will adequately fit the three size-group means of

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Table 1. *Size-group means*

(Each mean is the mean of replicate-means and the standard errors are based on the variance of replicate-means with 5 d.f. Ages are in days, weights in grams.)

		Large	Control	Small
Females				
Generation 9				
Number	n	44	47	45
Age at puberty	A_P	32·32 ± 1·18	36·26 ± 1·26	37·28 ± 1·17
Weight at puberty	W_P	20·72 ± 0·53	17·98 ± 0·30	15·53 ± 0·20
3-week weight	W_3	10·38 ± 0·60	9·31 ± 0·58	7·51 ± 0·35
6-week weight	W_6	25·23 ± 0·65	19·98 ± 0·79	16·63 ± 0·24
Generation 10				
6-week weight	W_6	24·57 ± 0·71	18·60 ± 0·52	15·45 ± 0·24
Final weight	W_F	41·83 ± 1·16	30·83 ± 1·22	24·60 ± 0·50
Males				
Generation 9				
Number	n	37	42	37
Age at puberty	A_P	45·51 ± 2·07	40·35 ± 1·14	45·11 ± 1·06
Weight at puberty	W_P	31·62 ± 1·35	23·74 ± 0·87	20·64 ± 0·38
3-week weight	W_3	11·47 ± 0·51	9·86 ± 0·25	7·88 ± 0·33
6-week weight	W_6	31·02 ± 0·95	24·73 ± 0·68	20·36 ± 0·52
Generation 10				
6-week weight	W_6	29·15 ± 0·94	22·04 ± 1·24	18·15 ± 0·30
Final weight	W_F	45·85 ± 1·29	35·97 ± 1·51	28·52 ± 0·58

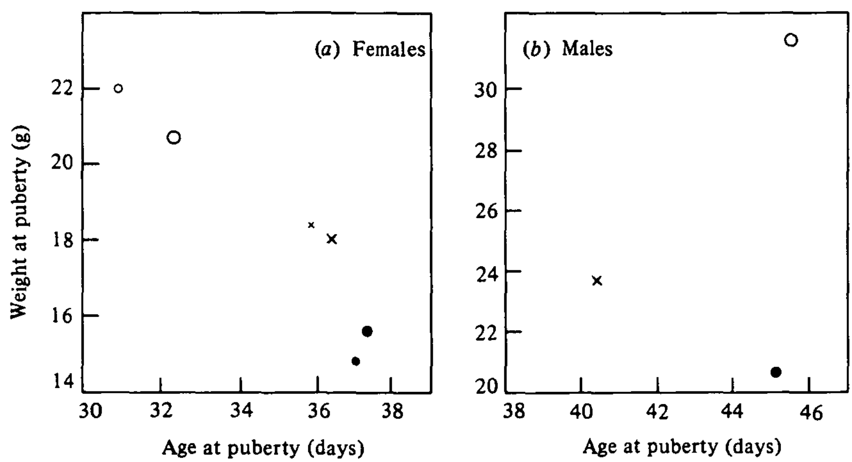

Fig. 3. Size-group means of weight at puberty and age at puberty. Open circles, large; crosses, control; filled circles, small. The smaller symbols in (*a*) refer to generation 18.

generation 9 in Fig. 3. Thus there are no good grounds for thinking that the Large and Small size-groups are asymmetrical or inconsistent.

The males, in Fig. 3 (*b*), show a different picture. The weights at puberty are different, all the differences between size-groups being significant. The Large and Small mice, however, have the same age at puberty, both being significantly older

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than the Controls. Thus puberty in males seems to be age-dependent, the regression of W_P on A_P being like Fig. 1 (*b*). This conclusion, however, is a little dubious on account of the anomalous position of the Controls. It will be remembered that a smaller percentage of the Controls were fertile at their first plug, but their age at the first fertile plug was also below those of the Large and Small groups, so this does not seem able to account for their anomalous position.

Relative importance of weight and age

In the females the occurrence of puberty depends on both weight and age. How can one assess the relative importance of weight and age as determinants of puberty? The two are in different units, grams and days, so they cannot be directly

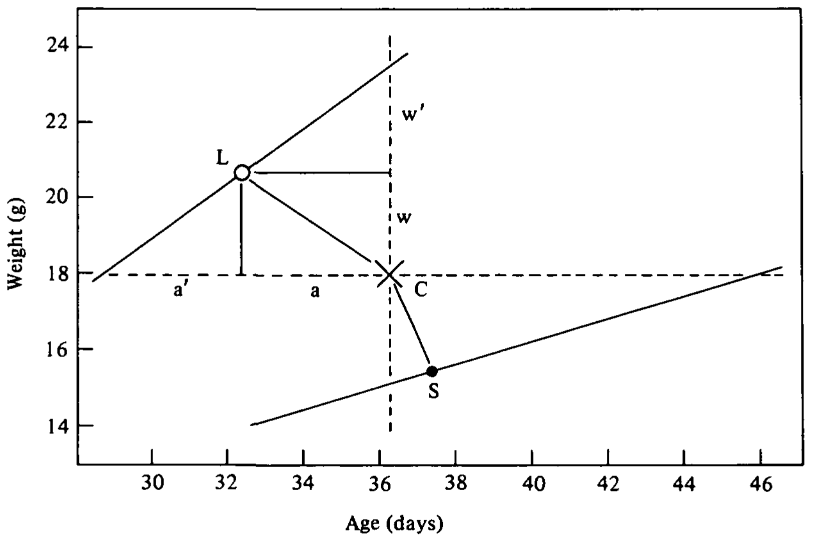

Fig. 4. Diagram to illustrate the relative importance of weight and age, as explained in the text.

compared. We can, however, render them comparable in the following way. We first find the 'equivalence' of grams and days as determinants of puberty. Fig. 4 shows the weight and age at puberty of the three size-groups with the approximate growth curves of the Large and Small groups. Let the values of the Controls be considered as 'targets'. The Large females reach the target weight when they are still a long way below the target age. Puberty is therefore deferred until the effect of being under age balances the effect of being overweight. When puberty occurs the excess of weight is 'equivalent' to the deficiency of age. Thus, for the differences between the Large and Control females

$$W_P(L) - W_P(C) \quad \text{is equivalent to} \quad A_P(L) - A_P(C)$$

or, referring to the lengths of the lines marked in Fig. 4,

$$w \text{ grams is equivalent to } a \text{ days.}$$

Taking the values for the Large and Control groups from Table 1 we find

2·74 grams is equivalent to −3·94 days

or

1 g is equivalent to −1·44 d

or

0·70 g is equivalent to −1 d.

This latter figure of −0·70 g/d is the regression of W_P on A_P, which is the slope of the line joining the L and C points in Fig. 4. The negative sign indicates that weight and age are antagonistic; an excess of weight is balanced by a deficiency of age.

Approximate standard errors of the regression slope can be calculated from the sampling variances of the mean W_P and mean A_P, which are available for the generation-9 data; they are the squares of the standard errors given in Table 1. The L–C regression slope is $-0·70 \pm 0·34$, and the S–C slope is $-2·4 \pm 4·1$. In view of the very large standard error of the S–C slope it would be pointless to calculate the weight and age equivalence from the Small mice. Averaging the size-groups by taking the linear regression fitted to the three points of puberty gives $1·0 \pm 0·3$ g, equivalent to −1 d.

To render age in days commensurate with weight in grams we have to find the weight increment that corresponds to a particular age increment. This can be done if the growth rate is known and is assumed to be constant over the relevant period. The growth increment corresponding to the age increment of a days is marked w' in Fig. 4, and $w' = Ga$, where G is the growth rate in grams per day. The growth rate of the Large females at the mean age of puberty was estimated as approximately 0·75 g/d. (Details of how this estimate was made will be given in a later section.) As seen above, $a = -3·94$ d, so $w' = 0·75 \times (-3·94) = -2·96$ g. Thus 2·74 grams of weight (i.e. w) is equivalent to −2·96 'grams of age' (i.e. w').

To see how these values are to be converted into the relative importance of weight and age we change our viewpoint and consider the prediction of puberty and the errors of this prediction. The weight and age at puberty of the Controls can each be regarded as predictors of the weight at puberty of the Large group. Predicted from the weight of the Controls, the error in the weight of the Large is w, and predicted from the age of the Controls the error in the weight of the Large is w'. The relative importance of weight and age as determinants of puberty is the inverse of the relative errors. Thus, neglecting the negative sign which is now irrelevant, the relative importance of weight can be expressed as $w'/w = 2·96/2·74 = 1·08$, which means that weight is 1·08 times as important as age.

The above calculation can be simplified by noting that the regression of W_P on A_P is $b = w/a$. So $w = ba$ and, as seen above, $w' = Ga$. Therefore $w'/w = G/b$. Thus only the growth rate and the regression of W_P on A_P need be known to evaluate the relative importance. The relative importance can equally well be assessed by considering the errors in estimating age at puberty. The relative importance of age is then $a'/a = b/G = 0·93$.

The interpretation of the size-group means leads to the conclusion that weight

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and age are of roughly equal importance as determinants of female puberty. It should be emphasized that this is only a very rough estimate because growth rates are not the same in all individuals and are not constant, and because only the Large and Control groups have been used. It should be noted also that the 'equivalence' of grams and days might be found to differ according to the age of puberty for the following reason. As growth proceeds the proportion of fat in the growth increment increases, and the occurrence of puberty may be influenced differently by lean weight and fat weight (Frisch, Hegsted & Yoshinga, 1977).

The data for male puberty in Fig. 3(*b*) cannot be treated in the above manner because the Controls are not intermediate in age. If there were no Controls and we had only the Large and Small groups to compare we would conclude that male puberty is 100% age-dependent.

The foregoing evaluation of the relative importance of weight and age refers to the size-groups. It describes how the occurrence of puberty has reacted to the genetic changes of growth rate produced by selection. It does not tell us anything about differences of growth rate between individuals within the size-groups. Differences within the size-groups are considered in the next sections.

(ii) *Replicates within size-groups*

We next consider the replicates in each size-group. Fig. 5 shows the mean weight at puberty (W_P) of each replicate plotted against its mean age at puberty (A_P). The broken line connects the means of the size-groups. The continuous straight lines are the regressions of W_P on A_P fitted within each size-group. The regression coefficients are given in Table 2.

Table 2. *Regression* (±S.E.) *of weight at puberty on age at puberty, based on replicate-means within size-groups, and tests of significance of differences between the slopes and the elevations*

(Weights are in grams, ages in days.)

	Large	Control	Small	Pooled within size-groups
Females				
b (W_P on A_P)	0·34 ± 0·15	−0·16 ± 0·09	0·09 ± 0·08	0·08 ± 0·08
t (D.F.)	2·33 (4)	1·85 (4)	1·20 (4)	0·99 (14)
$F_{2,12}$ (slopes)	—	—	—	5·68*
$F_{2,14}$ (elevations)	—	—	—	(36·39***)†
Males				
b (W_P on A_P)	0·46 ± 0·23	0·40 ± 0·33	−0·05 ± 0·18	0·36 ± 0·14
t (D.F.)	1·99 (4)	1·20 (4)	0·29 (4)	2·57* (14)
$F_{2,12}$ (slopes)	—	—	—	0·87
$F_{2,14}$ (elevations)	—	—	—	44·16***
Sexes combined				
b (W_P on A_P)	0·43 ± 0·22	0·09 ± 0·54	0·03 ± 0·27	0·25 ± 0·13
t (D.F.)	2·00 (9)	0·16 (9)	0·09 (9)	1·99 (29)

* $P < 0·05$, *** $P < 0·001$.

† This test of significance is not strictly valid because the slopes differ significantly.

The females, in Fig. 5 (*a*), show a picture totally different from that shown by the size-group means. Within each size-group the replicates reach puberty at nearly the same weight but at widely different ages. The regressions of W_P on A_P within size-groups are not significantly different from zero, indicating weight-dependence of puberty in females, as in Fig. 1 (*a*), with age having no significant effect on the occurrence of puberty. The replicates in the different size-groups will clearly not all fit on a single regression line of W_P on A_P. Significance tests are given in Table 2.

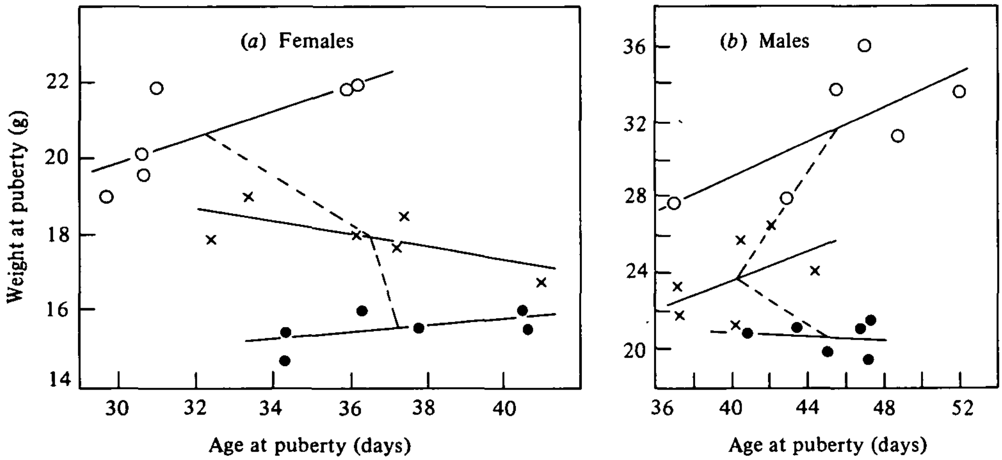

Fig. 5. Replicate-means of weight at puberty and age at puberty. Open circles, large; crosses, control; filled circles, small. Continuous lines are regressions of weight on age within each size-group (see Table 2). Broken lines connect the size-group means.

The males, in Fig. 5 (*b*), present a picture that looks much like that of the females. The three regression slopes do not differ significantly from each other and none is itself significantly different from zero, but unlike the females the pooled regression is significantly different from zero. The differences of elevation of the regression lines are very highly significant, showing that the replicates in the different size groups will not fit on a single regression line.

The two sexes do not differ significantly from each other in any of the size-groups. The combined regressions, pooled within sexes, are given in Table 2. None of these is significantly different from zero, but the regression in the large group and the regression pooled over size-groups both approach significance ($P = 0{\cdot}076$ and $0{\cdot}056$ respectively). If these positive regressions of W_P on A_P are real, could they be accounted for by differences of developmental rate and life-span? It was pointed out in the introduction that a positive regression, as in Fig. 1 (*d*), is expected if the larger groups develop more slowly, and if they develop more slowly they might be expected to have longer life-spans. Data on the life-spans of the replicates were available from generation 10 and will be summarized later. There was, however, no significant correlation between age at puberty and life-span, so differing life-spans among the replicates do not seem able to account for a positive regression of W_P on A_P.

Though females and males have similar regressions of W_P on A_P, a marked contrast between the sexes is revealed by analysis of variance, as follows. Hierarchical analyses of variance were carried out for both W_P and A_P and the components of variance between replicates within size-groups were calculated. Table 3 summarizes the results in terms of significance levels and gives the components as percentages of the totals within size-groups. In females, replicates differ significantly in A_P but not in W_P. In males the situation is reversed; replicates differ significantly in W_P but not in A_P. In females, the between-replicate

Table 3. *Significance of differences between replicates within size-groups in respect of age at puberty* (A_P) *and weight at puberty* (W_P)

(σ^2_b % is the component of variance between replicates pooled within size-groups as a percentage of the total individual variance within size-groups.)

	Females					Males				
	L	C	S	Pooled	σ^2_b %	L	C	S	Pooled	σ^2_b %
A_P	**	**	**	***	27	—	—	—	—	2
W_P	—	—	—	—	8	**	*	—	***	26

—, Non-significant; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Table 4. *Components of variance between replicates within each size-group, in respect of weight at puberty* (W_P) *and weight at the fixed ages of 3 weeks* (W_3) *and 6 weeks* (W_6)

	Females			Males		
	L	C	S	L	C	S
W_3	1·88	1·82	0·45	—	—	—
W_6	2·14	3·08	0·05	4·45	1·40	0·47
W_P	0·86	0·03	0·06	8·82	3·04	(−0·25)

component as a percentage of the total variance of individuals within size-groups is 27 % for W_P and 8 % for A_P; in males it is 2 % for W_P and 26 % for A_P. Thus the replicates within size-groups indicate mainly weight-dependence of puberty in females and mainly age-dependence in males. Table 4 gives the variance of weight at puberty for comparison with the variance of weight at a fixed age. As pointed out in the introduction, the difference in these variances depends on the extent to which puberty is weight- or age-dependent. The fixed ages for which we have data are at 3 weeks and 6 weeks. The mean age of puberty in females is between 4·5 and 5·5 weeks, so the variance of weight at the mean age of puberty should be somewhere between the variances at 3 and at 6 weeks. The mean age of puberty in males is close to 6 weeks, so the variance at 6 weeks will give a reasonable comparison. The variances in Table 4 are the components of variance between replicates within each size-group. In females the variance of W_P is much less than the variance at fixed age, which indicates mainly weight-dependence. In males the variance of W_P is greater than the variance of W_6 in the Large and Control groups. With pure-age-dependence the two would be expected to be equal, so by the criterion of variances the Large and Control replicate-means indicate pure age-dependence of male puberty. The Small males gave a negative estimate of the W_P component and the same conclusions cannot be drawn about them.

The replicate-means are consistent with the size-group means in showing that males and females differ, male puberty being less weight-dependent than female puberty. They are consistent also in that male puberty seems to be purely age-dependent. There is, however, a puzzling inconsistency in the females. By the criterion of the regression of W_P on A_P the replicate-means indicate pure weight-dependence of female puberty, whereas the size-group means showed weight and age to be about equally important.

(iii) *Individual values and 'developmental' variance*

The individual values of weight and age at puberty are plotted in Fig. 6. The replicates in each size-group are not distinguished. The regression of W_P on A_P tends to be positive, particularly in the Large mice. The regressions in the different size-groups are similar to those of the replicates in Fig. 5, though they are more strongly positive. In the case of the individual values an explanation of the positive regressions can be found in what may be termed 'developmental' variance. This will be explained before the regressions are further commented on.

Developmental variance

Consider a number of individuals all growing along the same growth curve. We cannot expect them all to reach puberty at the same point on the curve; the event of puberty will be distributed along the growth curve as indicated in Fig. 7(*a*). If puberty is an event that signals a particular 'developmental age' we may say that individuals vary in their developmental age at any point of their chronological age; or alternatively that individuals vary in the developmental age at which puberty occurs. This variation among individuals following the same growth curve will therefore be called 'developmental' variance. It causes variation of both W_P and A_P. It may be both genetic and environmental in origin, and it is independent of variation of growth rate or weight at a fixed age. The existence of this developmental variation of puberty in female mice has been proved by a selection experiment by Drickamer (1981). Selection in both directions was made for age at puberty. Responses in both directions were obtained, with a realized heritability of 48·5 %, but the growth rate was not changed. The differences between the means of the size-groups and of the replicates which have been the subject of the previous sections are not subject to the developmental variation, or at most are affected by only a small fraction of it. Developmental variance is thus a factor affecting the relation of W_P to A_P that is present in individual values but not in group means. The way in which developmental variance affects the relation of W_P to A_P is as follows.

If all individuals really were growing along the same growth curve as in Fig. 7(*a*), then W_P and A_P would be completely correlated positively, and the regression of W_P on A_P would be simply a measure of the growth rate. Now consider individuals growing along different growth curves as in Fig. 7(*b*) and (*c*),

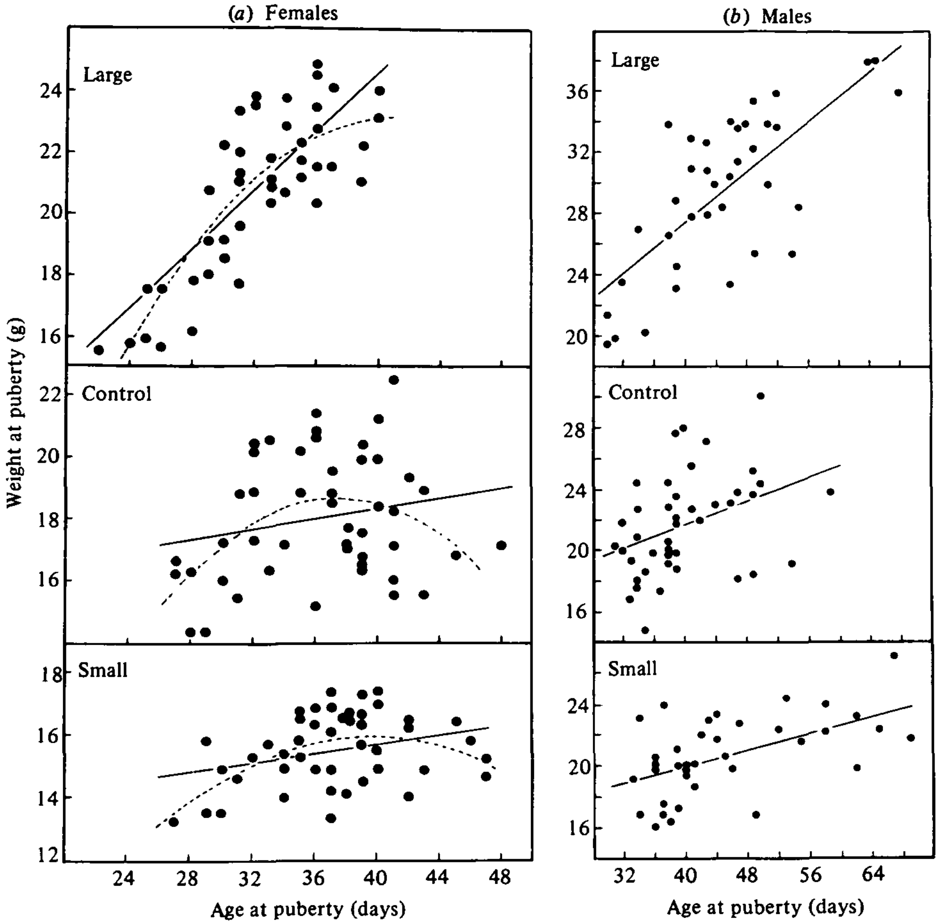

Fig. 6. Individual values of weight at puberty and age at puberty. For regressions see Table 5.

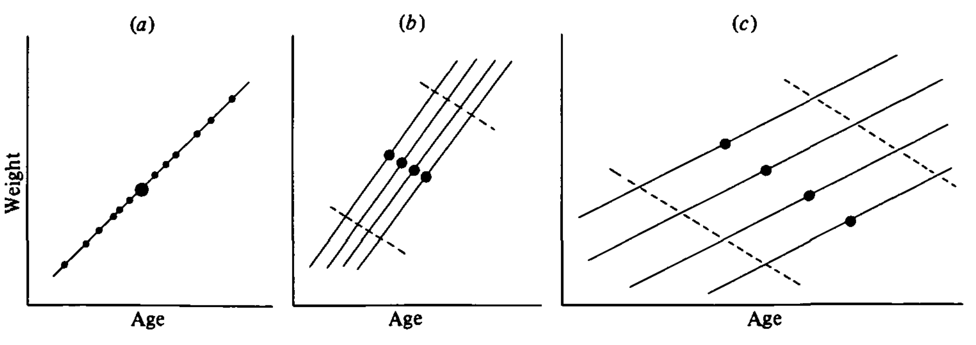

Fig. 7. Diagram illustrating 'developmental' variance of puberty, as explained in the text.

where the growth curves are shown for simplicity as linear and parallel. The point on each growth curve marks the mean, or expected, weight and age at puberty of individuals growing along that curve. These expected points of puberty are shown as having a negative regression of W_P on A_P like the size-group means in females. The developmental variance about the mean point of puberty of each growth curve is assumed to be the same for all growth curves. The extent of the variation due to developmental variance is indicated by the range of the variation shown as broken lines in the figures. The individual points of puberty will be distributed within the parallelogram bounded by the range of developmental variance and by the upper and lower growth curves. Inspection of the figures will show that the regression of W_P on A_P must tend to be positive. It is not possible to be precise about the magnitude of the regression because this depends on too many unknown factors – the growth rate, the variance of growth rate, the variance of weight at fixed age, the regression in the expected values, and how the developmental variance is expressed in individuals with different growth rates. By comparison of Fig. 7 (*b*) with (*c*) it can be seen, however, that the regression will be greater if growth is faster or if the growth curves are closer together (i.e. with less variance of weight at fixed age) as in Fig. 7 (*b*), than if growth is slower or the growth curves further apart (i.e. with more variance of weight at fixed age) as in Fig. 7 (*c*). The observed regressions agree with this expectation, in that the Large mice have the highest growth rates and the highest regressions.

The real growth curves are not linear, the growth rates being greater at first and less later. Therefore the regression of W_P on A_P should be curvilinear, being steeper at the earlier ages and less steep later. Both linear and curvilinear regressions were calculated, the curvilinear being a second-order polynomial. The regression coefficients are given in Table 5. The curvilinear regression gave a significantly better fit than the linear in the females of all three size-groups, though the shapes of the curves fitting the Control and Small groups are obviously unrealistic. The curvilinear regressions did not significantly improve the fit in any of the males. Both regression lines are drawn for the females in Fig. 6, but only the linear regressions for males. The linear regressions are all positive and significant in most cases; they are not significantly different in the two sexes.

The positive and curvilinear regressions are in general agreement with previous studies of female puberty. For example, Wilen & Naftolin (1978) found a positive regression of W_P on A_P in rats. The regression was higher in 'well-fed' rats ($b = 3{\cdot}4 \pm 0{\cdot}43$) than in rats with a lower growth rate resulting from feed-restriction ($b = 1{\cdot}23 \pm 0{\cdot}20$). Significant curvilinearity was found by Eisen (1973) in mice, the regression of W_P on A_P having the same general shape as found here in the Large females.

Estimates of variances

It is possible to get estimates, at least rough ones, of the developmental variances. The developmental variance of W_P or of A_P is the variance that would be observed if all individuals followed the same growth curve, or in other words if weights at all fixed ages were held constant. We have weights of individuals at two fixed ages, 3 weeks (W_3) and 6 weeks (W_6). By holding these two weights

Table 5. *Regression* (± S.E.) *of* W_P *on* A_P *from individual values, within size-groups*

(The linear regression is $y = a + bx$ and the curvilinear is $y = a + b_1x + b_2x^2$, where $y = W_P$ and $x = A_P$. The units are grams and days. For numbers of animals see Table 1.)

		Females			Males		
		Large	Control	Small	Large	Control	Small
				Linear			
	a	5·2	12·7	15·1	13·0	15·8	14·7
	b	0·48 ± 0·06	0·08 ± 0·06	0·075 ± 0·036	0·41 ± 0·07	0·20 ± 0·07	0·13 ± 0·04
	r^2	0·64	0·04	0·09	0·53	0·15	0·29
Regression		$P < 0·001$	$P \sim 0·2$	$P \sim 0·05$	$P < 0·001$	$P < 0·02$	$P < 0·001$
				Curvilinear			
	a	−20·8	−19·6	−7·7	−4·6	−10·0	+10·2
	b_1	2·15 ± 0·64	2·04 ± 0·69	1·19 ± 0·39	1·18 ± 0·49	1·43 ± 0·81	0·32 ± 0·40
	b_2	−0·026 ± 0·010	−0·027 ± 0·009	−0·015 ± 0·005	−0·008 ± 0·005	−0·014 ± 0·009	−0·002 ± 0·004
	R^2	0·69	0·19	0·24	0·56	0·20	0·30
Curvilinearity		$P < 0·02$	$P < 0·01$	$P < 0·01$	$P > 0·1$	$P > 0·1$	$P > 0·5$

constant the remaining variance should be a reasonably good approximation of the developmental variance. Accordingly multiple regressions of W_P on W_3 and W_6, and also of A_P on W_3 and W_6, were calculated and the residual variances (i.e. the mean square for deviations from regression) were taken as estimates of the developmental variance of W_P and of A_P respectively. The regressions will be considered more fully later; here we are concerned only with the residual variances These, labelled developmental, are given in Table 6, with the observed (total) variances for comparison. (The variances of W_3 and W_6 are also given though no conclusion will be drawn from them.)

Table 6. *Variances of individual values within size-groups, and estimates of developmental variances*

	Females			Males		
	L	C	S	L	C	S
Variances						
Observed						
W_3	3·60	3·06	2·31	4·30	4·37	3·58
W_6	4·05	7·59	2·39	11·50	8·64	6·59
W_P	7·00	4·08	1·34	26·78	10·95	6·52
A_P	19·16	24·88	21·89	83·67	42·83	105·24
Developmental						
W_P	6·48	3·62	1·24	13·29	5·33	4·12
% of observed	93	89	93	50	49	63
A_P	8·77	9·43	12·59	84·82	41·84	100·64
% of observed	46	38	57	100	98	96
Growth rate, g/d						
From $(\sigma^2_W/\sigma^2_A{}^{\frac{1}{2}}$	0·86	0·62	0·31	0·40	0·36	0·20
From $(\sigma^2_W/\sigma^2_A)^{\frac{1}{2}}$	0·75	0·40	0·30	0·41	0·42	0·20

Consider the females first. The developmental variance of weight at puberty amounts to about 90% of the total variance of W_P, the remaining 10% being associated with individual differences in the weights at fixed ages. The developmental variance of age at puberty, on the other hand, amounts to roughly 50% of the total, leaving 50% as being associated with differences in weights at fixed ages. The data from individuals therefore seem to show female puberty to be mainly weight-dependent, though it is not possible to be precise about the relative importance of weight. In males the situation is reversed; the variance of W_P contains roughly 50% of developmental variance, but the variance of A_P is virtually all developmental variance. (The slight excess of the developmental variance over the total in Large males is due to expressing these as mean squares rather than as sums of squares.) The individuals therefore show male puberty to be almost entirely age-dependent, though again it is not possible to be precise.

A test of the validity of the idea of developmental variance and of the reliability of its estimates can be made as follows. Developmental variance causes variation of both W_P and A_P. The amounts of the two variances so caused are simply related to each other by the growth rate. Consider the individuals with the same growth curve depicted in Fig. 7(*a*). Deviations of individuals from the mean are related thus (dropping the subscript P for the moment): $(W-\bar{W})/(A-\bar{A}) = G$, where G is the growth rate. All the variance here is developmental because there are no differences in growth rate. Therefore, if growth rates are the same in all individuals, the developmental variances will be related thus: $\sigma^2_W/\sigma^2_A = G^2$, and the square root of the ratio of the developmental variances estimates the growth rate. The growth rates estimated in this way are given in Table 6. The observed growth rates needed for comparison are the growth rates at the mean age of puberty. These were calculated from the weekly weights available for the generation-10 mice. The weekly weights were first adjusted proportionately to the 6-week weights of the generation-9 mice (which gave the puberty data), and the growth rate at the mean age of puberty was then obtained by interpolation between the growth rates in two consecutive weeks. The estimates so obtained are given in the last line of Table 6. The agreement between the two estimates is reasonably good in view of the fact that the assumed equality of individual growth rates is certainly not true. The test therefore shows that the idea of developmental variance and the estimates of it cannot be seriously wrong.

The conclusions to be drawn from the analysis of the individual values are as follows. The existence of developmental variation of puberty accounts for the tendency for individuals that are heavier at puberty to be also older, i.e. for the positive regression of W_P on A_P seen particularly in the Large mice. When the developmental variance is estimated and removed we find that individuals show female puberty to be mainly weight-dependent, as was seen in the replicate-means, and male puberty to be almost wholly age-dependent, as was seen in the size-group means. The individual values do not help to resolve the inconsistency between size-groups and replicates in the degree of weight-dependence of female puberty.

Partial regressions on W_3 and W_6

We have seen above that some variation of weight and age at puberty was not developmental variance and was consequently variance associated with individual differences of weight at the fixed ages of 3 and 6 weeks. By means of the partial regressions on W_3 and W_6 we can find out how weights at these ages affect weight and age at puberty. Partial regressions were calculated from the individual values within each size-group, disregarding replicates. The results are given in Table 7.

The males will be commented on first because the conclusions are straightforward. Age at puberty is not affected by W_3 or by W_6. Weight at puberty is not affected by W_3 but is strongly affected by W_6. This again confirms the age-dependence of male puberty. The partial regression, b_2, of W_P on W_6 is approximately 1, which is as expected in view of the fact that 6 weeks is near to the mean age at puberty.

Now consider the females. In contrast to the males, age at puberty is strongly affected by both W_3 and W_6. Both partial regression coefficients are negative, which means simply that the heavier animals at either age reach puberty at an earlier age. Weight at puberty is, however, also affected by both W_3 and W_6, significatly so when the size-groups are pooled, which means that differences in weight at these ages do have some effect on the weight at puberty. The two partial regression

Table 7. *Partial regressions* ($\pm$ S.E.) *on weights at 3 weeks* (W_3) *and at 6 weeks* (W_6)

(The regression equation is $y = a + b_1 W_3 + b_2 W_6$, where y is weight at puberty (W_P) or age at puberty (A_P).)

	Large	Control	Small	Pooled within size-groups
Females				
Error D.F.	41	44	42	131
W_P				
b_1	-0.54 ± 0.24*	-0.12 ± 0.26	-0.15 ± 0.16	-0.33 ± 0.13*
b_2	0.14 ± 0.23	0.34 ± 0.17	0.34 ± 0.16	0.34 ± 0.11**
A_P				
b_1	1.55 ± 0.28***	-0.32 ± 0.42	-1.26 ± 0.51*	-1.21 ± 0.22***
b_2	-0.28 ± 0.27	-1.28 ± 0.27***	-0.95 ± 0.50	-0.76 ± 0.17***
Males				
Error D.F.	34	39	34	111
W_P				
b_1	-0.42 ± 0.41	0.01 ± 0.25	-0.28 ± 0.31	-0.26 ± 0.19
b_2	1.28 ± 0.25***	0.82 ± 0.17***	0.79 ± 0.23**	1.02 ± 0.13***
A_P				
b_1	-0.010 ± 0.010	-0.007 ± 0.007	-0.013 ± 0.015	-0.011 ± 0.006
b_2	0.008 ± 0.006	-0.001 ± 0.005	-0.004 ± 0.011	0.003 ± 0.004

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

coefficients, pooled within size-groups, are of about the same magnitude but of opposite sign. The meaning of this may be made clearer by the following consideration. Both regression coefficients reflect the effect of 3- to 6-week weight-gain, G. The regression equation is

$$W_P = a + b_1 W_3 + b_2 W_6.$$

If we substitute in turn $W_6 = W_3 + G$ and $W_3 = W_6 - G$ we get the equation in the following two forms:

$$W_P = a + (b_1 + b_2) W_3 + b_2 G$$
$$W_P = a + (b_1 + b_2) W_6 - b_1 G.$$

We can now see that the two regression coefficients having the same magnitude but opposite sign means that W_P depends only on G and not at all on either W_3 or W_6 separately. It seems therefore that it is the 3- to 6-week weight-gain and not either the 3-week or the 6-week weight itself that affects weight at puberty in females.

Could the weight-gain, G, possibly resolve the inconsistency between size-groups and replicates within the size groups? Unfortunately it does not. Regressions of W_P on G in females were calculated from replicate-means within size-groups. The regression slopes in the three size-groups were not significantly different from each other but the elevations were ($P < 0.05$), proving that the size-groups are inconsistent with the replicates within size-groups.

(iv) *Final weight*

Taylor (in the Press) has shown that over a wide range of mammalian species female puberty occurs at a weight that is a nearly constant fraction of the mature weight, namely at about 45 % of mature weight. It is therefore of interest to see whether this is true also of these mice and, in particular, to see whether the size-groups and the replicates are consistent in this respect.

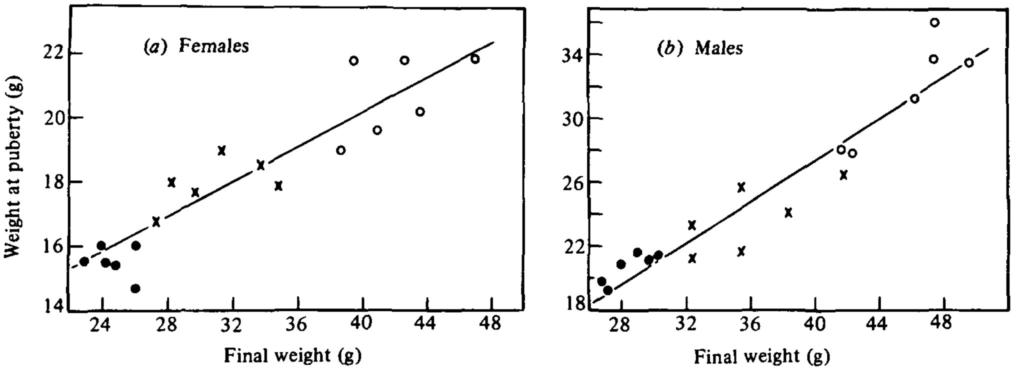

Fig. 8. Replicate-means of weight at puberty and final weight. Open circles, large; crosses, control; filled circles, small. For regressions see Table 8.

It will be remembered that weights beyond 6 weeks are not available for the individuals that gave records of puberty, but were available for the next generation (generation 10). We can therefore only work with replicate-means and not with individual values. The 'mature' weight was taken to be the final weight when growth appeared to have ceased. This was at the age of about one year, when natural deaths had started to deplete the samples (5 % of females had died before 1 year). The final weights were estimated as the mean weights at 46, 50 and 54 weeks. The mean numbers of animals per replicate at these ages were 12 females and 9 males. A point of interest about the life-time growth is that all the Large replicates grew to a maximum weight near the end of their life, whereas large strains have previously been found to reach a maximum weight about half way through their life, after which their weights fell to near the control levels (Roberts, 1961; Eklund & Bradford, 1977). The mean final weights of the size-groups are given in Table 1, and the mean 6-week weights of the generation-10 mice are given there also. It will be seen that the 6-week weights were a little lower in generation 10 than in generation 9, but it is not known if the final weights would also have been different. No attempt was made to adjust the final weights.

Fig. 8 shows the weights at puberty (W_P) of the generation-9 replicates plotted against the final weights (W_F) of the generation-10 replicates. The regression lines drawn are the overall regressions fitted to all the replicate-means disregarding size-groups. Table 8 gives the separate regressions within size-groups. The size-groups do not differ significantly in either the slopes or the elevations of the regression lines. Replicates and size-groups are therefore consistent in the relation of weight at puberty to final weight. This consistency, however, may be due more to imprecision than to reality, and it does not explain the inconsistency between replicates and size-groups seen in Fig. 5.

Since replicates and size-groups are consistent, the relation of W_P to W_F can best be expressed as the overall regression disregarding size-groups. The overall regressions are also given in Table 8, and are drawn in Fig. 8. The intercepts are not zero, particularly in the females, so the ratio of W_P to W_F is not the same in the three size-groups. The ratios W_P/W_F, given in Table 8, range from 50 to 63 %

Table 8. *Regressions* (b ± S.E.) *of weight at puberty* (W_P) *on final weight* (W_F) *based on replicate means*

(A) Size-groups separately. (B) Variance ratios testing differences of slopes and elevations, and overall regression equations with size-groups disregarded.)

(A)

	Large	Control	Small	Pooled within size-groups
Error D.F.	4	4	4	14
Females				
b	0·21 ± 0·18	0·13 ± 0·10	−0·12 ± 0·20	0·15 ± 0·08
r^2	0·26	0·30	0·08	0·19
W_P/W_F	0·496 ± 0·014	0·586 ± 0·019	0·633 ± 0·017	
(adj.)	0·48	0·55	0·59	
Males				
b	0·93 ± 0·24*	0·41 ± 0·20	0·56 ± 0·18*	0·62 ± 0·13***
r^2	0·78	0·50	0·70	0·60
W_P/W_F	0·689 ± 0·015	0·662 ± 0·021	0·724 ± 0·008	
(adj.)	0·65	0·59	0·65	

(B)

Variance ratios	Female	Male
$F_{2,12}$ slopes)	0·47	1·95
$F_{2,14}$ (elevations)	2·17	2·26

Overall regression equations (with standard errors)

Females: $W_P = (8{\cdot}93 \pm 0{\cdot}95)^{***} + (0{\cdot}28 \pm 0{\cdot}03)^{***} W_F$ ($r^2 = 0{\cdot}86$)
Males: $W_P = (1{\cdot}75 \pm 1{\cdot}92) + (0{\cdot}64 \pm 0{\cdot}05)^{***} W_F$ ($r^2 = 0{\cdot}91$)

* $P < 0{\cdot}05$; *** $P < 0{\cdot}001$.

in females and from 66 to 72 % in males. Thus males are not only older than females at puberty but they are also more 'mature' in relation to their final weights. The sexes differ significantly in their regression coefficients of W_P on W_F both pooled within size-groups ($P < 0{\cdot}01$) and overall ($P < 0{\cdot}001$). The regressions are much higher in males. This is a consequence of the age-dependence of male puberty and also of the later age of male puberty, because weights at fixed and later ages will be more closely related to final weight than weights at variable and earlier ages.

The values found for the ratio W_P/W_F are much higher than the value of 45 % found by Taylor (in the Press) for other mammalian species. The values found may have been spuriously high because of differences between the two generations. The 6-week weights of the generation-9 mice, which gave W_P, were on average about 8% higher than those of the generation-10 mice, which gave W_F. The final weights might have been similarly higher in generation 9 than in generation 10. Adjustment of W_F in proportion to the 6-week weights gives the values entered as W_P/W_F (adj.) in Table 8. These adjusted values are not much changed and are still much above 45%.

Longevity

Though not strictly relevant to the problems of puberty, it is worth recording the life-spans of the generation-10 mice. The mean ages at death in the three size-groups are given in Table 9. There were significant differences, in both sexes,

Table 9. *Mean age at death in weeks* ± S.E., *based on replicate-means*

(The mean number of mice per replicate was 12 females and 11 males.)

	Large	Control	Small
Females	89·9 ± 4·8	98·9 ± 3·2	97·1 ± 5·6
Males	88·6 ± 7·0	104·4 ± 6·1	105·8 ± 4·0

between replicates within size-groups. The replicate-means in the two sexes, however, were insignificantly correlated ($r = 0{\cdot}22$). There was no relation between age at puberty and longevity. The differences between the sexes were small and insignificant. The Large mice had a shorter life-span than the Control or Small, the mean ratio of Large/Small being 0·88, but the difference is not significant. Large mice have previously been reported to have shorter life-spans than small or unselected strains. Roberts (1961) found a ratio (large/small) of 0·90 in one comparison and 0·65 in another pair of strains; Eklund & Bradford (1977) found a large/control ratio of 0·57.

(v) *Environmental effects – litter size*

There is much evidence, some of which is cited in the discussion, that when differences in growth rate are environmentally caused, puberty in females occurs at a constant weight irrespective of the age at which this weight is attained. The size of the litter in which the individual was reared was the only environmental factor in the present data that could be looked at from this point of view. Litter size is well known to affect body weight at least up to 6 weeks of age. The effects of litter size on weight and age at puberty were accordingly examined. The litter size is the number of live young at birth in the litter in which the individual was reared. The regressions of W_P and of A_P on litter size were calculated within size-groups without distinguishing replicates. The results, given in Table 10, show that in females litter size had a significant effect on age at puberty but had virtually no effect on weight at puberty. This is as was expected from the previous evidence. The results for males are inconclusive. The effect on W_P is significant in the Small mice, larger litter size causing smaller weight at puberty, as expected if male puberty is age-dependent. Pooled over size-groups, however, the effect is non-significant. The effect on age at puberty is positive, as in females, but non-significant.

It is possible that differences of litter size might account for the inconsistency between replicates and size-groups in Fig. 5. There were, however, only small differences of litter size, and adjustments by regression to a standard litter size did nothing to resolve the inconsistency.

Table 10. *Regressions* (± s.e.) *of weight* (W_P) *and age* (A_P) *at puberty on litter size, within size-groups*

(The values for each litter size were weighted by the number of mice with that litter size. The degrees of freedom are taken as two less than the number of different litter sizes represented.)

	Large	Control	Small	Pooled within size-groups
Females				
Error d.f.	8	5	6	21
W_P	0·16 ± 0·18	−0·13 ± 0·23	−0·13 ± 0·11	0·01 ± 0·11
A_P	0·88 ± 0·24**	1·02 ± 0·26*	0·54 ± 0·51	0·76 ± 0·20**
Males				
Error d.f.	8	8	6	24
W_P	−0·48 ± 0·46	0·02 ± 0·22	−0·47 ± 0·15*	−0·27 ± 0·20
A_P	0·33 ± 0·65	0·60 ± 0·33	0·50 ± 0·67	0·47 ± 0·30

* $P < 0{\cdot}05$; ** $P < 0{\cdot}01$.

4. DISCUSSION

The question at issue is: how are weight and age at puberty affected by differences in growth? Puberty in females will be considered first. There have been many studies of female puberty in farm animals, laboratory mammals and man. Only a limited acquaintance with this previous work is needed to produce bewilderment at the inconsistency of the results. Possible reasons for a few of the inconsistencies may, however, be discerned. In considering how growth rate, or body size in general, affects weight at puberty (W_P) and age at puberty (A_P) we have to recognize three kinds of variation: (1) environmentally caused variation in growth; (2) genetically caused variation in growth; and (3) the 'developmental' variation of puberty discussed above in connexion with individual values. The developmental variation is variation of W_P and A_P among individuals with the same growth curve. It may be both genetic and environmental in origin.

Environmentally caused variation in growth has been widely studied, mainly by differences in the level of nutrition. In the main this variation has little effect on W_P, so that there appears to be a minimum, or critical, weight for the attainment of puberty, and the variation of growth consequently affects A_P, the faster-growing individuals reaching puberty earlier. This relationship has been found, for example, in cattle by Crichton, Aitken & Boyne (1959), Dalton *et al.* (1980), Little *et al.* (1981); in rats by Wilen & Naftolin (1978); in chickens by Soller *et al.* (1982); and in man (i.e. girls) by Frisch (1972). The well-known secular increase of human growth rate has been accompanied by a reduction of the age at puberty (Wyshak &

Frisch, 1982) but no change in the weight at puberty (Frisch, 1972). The conclusion from the present work, though based on very little data, was in agreement with these previous studies; weight at puberty in females was not affected by environmentally caused differences in growth, while age at puberty was. There are, however, exceptions where nutritional differences have affected both age and weight at puberty, for example in cattle (Mathai & Raja, 1976), pigs (Schilling & Schroder, 1977), and mice (Nelson, 1976; Hansen *et al.* 1983). In all these cases the faster-growing individuals were heavier and younger at puberty, like the size-groups in the present study.

Genetically caused differences in growth have shown the most marked inconsistencies in their effects on puberty. Genetically caused differences in growth may result from deliberate selection, as in the present work, or may appear as differences between breeds. Changes produced by selection will be considered first. Selection in mice for increased growth or weight at fixed age has produced all four possible combinations of change of W_P and A_P. In all these studies puberty was assessed by vaginal opening. Heavier and younger puberty was found by Bakker, Nagai & Eisen (1977) following selection for increased 3- to 6-week growth, and in the present experiment following selection for 6-week weight. Heavier and older puberty was found by Bakker *et al.* (1977) following selection for 6-week weight, and by Crane *et al.* (1972) following selection for 6-week weight on a 'low' diet. Increased W_P with no change in A_P was found by Crane *et al.* (1972) following selection for 6-week weight on a 'high' diet. And, finally, reduced A_P with no change of W_P was found by Yamada & Hamada (1978) following selection for 8-week weight. In comparisons of breeds, differences of both W_P and A_P seem to predominate, but with inconsistency of the sign of the association. Association of higher W_P with lower A_P (heavier and younger) has been found in cattle (Pleasants, Hight & Barton, 1975), sheep (Quirke, 1979), pigs (Hutchens, Hintz & Johnson, 1982), and rats (Clark & Price, 1981). Association of higher W_P with higher A_P (heavier and older) has been found in cattle (Laster, 1976) and in sheep (Dickerson & Laster, 1975).

In the present work there was a conspicuous internal inconsistency when different strains, or 'breeds' were compared. When the strains differing much in body size were compared, i.e. the Large, Control and Small size-groups, there was a negative association of W_P and A_P, the Large mice being heavier and younger at puberty. However, when strains differing less in body size were compared, i.e. the replicates within each size-group separately, puberty occurred at constant weights in each size-group, but at different ages. The differences in growth rate between the replicates thus led to different ages at puberty but did not affect weights at puberty. This is what would have been expected if the differences of growth were environmentally caused, but there was no known environmental cause, and so the differences of growth between the replicates must have been genetic, just like the differences between the size-groups. The only distinction is that the size-group differences were brought about by selection while the replicate differences were brought about by random drift. Associations of characters with body size that are different between and within groups are frequently found (Clutton-Brock & Harvey, 1979). A well-known example is litter size: larger species tend to have smaller litters, but larger individuals within species tend to have larger litters. It seems unlikely, however, that a common cause can be involved for such differences of association and for the inconsistency of puberty.

The existence of developmental variation has been proved in mice by Drickamer (1981). Selection in both directions for age at puberty changed age at puberty without affecting growth rate, so that the earlier maturing lines were lighter and the later maturing lines were heavier at puberty. Developmental variance may provide a clue to some of the inconsistencies in breed comparisons noted above. Developmental differences without differences of growth rate will result in a positive association of W_P with A_P, i.e. breeds that are heavier at puberty will be older. One may postulate that differences in growth rate without developmental differences generally result in a negative association of W_P with A_P, as in the comparison of the size-groups in the present experiment. Then, if two breeds differ in growth rate but not in the developmental age of puberty, the faster growing will be heavier and younger at puberty. If breeds differ in both growth rate and development, one tending to give a negative and the other a positive association of W_P with A_P, then the outcome might be differences of age but not of weight at puberty. This is what was found in the present experiment when replicates within size-groups were compared. A possible explanation of the inconsistency between size-groups and replicates is therefore that the size-groups differed in growth rate but not in development, while the replicates within size-groups differed in both growth rate and development. This explanation, however, is only a possible one without any evidence to support it.

Another possible explanation of some of the inconsistencies noted above may lie in the body composition. There is evidence from rats (Frisch *et al.* 1977) and women (Frisch & McArthur, 1974; Frisch, 1980) that the ratio of fat to lean is more constant at puberty than body weight itself is, puberty occurring when a critical body composition is reached. Differences of body composition might account for some of the inconsistencies noted. Unfortunately no data on the mice studied here were available from which puberty could be related to body composition.

Turning now to puberty in males, the results of the present study are fairly clear. They are also consistent with the little that is known from previous studies. First, puberty occurred later in males than in females, by 13 days in the Large mice, 4 days in the Controls and 8 days in the Small mice, the difference ranging from 11 to 41 % of the female age at puberty. It must be remembered that female puberty was assessed by vaginal opening. Fertile mating, however, would not be possible till the first oestrus, which occurs later than vaginal opening. The difference between the sexes in reaching functional puberty may therefore not have been very great. A greater difference between the sexes than found here was reported in rats by Allrich *et al.* (1981), males reaching puberty 25 days (= 68 %) later than females. Here female puberty was also assessed by vaginal opening but the first oestrus occurred within one day of vaginal opening. In man also, it is thought that boys reach puberty later than girls (Frisch & Revelle, 1969, 1971). This conclusion is based on the finding that the adolescent growth spurt occurs 2 years (= 18 % later in boys than in girls.

The second conclusion about the male mice is that male puberty is almost wholly age-dependent, males of different strains tend to reach puberty at the same age irrespective of their weight. Here again there is similar evidence from rats and man. Allrich *et al.* (1981) conclude that their results 'suggest that age of the male may be a more important factor than body weight in determining the onset of mating ability'. The evidence on boys is based again on the adolescent growth spurt (Frisch & Revelle, 1969, 1971). More variation in weight was found in boys than in girls at the initiation of the growth spurt and at the period of maximum growth rate, indicating less weight-dependence of puberty in boys than in girls.

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