Theor Appl Genet (1988) 76:148–156

Phenotypic and genetic variability of estimated growth curve parameters in mice

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Received July 14, 1987; Accepted December 17, 1987
Communicated by L. D. Van Vleck

Summary. Data from 1,919 outbred ICR mice were used to examine the potential usefulness of growth curve parameters as selection criteria for altering the relationship between body weight and age. A logistic growth function was used to model growth through 12 weeks of age. Estimates of asymptotic weight (A), maximum growth rate (r) and age at point of inflection (t*) were obtained by nonlinear least-squares. A log transformation was also used to stabilize residual variance. Phenotypic and genetic parameters were estimated for the estimated growth curve parameters and for body weights at 2, 3, 4.5, 6, 8 and 12 weeks of age. Heritabilities of estimated growth curve parameters (obtained with and without a log transformation, respectively) were: A (0.28 ± 0.07, 0.28 ± 0.07), r (0.35 ± 0.07, 0.53 ± 0.09) and t* (0.41 ± 0.08, 0.44 ± 0.08). Estimated genetic correlations suggest that t* may be useful in selecting for rapid early growth without increasing mature weight.

Key words: Growth curve – Genetic parameters – Heritability – Mice

Introduction

The relationship between body weight and age is particularly important in meat animals such as beef cattle. Because this relationship is of interest throughout an animal's lifetime, it is critical to study it as a whole rather than in isolated pieces (Cartwright 1970; Dickerson 1978). Fitzhugh (1976) suggested that a 'desirable' pattern of growth would be one characterized by small birth weight relative to dam size in order to reduce dystocia, rapid early growth and small mature size in the parental stocks so as to have a low maintenance cost.

The age-weight relationship could be altered through selection and a criterion is required for this. Selection studies with farm animals are expensive to conduct because of high cost and long generation intervals. Laboratory mice provide a model for examining the potential usefulness of alternative selection criteria before application to farm animals (Roberts 1965; Eisen 1974).

Eisen (1974, 1976) discussed selection criteria for increasing early growth without affecting mature weight in mice. Single trait selection for body weight at a given age or weight gain in a specified period was found to be ineffective for this purpose. Such selection increased growth rates and body weight throughout the animal's lifetime. McCarthy and Bakker (1979) selected mice for increased 5 week and decreased 10 week body weight using independent culling levels and obtained a 1% increase in 5 week body weight and a 2% decrease in both 10 week and 21 week weights. Wilson (1973) selected for an increased ratio of 3–6 week to 3–9 week body weight gain. After 8 generations of selection, there were decreases of 1%, 1% and 8% in body weights at 3, 6 and 9 weeks of age, respectively, relative to the control lines. These experiments suggest that index selection may alter the relationship between weight and age but progress is likely to be slow.

This relationship can be described with a growth function. In these functions, growth rate first increases with age and then decreases as the animal approaches maturity, which gives a sigmoid body weight-age plot (Brody 1945; Parks 1982). The nonlinear Richards' function, or special cases of it, are commonly used to model growth in animals (Parks 1982). Parameters describe various

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aspects of growth and provide potentially useful criteria for altering the age-weight relationships by genetic means. The objective of this study was to examine the possible usefulness of growth curve parameters as selection criteria to accomplish the above in mice.

Exprimental procedures

In November 1981, 55 male and 110 female ICR outbred mice were obtained from each of two sources: Dominion (Flow) Laboratories and Harlan Sprague-Dawley. Mice were approximately 6 weeks old and arrangements were made with the suppliers for the mice to come from different litters so as to attain as wide a genetic sampling as possible.

Males and females were randomly allocated to each of two groups (batches) for ease of management. Within batches, each male from one source was mated to two females from the other source to maximize heterozygosity in the foundation stock. Matings in the two batches were separated by a 2 week period to facilitate work load; this arrangement was maintained throughout the experiment and the batches remained genetically closed throughout. Progeny from these matings are referred to as generation 1.

To produce subsequent generations, 50–60 males and 100–120 females per batch were randomy selected on a within-family basis. Whenever possible, males and females were selected from different sire families and litters, respectively. Matings (2 females per male) were random but pairings between full or half-sibs were avoided to restrict inbreeding. Expected effective population size and rate of increase of inbreeding in each batch are 133–160, and 0.18%–0.22% per generation, respectively (Falconer 1981).

Mice of generation 0 were put in breeding cages at about 9–11 weeks of age for a period of 14 days. Females that died during the mating period were replaced immediately; males were replaced 3 days post-death to reduce sire identification errors. Females were moved into individual boxes and search for pups began 18 days after the beginning of matings. Litters born in generation 1 were standardized at 1 day of age to 8 pups per litter. This was at random, within sexes, aiming for a 1:1 sex ratio. When there were not enough individuals in a litter, pups were cross-fostered from litters born on the same day. Litters born in subsequent generations were standardized to 6 pups per litter, because of limitations in space. At 2 weeks of age, mice were marked individually using toe notching. Pups were weaned at 3 weeks of age and assigned to post-weaning cages with 6–10 mice of the same sex from different litters, whenever feasible.

Individual weights were routinely taken on all mice at 2, 3, 4.5, 6, 8 and 12 weeks of age to the nearest 0.1 gram. Tail lengths were recorded at 6 and 12 weeks of age to the nearest 0.1 cm. After taking 12 week body weights, males and females were randomly selected to produce the following generation and mated immediately following the above procedures.

Selection of a nonlinear growth model

A growth curve is usually sigmoid provided that a large range of ages is represented. Many functions can produce this general shape, and it is not practical to consider all of these to assess which one is "best". Attention was restricted to the Richards' family of growth functions (Richards 1959, 1969), because parameters could be related to various aspects of growth that were of biological interest. Also, the most commonly used growth curves are special cases of the Richards' function. This can be written (Fitzhugh 1976)

$$E(y_t) = A(1 \pm Be^{-kt})^m \qquad (1)$$

where $E(y_t)$ = expected body weight at age t, A = asymptotic weight, B = integration constant, k = maturing rate and m = inflection parameter. In (1), the positive sign applies when $m < 0$, and the negative when $m \geq 1$. The parameter A relates to mature body weight; B is connected to relative weight at time 0; k describes the rate at which mature weight is achieved, and m gives the fraction of mature weight at which growth rate is maximum.

In estimating the parameters of (1) using iterative methods such as nonlinear least-squares, complications can arise with convergence of the solutions; this is particularly true for m (Rutledge et al. 1972; Brown et al. 1976; McCarthy and Bakker 1979). This problem can be avoided by assuming that m is known. In fact, $m = 1$ gives the Brody function, $m = 3$ gives the Von Bertalanffy function, $m = -1$ yields the logistic function and $m \to \infty$ produces the Gompertz function (Fitzhugh 1976; Parks 1982).

In order to find an appropriate value for m, a group of randomly chosen mice was weighed more frequently than the population as a whole. This group consisted of 37 mice (generation 3, batch 2) from 19 litters born on the same day and standarized to 8 pups per litter, 4 males and 4 femals. One male and one female were selected at random from each of the 19 litters; one of the animals died. Prior to 3 weeks of age, these mice were handled as those in the rest of the colony. From 3–12 weeks of age, they were weighed twice per week, and weekly from 12–28 weeks of age. Mice from this group were not used as parents.

Estimation of m in (1) by nonlinear least-squares using records from this group suggested the logistic function for application in the full data set. The function was then reparameterized to facilitate interpretation. With $m = -1$, putting $B = \exp(\ln B)$ in (1) leads to

$$E(y_t) = A[1 + e^{k(\ln B/k - t)}]^{-1} . \qquad (2)$$

Following Fitzhugh (1976), let

$$t^* = \ln B/k$$

and

$$r = kA/4$$

where t* is the age at which growth rate is maximum (point of inflection of the curve) and r is maximum growth rate. Using these, (2) becomes

$$E(y_t) = A[1 + e^{4r(t^* - t)/A}]^{-1} . \tag{3}$$

In this form, the parameters have the following interpretation: A (asymptotic weight) is mature weight, r is maximum growth rate, and t* (age at point of inflection) is related to age at puberty (Monteiro and Falconer 1966). With this reparameterization, convergence would be directly for parameters of biological interest and not for some function of them, which is more reasonable from an estimation viewpoint. Also, it facilitates the choice of initial guesses for iteration.

Body weights at day 1 (estimated by dividing litter weight at day 1 by litter size) and at 2, 3, 4.5, 6, 8 and 12 weeks in the 37 mice were used to estimate all parameters in (3). Predicted body weights were compared with observed values to examine possible biases. The reason for this was that the full data set included only those body weights.

Estimation of growth curve parameters in the full data set

Estimation was by nonlinear least-squares (Draper and Smith 1966; Daniel and Wood 1971) via Marquardt's (1963) algorithm. This procedure has been used previously for estimating growth curve parameters in mice and cattle (e.g.: Carmon 1965; Eisen et al. 1969; Timon and Eisen 1969; Rutledge et al. 1972; Brown et al. 1976; McCarthy and Bakker 1979; Goonewardene et al. 1981; Parratt and Barker 1982). In general, residual variance of body weight would be expected to increase as the body weight of the animal increases with age. A logarithmic transformation of body weights was used to deal with this problem. In this case, the "errors" in the original scale of the observations would be assumed to be multiplicative. Nonlinear least-squares estimates of growth curve parameters in (3) and in its log-transformed version were obtained for each of 1,919 mice from generations 2 and 3, with batches 1 and 2 represented in each generation. Growth curves were fitted using the following records: estimated body weight at day 1 and body weights at 2, 3, 4.5, 6, 8 and 12 weeks of age. Records from generation 1 were not used because at this point the population was expected to be far from linkage equilibrium, thus making this data unsuitable for estimation of genetic parameters (Cockerham 1954).

Estimation of genetic parameters

Body weights at 2, 3, 4.5, 6, 8 and 12 weeks, tail lengths at 6 and 12 weeks of age and estimates of A, r and t* (both untransformed and transformed models) in the 1,919 mice were used to estimate genetic and phenotypic parameters.

The following mixed linear model was used:

$$y_{ijklm} = S_i + G_j + SG_{ij} + s_{jk} + d_{jkl} + e_{ijklm} \tag{4}$$

where

y_{ijklm} = observed or estimated value of variate;
S_i = fixed effect of sex i;
G_j = fixed effect of generation-batch j;
SG_{ij} = fixed effect of an interaction between sex i and generation-batch j;
s_{jk} = random effect of sire k in generation-batch j;
d_{jkl} = random effect of dam 1 mated to sire k in generation-batch j
e_{ijklm} = random residual.

It was assumed that $s_{jk} \sim (0, \sigma_s^2)$, $d_{jkl} \sim (0, \sigma_d^2)$, $e_{ijklm} \sim (0, \sigma_e^2)$, with all covariances between pairs of random variables in the model being null. Estimates of variance and covariance components were obtained by Method 3 (Henderson 1953) using the package LSML76 (Harvey 1977).

Ignoring non-additive effects, the following relationships hold (Willham 1963)

$$\sigma_s^2 = 0.25\,\sigma_{Ao}^2$$
$$\sigma_d^2 = 0.25\,\sigma_{Ao}^2 + \sigma_{AoAm} + \sigma_{Am}^2 + \sigma_{Em}^2$$
$$\sigma_e^2 = 0.50\,\sigma_{Ao}^2 + \sigma_E^2$$

where σ_{Ao}^2 is additive "direct" genetic variance, σ_{Am}^2 is additive genetic variance of maternal effects, σ_{AoAm} is covariance between direct and maternal genetic effects, σ_{Em}^2 is variance of maternal environmental effects and σ_E^2 is variance of individual enviromental effects. Although there are five unknown parameters, only three variances (or linear functions thereof) can be estimated using (4). Similarly, covariance components between pairs of traits can be written in terms of genetic and environmental components of covariance.

Heritabilities of direct genetic effects and genetic and phenotypic correlations were of main interest. Formulae for these parameters are

$$h_0^2 = 4\,\sigma_s^2/(\sigma_s^2 + \sigma_d^2 + \sigma_e^2)$$
$$r_{Ao} = \sigma_{ss'}/(\sigma_s^2\,\sigma_{s'}^2)^{1/2}$$

and

$$r_p = (\sigma_{ss'} + \sigma_{dd'} + \sigma_{ee'})/[(\sigma_s^2 + \sigma_d^2 + \sigma_e^2)(\sigma_{s'}^2 + \sigma_{d'}^2 + \sigma_{e'}^2)]^{1/2}$$

respectively; $\sigma_{ss'}$, $\sigma_{dd'}$ and $\sigma_{ee'}$ are sire, dam and residual covariance components between two traits, respectively. The above expressions were estimated replacing the unknown variance and covariances components by Method 3 estimates. Standard errors of estimates were approximated as outlined by Dickerson (1969).

Results and discussion

Model selection

In spite of the large number of body weights per animal, convergence was slow. An average of 34.2 rounds of iteration was required for convergence, and in 3 out of the 37 cases, over 50 rounds were needed. This slow rate of convergence would have made the Richards' function (1), with all parameters unknown, unfeasible for use in the large data set. Estimates of the m parameter ranged from -1.53 to -0.91, with a mean of -1.17 ± 0.20. Although these results suggest the logistic function as adequate for describing growth of mice, it should be noted that the coefficient of variability of the estimates of m is very high.

When the parameters of (3) were estimated using body weights through 12 weeks of age only, some undesirable features of the logistic function were observed. For example, estimated body weight at day 1 was overpredicted by about 56%, on average, and body weight at 12 weeks of age was underpredicted by about 8% (Table 1). This tendency of the logistic model to underpredict later weights in life has also been noted by other workers (Eisen et al. 1969; Timon and Eisen 1969; Rutledge et al. 1972).

Growth curve parameters in the full data set

Means and standard deviations of estimated growth curve parameters in 1,919 mice are in Table 2. Mean estimated asymptotic weight (A) was 36.4 g in both untransformed and log-transformed models, in agreement with the 35.0 g obtained by Rutledge et al. (1972), whose ICR mice were also weighed through 12 weeks of age. However, it was higher than the estimated asymptotic weight found with mice weighed through 8 weeks of age (Eisen et al. 1969), but smaller than the value reported by Timon and Eisen (1969) working with mice weighed through 14 weeks of age. Mean estimated maximum growth rate (r) was slightly smaller in the untransformed model (1.1 g/day) than in the log-transformed one (1.4 g/d); the mean value of r was larger than estimates found in the literature (Eisen et al. 1969; Timon and Eisen 1969; Rutledge et al. 1972). Mean age at point of inflection (t*) was larger in the untransformed model (21.2 days) than in the logarithmic version (20.4 days). These estimates are smaller than those found by Eisen et al. (1969) and Rutledge et al. (1972).

Least-squares estimates of marginal means of estimated growth curve parameters by sex, i.e., averaged over generation-batches, sires and dams, are in Table 3. Males had larger estimated asymptotic weights, faster estimated maximum rates of gain and later ages at point of inflection than females, in agreement with previous work with ICR mice (Eisen et al. 1969; Timon and Eisen 1969; Rutledge et al. 1972).

Table 1. Means of observed and predicted body weight at several ages using the logistic growth function in 37 ICR mice

Age (weeks)	Observed (O) (g)	Predicted (P) (g)	$\frac{P-O}{O} \times 100$
0	1.6	2.5	56.3
2	10.7	9.7	−9.3
3	15.8	16.8	6.3
4.5	28.6	27.5	−3.8
6	32.5	32.6	0.3
8	35.3	34.8	−1.4
12	38.3	35.3	−7.8

Table 2. Means and standard deviations of estimates of mature weight (A), maximum growth rate (r) and age at puberty (t*)

Parameter	Model	
	Untransformed	Logarithmic
A (g)	36.4 ± 5.2	36.4 ± 5.2
r (g/day)	1.1 ± 0.2	1.4 ± 0.2
t* (days)	21.2 ± 2.0	20.4 ± 1.9

Table 3. Least-squares estimates and standard errors of estimated mature weight (A), maximum growth rate (r) and age at point of inflection (t*), by sex

Parameter	Model[a]			
	Untransformed		Logarithmic	
	Males	Females	Males	Females
A (g)	40.2	32.9	40.2	32.9
r (g/day)	1.3	0.9	1.5	1.3
t* (days)	22.3	20.2	21.7	19.4

[a] Standard errors were 0.2, 0.01 and 0.1 for estimates of A, r and t*, respectively, in both sexes

Heritability estimates

Heritability estimates of estimated asymptotic weight (Table 4) were 0.28 ± 0.07 in both models. These estimates are higher than the 0.08 found by Carmon (1965) and the 0.18 obtained by Rutledge et al. (1972). Heritability of estimated maximum growth rate was estimated at 0.35 ± 0.07 and at 0.53 ± 0.09 in untransformed and log-transformed models, respectively. These estimates are higher than the 0.28 found by Rutledge et al. (1972). Estimates for age at point of inflection were 0.41 ± 0.08

and 0.44 ± 0.08 in untransformed and log-transformed models, respectively; these are much higher than the 0.08 found by Rutledge et al. (1972). Heritabilities of these estimated parameters were also obtained by Eisen et al. (1969) and Timon and Eisen (1969) from full-sib analyses, so their estimates might be biased upwards by maternal and dominance variance. In general, it appears that estimated asymptotic weight, maximum growth rate and age at point of inflection are moderately heritable.

Heritability estimates for the various body weights and tail lengths are in Table 5. The heritability estimate for 2 week body weight (0.41 ± 0.08) was larger than previous estimates of 0.20 for 15 day weight (Rutledge et al. 1972), and of 0.05 to 0.37 for 12 day weight (Eisen et al. 1970; Rutledge et al. 1972; Jara-Almonte and White 1973; Slawinski 1974). The heritability estimate for 3 week weight was 0.55 ± 0.09, which was larger than previous estimates ranging from 0.11 to 0.45 (Rutledge et al. 1972; Hanrahan and Eisen 1973; Jara-Almonte and White 1973; Slawinski 1974; Frahm and Brown 1975; Dunnington et al. 1977; von Butler and Willeke 1982). The estimate for 4.5 week body weight (0.51 ± 0.08) was also larger than the 0.20 and 0.23 obtained by Rutledge et al. (1972) and Cheverud et al. (1983), respectively. However, estimates of 0.23 ± 0.07 and 0.28 ± 0.07 for 6week and 8week body weight, respectively, agree well with others (Legates 1969; Rutledge et al. 1972; Falconer 1973; Hanrahan and Eisen 1973; Jara-Almonte and White 1973; Rutledge 1974; Slawinski 1974; Dunnington et al. 1977; Nagai et al. 1978; von Butler and Willeke 1982; Cheverud et al. 1983). The heritability estimate of 12 week body weight of 0.32 ± 0.07 agreed with the 0.36 reported by Rutledge et al. (1972). Tail lengths were more heritable at 6 than at 12 weeks of age (0.51 ± 0.08 vs 0.13 ± 0.06); the reason for this difference in heritability is not clear. Rutledge et al. (1973) found an estimate of 0.44 of realized heritability of 6 week tail length.

Table 4. Heritability estimates of estimated growth curve parameters and approximate standard errors

Parameters	Model	
	Untransformed	Logarithmic
Asymptotic weight	0.28 ± 0.07	0.28 ± 0.07
Maximum growth rate	0.35 ± 0.07	0.53 ± 0.09
Age at point of inflection	0.41 ± 0.08	0.44 ± 0.08

Table 5. Estimates of heritability and approximate SE for body weight and tail lengths at several ages

Trait[a]	Estimate ± SE
W2	0.41 ± 0.08
W3	0.55 ± 0.09
W4.5	0.51 ± 0.08
W6	0.23 ± 0.07
W8	0.28 ± 0.07
W12	0.32 ± 0.07
T6	0.51 ± 0.08
T12	0.13 ± 0.06

[a] W2, W3, W4.5, W6, W8 and W12 are body weights at 2, 3, 4.5, 6, 8 and 12 weeks of age, respectively; T6 and T12 are tail lengths at 6 and 12 weeks of age, respectively

Estimates of genetic correlations

Genetic correlations between growth curve parameter estimates are given in Table 6. Consider first genetic correlations between estimates of the same parameter obtained with the two different models. The genetic correlation between asymptotic weight (A) estimated with the untransformed and the logarithmic models was 1.00. The genetic correlation between estimates of maximum growth rate (r) was 0.77 ± 0.07. This indicates that less than 60% of the genetic variation in maximum growth rate, using one model, would be accounted for by genetic variation for the same parameter in the other model. The

Table 6. Estimates of genetic correlations (with approximate SE) between estimated growth curve parameters

Items		Item[a]					
		Untransformed model			Log-transformed model		
		A	r	t*	A	r	t*
Untransformed:	A	1.00	1.07 ± 0.08	0.10 ± 0.16	1.00 ± 0.00	0.89 ± 0.04	0.16 ± 0.15
	r	–	1.00	0.13 ± 0.15	1.07 ± 0.08	0.77 ± 0.07	0.23 ± 0.14
	t*	–	–	1.00	0.10 ± 0.16	−0.16 ± 0.13	0.98 ± 0.01
Transformed:	A	–	–	–	1.00	0.89 ± 0.04	0.16 ± 0.15
	r	–	–	–	–	1.00	−0.19 ± 0.13
	t*	–	–	–	–	–	1.00

[a] A: asymptotic body weight; r: maximum growth rate; t*: age at point of inflection

genetic correlation between age at point of inflection (t*) estimated with the two models was 0.98 ± 0.01. Hence, the major discrepancy between the two models was in maximum growth rate. This is discussed further in the context of phenotypic correlations.

Within models, estimates of asymptotic body weight and maximum growth rate were highly correlated genetically: 1.07 ± 0.08 and 0.89 ± 0.04 in the untransformed and transformed models, respectively. This indicates that animals that have a genetic propensity to grow fast would be expected to produce progeny with larger mature weights. Age at point of inflection was lowly correlated genetically with estimated asymptotic weight, the estimates being not different from 0 as indicated by the approximate standard errors. Also, estimated maximum growth rates and age at point of inflection were lowly correlated, genetically. Estimates of this correlation were 0.13 ± 0.15 in the untransformed model and −0.19 ± 0.13 in the logarithmic version. The reason for this discrepancy in sign is unclear, but it is consistent with the conjecture that the r parameter would measure different underlying variables in the two models employed.

Genetic correlations between estimated growth curve parameters and body weights and tail lengths at various ages are in Table 7. The genetic correlation between asymptotic weight and body weight at a given age was always positive and increased in value as the animal aged; the correlation with body weights at 6 and 8 weeks of age was perfect. Coupled with the heritability estimates in Tables 4 and 5, this implies that selection for body weight at 6 or 8 weeks of age would result in approximately the same genetic change for estimated asymptotic body weight as direct selection for the latter (Falconer 1981). Obtaining an estimate of asymptotic weight involved recording animals until 12 weeks of age. Hence, if mortality is high, selection intensity may be lower in direct selection for estimated A than in indirect selection for body weight at 6 or 8 weeks.

Genetic correlations between estimated maximum growth rate and the various body weights were all positive. In the untransformed model, this genetic correlation increased monotonically from 0.22 ± 0.14 at 2 weeks of age, to 1.12 ± 0.08 at 12 weeks of age. In the transformed model, the genetic correlation increased from 0.64 ± 0.08 at 2 weeks of age to a maximum of 0.92 ± 0.05 at 6 weeks. These estimates reinforce the hypothesis that the r parameter may reflect different aspects of growth in the two models.

The genetic correlation between estimated age at point of inflection and body weight was strongly negative through 3 weeks of age, and approached zero thereafter, the two models given essentially the same result. These correlations suggest that selection for decreased age at point of inflection (or age at puberty) would increase earlier body weights with little, if any, effect on later weights. This type of selection might be conducted in species where animals are marketed at early ages. Falconer (1984) provides a comprehensive discussion of this problem. In general, estimates of genetic correlations between estimated growth curve parameters and tail lengths were low and smaller than their standard errors in several cases.

Estimated genetic correlations between the various body weights and tail lengths are in Table 8. The genetic correlations between body weights (see abbreviations in Table 5) were positive. Correlations between pre-weaning (W2 and W3) and post-weaning (W4.5, W6, W8, W12) weights decreased as time between weights increased. For example, the genetic correlation between W2 and W3 was 0.99 ± 0.02 while that between W2 and W12 was

Table 7. Estimates of genetic correlations (with approximate SE) between estimated growth curve parameters, and body weights and tail lengths at several ages

Variate[b]	Variate[a]					
	Untransformed model			Log-transformed model		
	A	r	t*	A	r	t*
W2	0.16 ± 0.15	0.22 ± 0.14	−1.02 ± 0.16	0.16 ± 0.15	0.64 ± 0.08	−1.01 ± 0.16
W3	0.57 ± 0.10	0.53 ± 0.10	−0.76 ± 0.14	0.56 ± 0.10	0.72 ± 0.06	−0.73 ± 0.14
W4.5	0.92 ± 0.05	0.99 ± 0.02	−0.29 ± 0.13	0.92 ± 0.05	0.79 ± 0.05	−0.19 ± 0.13
W6	1.10 ± 0.04	1.06 ± 0.04	0.00 ± 0.17	1.10 ± 0.04	0.92 ± 0.05	0.10 ± 0.16
W8	1.00 ± 0.00	1.07 ± 0.08	0.10 ± 0.16	1.00 ± 0.00	0.89 ± 0.04	0.16 ± 0.15
W12	0.91 ± 0.05	1.12 ± 0.08	−0.19 ± 0.14	0.91 ± 0.05	0.80 ± 0.07	−0.05 ± 0.15
T6	0.25 ± 0.14	0.04 ± 0.14	−0.07 ± 0.13	0.25 ± 0.14	0.24 ± 0.12	−0.09 ± 0.13
T12	0.08 ± 0.23	−0.32 ± 0.20	−0.19 ± 0.21	0.08 ± 0.23	0.06 ± 0.19	−0.19 ± 0.21

[a] A: asymptotic body weight; r: maximum growth rate; t*: age at point of inflection

[b] W2, W3, W4.5, W6, W8 and W12 are body weights at 2, 3, 4.5, 6, 8 and 12 weeks of age, respectively; T6 and T12 are tail lengths at 6 and 12 weeks of age, respectively

Table 8. Estimates of genetic correlations (with approximate SE) between body weights and tail lengths at several ages

Variate[a]	Variate[a]							
	W2	W3	W4.5	W6	W8	W12	T6	T12
W2	1.00	–	–	–	–	–	–	–
W3	0.99 ± 0.02	1.00	–	–	–	–	–	–
W4.5	0.57 ± 0.09	0.80 ± 0.05	1.00	–	–	–	–	–
W6	0.22 ± 0.16	0.76 ± 0.09	1.05 ± 0.04	1.00	–	–	–	–
W8	0.16 ± 0.15	0.56 ± 0.10	0.92 ± 0.05	1.10 ± 0.04	1.00	–	–	–
W12	0.12 ± 0.15	0.76 ± 0.08	1.00 ± 0.05	1.12 ± 0.06	0.91 ± 0.05	1.00	–	–
T6	0.15 ± 0.13	0.33 ± 0.11	0.22 ± 0.12	0.07 ± 0.16	0.25 ± 0.14	0.28 ± 0.13	1.00	–
T12	−0.06 ± 0.21	0.57 ± 0.18	−0.04 ± 0.20	−0.38 ± 0.23	0.08 ± 0.23	0.31 ± 0.21	0.70 ± 0.17	1.00

[a] W2, W3, W4.5, W6, W8 and W12 are body weights at 2, 3, 4.5, 6, 8 and 12 weeks of age, respectively; T6 and T12 are tail lengths at 6 and 12 weeks of age, respectively

Table 9. Estimates of phenotypic correlations between estimated growth curve parameters

Variate		Variate[a]					
		Untransformed model			Log-transformed model		
		A	r	t*	A	r	t*
Untransformed:	A	1.00	0.43	0.53	1.00	0.78	0.48
	r		1.00	−0.19	0.43	0.56	−0.09
	t*			1.00	0.53	0.04	0.97
Transformed:	A				1.00	0.78	0.48
	r					1.00	−0.06
	t*						1.00

[a] A: asymptotic body weight; r: maximum growth rate; t*: age at point of inflection

0.12 ± 0.15, which was low in spite of a part-whole relationship. Genetic correlations between post-weaning weights ranged between 0.92 ± 0.05 and 1.12 ± 0.06. This agrees with other studies. Jara-Almonte and White (1973) reported a genetic correlation between 12 day weight and 3 week weight of 0.97. Estimates of genetic correlations between pre- and post-weaning weights have ranged from −0.02 to 0.75 (Jara-Almonte and White 1973; Hanrahan and Eisen 1973) and those involving post-weaning weights were close to 1.00 (Jara-Almonte and White 1973; Hanrahan and Eisen 1973; McCarthy and Doolittle 1977). Correlations between tail length at 6 weeks of age and body weights were positive and low. The genetic correlation between tail length at 12 weeks of age and body weights were erratic, ranging from −0.38 ± 0.23 (with body weight at 6 weeks) to 0.57 ± 0.18, with 21 day weight.

Mean estimated age at point of inflection was 20.4 or 21.2 (Table 2) and, as noted earlier, its genetic correlation with weaning weight was −0.76 ± 0.14 or −0.73 ± 0.14 (Table 7), depending on the model. However, the genetic correlations between age at point of inflection and weights later in life were very low. On the other hand, the genetic correlations between weaning weight (W3) and later weights were positive, ranging between 0.56 ± 0.10 and 0.80 ± 0.05 (Table 8). Hence, selection for early age at point of inflection or age at puberty, as opposed to selection for high weaning weight, would be expected to increase juvenile gain without a sizable concomitant increase in mature weights. Also, because age at point of inflection seems to be less heritable in this population than weaning weight (Tables 4 and 5), the expected increase in weaning weight due to selection for age at point of inflection would be less than that resulting from direct selection for high weaning weight (Falconer 1981). This could be interesting in regard to reducing negative effects due to large weaning weights, e.g., in beef cattle (Koch 1972).

Estimates of phenotypic correlations

Phenotypic correlations between estimates of growth curve parameters are in Table 9. Correlations between estimates of the same parameter obtained with the two models were high, except for maximum growth rate. The phenotypic correlation between estimates of A was 1.00, which suggests that the two estimates were essentially the same (see also Table 3). The correlation between t* values obtained with the two models was 0.97, so the difference between estimates in the two models was mainly due to a shift in mean value (Table 3). The correlation between estimates of r from the two models was only 0.56, which indicates that the relationship between the two corresponding estimators cannot be described by a simple linear transformation.

The phenotypic correlations between estimates of asymptotic weight and maximum growth rate in each of the two models were positive (0.43 and 0.78); animals that grow faster would be expected to reach a heavier mature weight than animals that grow slower. These estimates agree with the 0.51–0.57 obtained by Eisen et al. (1969), and with the 0.45 found by Rutledge et al. (1972).

Within models, phenotypic correlations between estimated asymptotic weight and age at point of infection were positive (0.53 and 0.48). This was also in agreement with previous estimates of 0.31–0.58 (Eisen et al. 1969), 0.35 (Timon and Eisen 1969) and 0.45 (Rutledge et al. 1972). Correlations between estimated maximum growth rate and age at point of inflection were negative and close to zero (−0.19 and −0.09), in agreement with estimates of −0.09 to −0.39 (Eisen et al. 1969), and −0.19 (Rutledge et al. 1972).

Phenotypic correlations between body weights and tail lengths and the parameters estimated with the two nonlinear models are in Table 10. Correlations between estimated asymptotic weight, body weights and tail lengths at the various ages were all positive. The correlation with body weights increased from 0.43 at 2 weeks of age to 1.00 at 8 weeks of age and then decreased to 0.72 at 12 weeks of age. This indicates a problem with the logistic model applied to mice: estimated asymptotic body weight is essentially 8 week weight but it seems to provide insufficient information on weights at older ages. The correlations between maximum growth rate, body weights and tail lengths were positive. Phenotypic correlations between maximum growth rate and body weights tended to increase, and then to decrease as the animal aged. In the untransformed model, the correlation increased from 0.25 at 2 weeks of age to 0.80 at 4.5 weeks, and then decreased to 0.43 at 12 weeks. This pattern was not as marked in the log-transformed model: the correlation increased from 0.68 at 2 weeks to 0.78 at 8 weeks, and then dropped to 0.61 at 12 weeks.

The phenotypic correlations between estimated age at point of inflection and body weights were negative through 4.5 weeks of age and positive at later ages; the correlations with tail length were negligible. Negative correlations at earlier ages indicate that animals that are heavier at such ages, especially during the pre-weaning period, would reach puberty earlier. The positive correlations at later ages suggest that animals that attained heavier mature weights had delayed puberty. There was fairly close agreement between the correlations obtained with the two models.

Phenotyopic correlations between body weights and tail lengths are shown in Table 11. Strong positive correlations between body weights were found, but tended to decline as the interval between weights increased. For example, phenotypic correlations ranged from 0.79 between 2–3 week body weights, to 0.38 between 2–12 week body weights. The phenotypic correlations are in good agreement with other estimates (Hanrahan and Eisen 1973; Jara-Almonte and White 1973; McCarthy and Bakker 1979). It is interesting to observe that while the phenotypic correlation between 6 and 12 body weight was 0.65, the one between tail lengths at these ages was 0.28. Body weight and tail length in mice seem to follow different growth trajectories.

Table 10. Estimates of phenotypic correlations between estimated growth curve parameters and body weights and tail lengths at several ages

Variate[b]	Variate[a]					
	Untransformed model			Log-transformed model		
	A	r	t*	A	r	t*
W2	0.43	0.25	−0.37	0.43	0.68	−0.49
W3	0.48	0.46	−0.41	0.48	0.74	−0.48
W4.5	0.68	0.80	−0.13	0.68	0.77	−0.09
W6	0.78	0.78	0.14	0.78	0.75	0.17
W8	1.00	0.43	0.53	1.00	0.78	0.48
W12	0.72	0.43	0.27	0.72	0.61	0.25
T6	0.16	0.13	−0.01	0.16	0.17	−0.02
T12	0.24	0.20	−0.00	0.24	0.24	−0.00

[a] A: asymptotic body weight; r: maximum growth rate; t*: age at point of inflection

[b] W2, W3, W4.5, W6, W8 and W12 are body weights at 2, 3, 4.5, 6, 8 and 12 weeks of age, respectively; T6 and T12 are tail lengths at 6 and 12 weeks of age, respectively

Table 11. Estimates of phenotypic correlations between body weights and tail length at several ages

Variate[a]	Variate[a]							
	W2	W3	W4.5	W6	W8	W12	T6	T12
W2	1.00	–	–	–	–	–	–	–
W3	0.79	1.00	–	–	–	–	–	–
W4.5	0.56	0.67	1.00	–	–	–	–	–
W6	0.45	0.53	0.77	1.00	–	–	–	–
W8	0.43	0.48	0.68	0.78	1.00	–	–	–
W12	0.38	0.43	0.57	0.65	0.72	1.00	–	–
T6	0.15	0.17	0.19	0.17	0.16	0.13	1.00	–
T12	0.21	0.22	0.24	0.28	0.24	0.21	0.28	1.00

[a] W2, W3, W4.5, W6, W8 and W12 are body weights at 2, 3, 4.5, 6, 8 and 12 weeks of age, respectively; T6 and T12 are tail lengths at 6 and 12 weeks of age

Conclusions

In conclusion, selection for estimated asymptotic body weight or maximum growth rate would be expected to increase body weight at all ages. This can be accomplished with less difficulty by selecting for body weight. However, selection for an earlier age at point of inflection (age at puberty) would seem promising in the sense that the trait was moderately heritable (0.41–0.44) and the genetic correlations were favorable. It would appear feasible to increase juvenile growth without affecting mature body weight.

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