Theor. Appl. Genet. 51, 249-260 (1978)

Direct and Maternal Genetic Effects on Body Weight Maturing Patterns in Mice*

W.R. Williams, E.J. Eisen, J. Nagai** and H. Bakker***
Department of Animal Science, North Carolina State University, Raleigh, North Carolina (USA)

Summary. Direct and maternal genetic effects were evaluated for maturing patterns of body weight in mice using a crossfostering design. Crossfostering was performed in one group using dams from populations selected for rapid growth rate (M16 and H_6) and their reciprocal F_1 crosses. A second crossfostering group consisted of dams from the respective control populations (ICR and C_2) and their reciprocal F_1's. Population differences were partitioned into direct and maternal effects due to genetic origin, correlated selection responses, heterosis and cytoplasmic or sex-linked effects. Degree of maturity was calculated at birth, 12, 21, 31 and 42 days of age by dividing body weight at each age by 63-day weight. Absolute and relative maturing rates were calculated in adjacent age intervals between birth and 63 days. Genetic origin effects (ICR vs. C_2; M16 vs. H_6) were significant for many maturity traits, with average direct being more important than average maternal genetic effects. In general, correlated responses to selection for maturity traits were larger in the M16 population (M16 vs. ICR) than in the H_6 population (H_6 vs. C_2) and correlated responses in average direct effects were larger than average maternal effects. Positive correlated responses in average direct effects were found for relative maturing rates at all ages and for absolute maturing rates from 31 to 63 days. Apparent correlated responses in degree of maturity were negative for M16 and H_6. However, further analysis suggested that the correlated response for degree of maturity in H_6 may be positive at later ages and negative at earlier ages. Direct and maternal heterosis for degree of maturity was positive in the selected and control crosses. Absolute and relative maturing rates showed positive heterosis initially, followed by negative heterosis. Reciprocal differences due to the cytoplasm or sex-linkage were not important for patterns of maturity.

Key words: Mice - Maternal Effects - Body Weight - Maturity - Sex-linkage

Introduction

Body weights and weight gains commonly have been used to compare growth in different individuals measured at a constant age. These measurements fail to distinguish the degree of development or proportion of mature weight attained at a specific age. Based on an observation by Brody (1945) that body weight at an immature age can be expressed as a proportion of mature size, Fitzhugh and Taylor (1971) defined degree of maturity, absolute maturing rate and relative maturing rate. These traits provide a novel description of growth, which can be used to distinguish differences in growth patterns among individuals that vary in their mature size.

The objective of the present study was to use degree of maturity, absolute maturing rate and relative maturing rate to evaluate growth patterns in growth-selected, control and crossbred mice. A multiple-group crossfostering design (Nagai, Bakker and Eisen 1976a, b) was used to partition average direct and average maternal genetic effects among populations. Reciprocal crosses between populations were used to determine the importance of direct and maternal heterotic and non-chromosomal effects on the maturing traits. This study was part of an experiment designed to evaluate direct and maternal genetic effects of correlated traits in growth-selected populations of mice (Nagai et al. 1976a,b; Bakker, Nagai and Eisen 1976; Eisen, Bakker and Nagai 1977).

* Paper No. 5244 of the Journal Series of the North Carolina Agricultural Experiment Station, Raleigh, Animal Research Institute Contribution No. 683 and Agricultural University at Wageningen Contribution No. 654-490-12

** On leave from the Animal Research Institute, Agriculture Canada at Ottawa, Ontario

*** On leave from the Department of Animal Husbandry, Agricultural University at Wageningen, the Netherlands

0040-5752/78/0051/0249/$ 2.40

Materials and Methods

Source of Data

The mouse populations, mating scheme and crossfostering design have been described by Nagai et al. (1976a). Briefly, the H_6 and M16 populations were developed by selection for large 6-week body weight and increased 3- to 6-week postweaning gain for 73 and 36 generations, respectively. The C_2 and ICR populations represent the respective controls. Both selected strains appear to have plateaued in their response to selection at the time this study was initiated. Direct responses to selection have been described by Legates (1969) for the H_6 population and by Eisen (1975) for the M16 population.

Matings between the H_6 and M16 populations and between the C_2 and ICR populations provided four reciprocal F_1 crosses ($H_6 \times$ M16, M16 $\times H_6$, $C_2 \times$ ICR, ICR $\times C_2$; male parent written first). Individuals within each of the 8 populations were randomly mated at about 9 weeks of age, avoiding sib matings, to produce 8 progeny groups. The selected crossfostering group consisted of dams from the H_6, M16, $H_6 \times$ M16 and M16 $\times H_6$ populations. Similarly, the control crossfostering group included the C_2, ICR, $C_2 \times$ ICR and ICR $\times C_2$ populations. Within each crossfostering group, replicate crossfostering sets were formed. Litters were standardized to 8 pups of 4 males and 4 females, when possible, and each dam nursed 2 of her own progeny and 2 from each of the other 3 dams. An attempt was made to allot a male and female from a litter to each nurse dam. Toe-clipping was performed at birth to distinguish line genotypes and again at 7 days to provide individual mouse identification. Progeny were weaned at 21 days of age, and 4 mice of the same sex and population were randomly caged together. Body weights were recorded at birth, 12, 21, 31, 42 and 63 days of age on all progeny. Body weights at 21 days and thereafter were adjusted for sex (Falconer and King 1953).

Definition of Traits

Fitzhugh and Taylor (1971) defined the following traits: Degree of maturity is the proportion of mature size (A) attained for body weight (Y_t) measured at a given stage (t) of development, $MATt = Y_t/A$. Absolute maturing rate is the change in degree of maturity over a time interval, $AMR\Delta t = \frac{dMATt}{dt} \doteq (MATt_2 - MATt_1)/(t_2 - t_1)$, where t_1 and t_2 represent different ages. Relative maturing rate is the maturing rate relative to the current degree of maturity, $RMR\Delta t = \frac{1}{MATt}\frac{dMATt}{dt} \doteq (\ell nY_{t_2} - \ell nY_{t_1})/(t_2 - t_1)$, which is equivalent to relative growth rate. To transform the data to measures of degree of maturity, individual weights at each age were divided by weight at 63 days, which was used as an approximate measure of mature size. These traits are denoted by MAT1, MAT2, MAT3, MAT4 and MAT5, respectively. Absolute and relative maturing rates were calculated between successive ages from birth to 63 days using the above formulas. Absolute maturing rates are denoted as AMR1 (birth to 12 days), AMR2 (12 to 21 days), AMR3 (21 to 31 days), AMR4 (31 to 42 days) and AMR5 (42 to 63 days). Relative maturing rates are written analogously as RMR1, RMR2, etc. with the numeric prefix referring to the successive time interval.

Statistical Analysis

The statistical model used was $Y_{ijk\ell m} = \mu + G_i + S_{j(i)} + A_{k(i)} + N_{\ell(i)} + (AN)_{k\ell(i)} + (SA)_{jk(i)} + (SN)_{j\ell(i)} + (SAN)_{jk\ell(i)} + e_{ijk\ell m}$, where $Y_{ijk\ell m}$ is an observation on the m^{th} individual of the k^{th} genetic population nursed by a dam of the ℓ^{th} genetic population in crossfostering set j of the selected or control group (i), μ = general mean; G_i = effect of the selected (i=1) or control (i=2) group; $S_{j(i)}$ = effect of the $j(i)^{th}$ crossfostering set ($j(1) = 1,2,\ldots,28$; $j(2) = 1,2,\ldots,48$; $A_{k(i)}$ = effect of the $k(i)^{th}$ population of genetic dam ($k(1)$, $k(2) = 1,\ldots,4$); $N_{\ell(i)}$ = effect of the $\ell(i)^{th}$ population of nurse dam ($\ell(1), \ell(2) = 1,\ldots,4$); $(AN)_{k\ell(i)}$, $(SA)_{jk(i)}$, $(SN)_{j\ell(i)}$, $(SAN)_{jk\ell(i)}$ represent interaction effects; $e_{ijk\ell m}$ = residual effect associated with the m^{th} mouse of the $(ijk\ell)^{th}$ subclass. The G_i, $A_{k(i)}$, and $N_{\ell(i)}$ are considered fixed effects while $S_{j(i)}$ is a random effect. The residual term, $e_{ijk\ell m}$, is assumed to be normally and independently distributed with zero mean and variance σ^2.

The appropriate error terms to test prenatal, postnatal and crossfostering group differences are the crossfostering set × prenatal, crossfostering set × postnatal and crossfostering set × prenatal × postnatal interaction mean squares, respectively. These interaction sums of squares were pooled to provide an experimental error to test prenatal, postnatal, prenatal × postnatal and crossfostering group sources of variation. The prenatal and postnatal effects were partitioned into a priori orthogonal and nonorthogonal linear contrasts. The contrasts for direct genetic effects are listed in Table 1. Contrasts for maternal genetic effects are similar, except that the effect of the selected genetic group must be deleted in the contrasts evaluating response to selection. The genetic interpretation of these contrasts (Dickerson 1969; Eisen 1973; Nagai et al. 1976b) is presented below.

Prenatal (Genetic Dam) Comparisons

The prenatal marginal means are means of full sib progeny of the same genetic population averaged across different postnatal maternal environments. Excluding genetic by nurse dam interactions, the environmental influence provided by the 4 nurse dams within a selected or control crossfostering set are expected to influence each genotype in a similar manner. Thus, prenatal mean comparisons should describe average direct genetic differences within the select or control groups, e.g. H_6 - M16, C_2 - ICR. Comparisons of prenatal means across select and control groups involve different maternal environments influencing select genotypes in one case and the control genotypes in the other. Thus, valid prenatal comparisons between the selected and control populations

Table 1. Linear contrasts developed to test differences in average direct and average maternal genetic effects resulting from genetic origin, correlated selection response, heterosis and reciprocal effects

Nature of contrast	Contrast	Selected line effects				Control line effects			
		H_6	M16	$H_6 \times$ M16	M16 $\times H_6$	C_2	ICR	$C_2 \times$ ICR	ICR $\times C_2$
Genetic origin	1	1	-1						
	2					1	-1		
Selection response	3	1				-1			
	4		1				-1		
	5	1	-1			-1	1		
Heterosis	6	-1	-1	1	1				
	7					-1	-1	1	1
	8	-1	-1	1	1	1	1	-1	-1
Reciprocal effects	9			1	-1				
	10							1	-1

require the assumption that the expected phenotype averaged across different postnatal maternal environments will reflect the genotype of the population.

Postnatal (Nurse Dam) Comparisons

Within a select or control crossfostering set, each of 4 nurse dams suckled 2 full sibs of her own and 2 full sibs from each of 3 other genetic populations. Therefore, the expected postnatal marginal mean represents the average maternal performance for the particular nurse dam population because the mean growth potential of progeny from the 4 selected (or control) populations is expected to be equal among the 4 nurse dam populations of concern. For the comparison of postnatal maternal performance within select or control groups, postnatal marginal means can thus be used to estimate the difference in average maternal genetic effects. However, for the comparison of postnatal maternal performance between selected and control groups, the different growth potential of progeny between the two groups must be taken into consideration. In terms of the model employed, postnatal marginal means can be written as $\mu + G_i + N_{\ell(i)}$, where G_i is the effect of the select (i=1) or control (i=2) group and $N_{\ell(i)}$ is the effect of the $\ell(i)^{th}$ population of nurse dam. The contrast for the difference in postnatal marginal means is

$$\mu + G_1 + N_{\ell(1)} - \mu - G_2 - N_{\ell(2)} = G_1 - G_2 + N_{\ell(1)} - N_{\ell(2)}.$$

The difference in postnatal marginal means between a selected and a control dam population provides the difference in average maternal genetic effects between the two populations plus the mean difference between the selected and control groups. This case is different from the comparison of prenatal means of a selected population with that of a control population, where two prenatal marginal means reflect solely average direct genetic effects.

Correlations

The phenotypic correlations among the traits were approximated from the covariance within full-sib families, pooled within populations. These full sibs were nursed by either their genetic dam or a foster dam. The expectation of the covariance within full-sib families is $1/2\ \sigma_{A_{ij}} + 3/4\ \sigma_{D_{ij}} + \sigma_{E_{ij}}$, where $\sigma_{A_{ij}}$, $\sigma_{D_{ij}}$ and $\sigma_{E_{ij}}$ represent the additive, dominance and environmental covariances ($i \neq j$) or variances ($i = j$) for traits i and j.

Results

The effects of selection and crossing the selected populations on body weights are shown in Fig. 1. The means plotted are based on progeny reared by their own genetic mother. The results show that selection in the M16

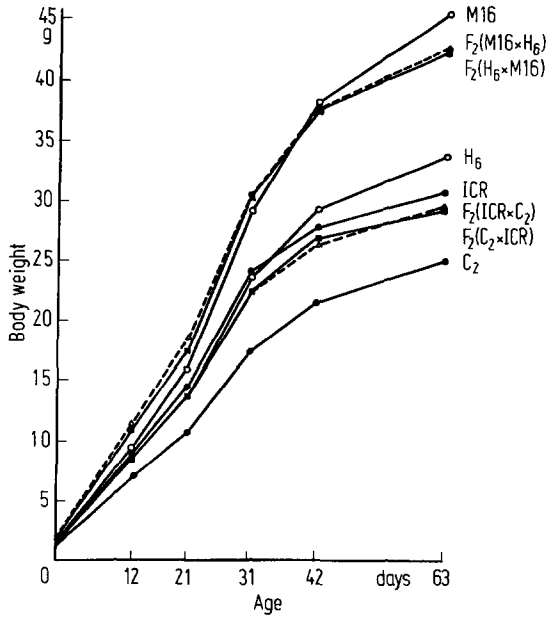

Fig. 1. Growth curves for the eight populations (means based on progeny reared by their own genetic mother)

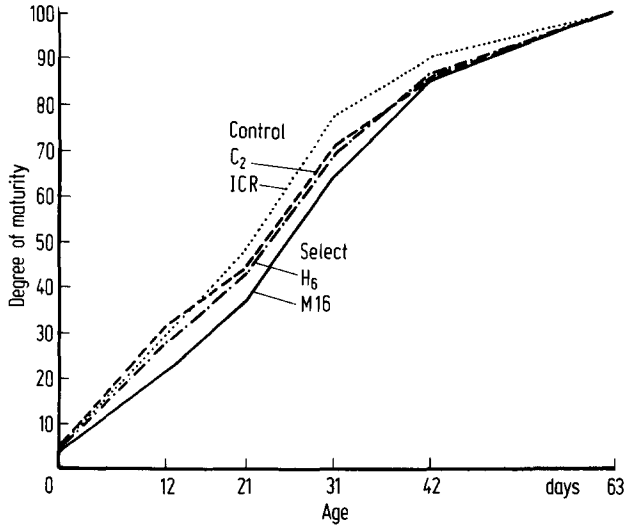

Fig.2. Plot of prenatal least-squares means for degree of maturity versus age for the control and selected populations

and H_6 populations has effectively increased growth rate compared with ICR and C_2, respectively, and that the selected and control crosses exhibited heterosis for body weight (Nagai et al. 1976b).

The magnitude of genetic diversity in maturing patterns is illustrated by the prenatal least-square means for degree of maturity plotted against age for the control and selected populations (Fig.2). Least-squares means, classified by population of genetic and nurse dams, are listed in Tables 2 to 4 for each maturing trait.

The analyses of variance for degree of maturity, absolute maturing rate, and relative maturing rate traits are found in Williams (1976). Mean squares for crossfostering groups (selected vs. control, crossfostering sets, prenatal populations (direct genetic), and postnatal populations (maternal genetic), for the most part, were significant ($P < .01$). The significant ($P < .01$) postnatal dam effect for degree of maturity at birth reflects the substained maternal influence on 63-day body weight since birth weights were similar among all postnatal dam populations within crossfostering groups (Nagai et al. 1976b). Prenatal by postnatal interactions were found to be nonsignificant, so that linear contrasts involving this interaction were not conducted. The absence of significant prenatal by postnatal interactions are essential assumptions for valid interpretation of the prenatal and postnatal mean comparisons. Previous investigations with mice have generally shown that prenatal line by postnatal line interactions are negligible for body weights and weight gains (White, Legates and Eisen 1968; LaSalle and White 1975; Nagai et al. 1976b).

Table 2. Least-squares means for degree of maturity traits classified by population of genetic dam and nurse dam[a]

Population	MAT1	MAT2	MAT3	MAT4	MAT5
	Genetic dam				
H_6	4.72	27.64	42.96	69.38	86.74
M16	3.63	21.45	36.28	64.35	85.15
$H_6 \times$ M16	4.23	25.15	41.44	71.20	87.93
M16 $\times H_6$	4.20	25.01	41.09	70.21	87.59
C_2	5.50	30.99	44.37	70.27	86.43
ICR	5.35	29.26	48.02	77.65	89.98
$C_2 \times$ ICR	5.29	29.85	45.85	76.21	88.87
ICR $\times C_2$	5.48	30.32	46.26	76.25	89.11
	Nurse dam				
H_6	4.33	23.12	38.49	67.47	86.02
M16	4.29	24.27	40.11	68.56	86.82
$H_6 \times$ M16	4.07	25.63	41.00	69.16	87.07
M16 $\times H_6$	4.10	26.23	42.17	69.95	87.50
C_2	5.60	27.42	44.07	73.96	88.11
ICR	5.34	30.60	46.06	75.00	88.78
$C_2 \times$ ICR	5.31	31.21	47.35	76.19	88.77
ICR $\times C_2$	5.35	31.19	47.02	75.22	88.74
Crossfostering group	Standard errors				
Select	.04	.21	.30	.46	.34
Control	.03	.16	.23	.36	.26

[a] Each mean and standard error has been multiplied by 100. Number of observations for the respective populations of genetic dam are 216, 200, 222, 223, 359, 370, 368, 373 and for populations of nurse dams are 215, 197, 226, 223, 355, 375, 362, 378

Differences Due to Genetic Origin, Selection Procedures and Drift

The base populations, derived from different foundations stocks, likely contain initial gene frequency differences at a number of loci influencing growth. Thus, the nature and magnitude of genetic variation among the two foundation population, ICR and C_2, could be quite distinct. Different selection criteria and heritabilities in the M16 and H_6 populations (Legates 1969; Eisen 1975) are also expected to increase the genetic distance between them. Furthermore, many generations of selection in finite populations may re-

Table 3. Least-squares means for absolute maturing rate traits classified by population of genetic dam and nurse dam[a]

Population	AMR1	AMR2	AMR3	AMR4	AMR5
	Genetic dam				
H_6	1.91	1.70	2.64	1.58	0.63
M16	1.48	1.65	2.81	1.89	0.71
$H_6 \times$ M16	1.74	1.81	2.98	1.52	0.57
M16 $\times H_6$	1.73	1.79	2.91	1.58	0.59
C_2	2.12	1.49	2.59	1.47	0.65
ICR	1.99	2.08	2.96	1.12	0.48
$C_2 \times$ ICR	2.05	1.78	3.04	1.15	0.53
ICR $\times C_2$	2.07	1.77	3.00	1.17	0.52
	Nurse dam				
H_6	1.57	1.71	2.90	1.69	0.67
M16	1.66	1.76	2.84	1.66	0.63
$H_6 \times$ M16	1.80	1.71	2.82	1.63	0.62
M16 $\times H_6$	1.84	1.77	2.78	1.60	0.60
C_2	1.82	1.85	2.99	1.29	0.57
ICR	2.11	1.72	2.89	1.25	0.53
$C_2 \times$ ICR	2.16	1.79	2.88	1.14	0.53
ICR $\times C_2$	2.15	1.76	2.82	1.23	0.54
Crossfostering group	Standard errors				
Select	0.016	0.019	0.034	0.033	0.016
Control	0.012	0.015	0.026	0.025	0.012

[a] Each mean and standard error has been multiplied by 100

Table 4. Least-squares means for relative maturing rate traits classified by population of genetic dam and nurse dam[a]

Population	RMR1	RMR2	RMR3	RMR4	RMR5
	Genetic dam				
H_6	14.73	4.91	4.80	2.05	0.68
M16	14.81	5.84	5.75	2.58	0.78
$H_6 \times$ M16	14.85	5.57	5.43	1.94	0.62
M16 $\times H_6$	14.88	5.54	5.37	2.04	0.64
C_2	14.41	4.01	4.59	1.91	0.70
ICR	14.17	5.53	4.80	1.40	0.51
$C_2 \times$ ICR	14.42	4.79	5.10	1.43	0.57
ICR $\times C_2$	14.27	4.72	5.02	1.44	0.56
	Nurse dam				
H_6	13.96	5.68	5.64	2.24	0.73
M16	14.44	5.62	5.38	2.18	0.68
$H_6 \times$ M16	15.37	5.24	5.24	2.13	0.67
M16 $\times H_6$	15.50	5.32	5.09	2.06	0.64
C_2	13.24	5.30	5.17	1.64	0.61
ICR	14.56	4.55	4.87	1.58	0.57
$C_2 \times$ ICR	14.77	4.65	4.77	1.42	0.57
ICR $\times C_2$	14.70	4.56	4.70	1.54	0.58
Crossfostering group	Standard errors				
Select	0.062	0.048	0.055	0.046	0.018
Control	0.048	0.037	0.042	0.036	0.014

[a] Each mean and standard error has been multiplied by 100

sult in mean changes due to genetic drift. Contrasts 1 and 2 (Table 1) were developed to evaluate average direct or average maternal genetic differences between the two selected populations and between the two control populations, respectively.

Average direct genetic effects for degree of maturity were greater ($P < .01$) in the H_6 population than in M16 at all ages (Table 5). Average direct genetic effects in H_6 were larger ($P < .01$) than in M16 for initial absolute maturing rate, followed by lower ($P < .01$) absolute maturing rates from 21 days onward. Relative maturing rates were smaller ($P < .01$) in the H_6 population from 12 to 63 days. Average direct genetic effects between the two control populations were quite distinct from those in the two selected populations. The C_2 population was more ($P < .01$) mature at birth and 12 days than ICR and less ($P < .01$) mature thereafter. Absolute and relative maturing rates in the C_2 population were greater ($P < .01$) between birth and 12 days, smaller ($P < .01$) between 12 and 31 days, and greater ($P < .01$) between 31 days and maturity, as compared with ICR.

Average maternal genetic differences were generally smaller than average direct genetic differences and were significant for fewer traits. Among the selected populations, average maternal genetic effects for degree of maturity at 12 and 21 days were lower ($P < .01$) for H_6. Absolute maturing rates revealed no significant differences, while relative maturing rates were greater ($P < .01$) between birth and 12 days for offspring suckling M16 dams and greater ($P < .01$) between 21 and 31 days for H_6 dams. Average maternal genetic effects showed similar trends in the controls. Average maternal genetic effects in the C_2 population increased ($P < .01$) degree of maturity at birth and decreased ($P < .01$) degree of maturity at 12 and 21 days, relative to ICR. The nursing influence of the ICR dams increased ($P < .01$) both absolute and relative maturing rates in the progeny they suckled between birth and 12 days, while the C_2 maternal effects increased ($P < .01$) relative maturing rates between 12 and 21 days and both absolute and relative maturing rates between 21 and 31 days of age.

Table 5. Average direct and average maternal genetic differences between H_6 and M16 and between C_2 and ICR in degree of maturity, absolute maturing rate, and relative maturing rate traits[a]

Trait	H_6 - M16		C_2 - ICR	
	Average direct	Average maternal	Average direct	Average maternal
MAT1	1.09**	0.04	0.15**	0.26**
MAT2	6.19**	-1.15**	1.73**	-3.18**
MAT3	6.68**	-1.62**	-3.65**	-1.99**
MAT4	5.03**	-1.09	-7.38**	-1.04
MAT5	1.59**	-.81	-3.55**	-.66
AMR1	0.43**	-.10	0.13**	-.29**
AMR2	0.05	-.05	-.60**	0.13
AMR3	-.16**	0.05	-.37**	0.10*
AMR4	-.31**	0.03	0.35**	0.03
AMR5	-.08**	0.04	0.17**	0.03
RMR1	-.08	-.48**	0.25**	-1.32**
RMR2	-.93**	0.06	-1.52**	0.75**
RMR3	-.95**	0.26**	-.21**	0.29**
RMR4	-.53**	0.06	0.52**	0.06
RMR5	-.10**	0.05	0.19	0.04

[a] Contrasts 1 and 2 have been multiplied by 100
* $P < .05$, ** $P < .01$

Table 6. Average direct genetic differences in degree of maturity, absolute maturing rate, and relative maturing rate traits resulting from correlated responses and differential correlated responses to selection[a]

Trait	H_6-C_2	SD[b]	M16-ICR	SD[b]	(H_6-C_2)-(M16-ICR)
MAT1	-.77**	-1.32	-1.71**	-2.93	0.94**
MAT2	-3.35**	-1.10	-7.82**	-2.58	4.47**
MAT3	-1.41**	-.32	-11.74**	-2.66	10.33**
MAT4	-.89**	-.13	-13.30**	-1.97	12.41**
MAT5	0.31	0.06	-4.83**	-.98	5.14*
AMR1	-.21**	-.91	-.51**	-2.22	0.29**
AMR2	0.21**	0.72	-.44**	-1.52	0.65**
AMR3	0.05	0.10	-.16**	-.32	0.21**
AMR4	0.11*	0.23	0.77**	1.62	-.66**
AMR5	-.01	-.04	0.23**	0.99	-.24**
RMR1	0.32**	0.35	0.64**	0.70	-.32**
RMR2	0.90**	1.29	0.31**	0.44	0.59**
RMR3	0.21**	0.26	0.95**	1.17	-.74**
RMR4	0.14*	0.21	1.19**	1.74	-1.04**
RMR5	-.02	-.07	0.27**	1.01	-.29**

[a] Contrasts 3, 4 and 5 have been multiplied by 100
[b] The correlated response in standard deviation units
* $P < .05$, ** $P < .01$

Correlated response to selection in maturing patterns

Correlated responses in maturing traits were evaluated by contrasts 3 and 4, while contrast 5 provides a test of homogeneous response to selection between the two selection regimes (H_6-C_2 and M16-ICR). The deviations of the selected populations from their respective controls were also expressed in standard deviation units. Results of these contrasts for average direct and maternal genetic effects are listed in Tables 6 and 7, respectively.

The portion of the correlated response due to average direct genetic effects, based on the H_6-C_2 contrast, reveals that selection for 6-week body weight decreased ($P < .01$) degree of maturity at birth, 12, 21 and 31 days. Absolute maturing rate for the H_6 population was smaller from birth to 12 days ($P < .01$) but larger in the 12- to 21-day ($P < .01$) and 31- to 42-day ($P < .05$) age intervals. Relative maturing rates were greater ($P < .01$) in the H_6 population between birth and 42 days. In standard deviation units, all of these traits exhibited greater correlated responses in the earlier stages of postnatal growth. The M16-ICR contrast for average direct genetic effects indicated a decreased ($P < .01$) degree of maturity at each age due to selection for postweaning gain. Absolute maturing rates were lower in M16 between birth and 31 days ($P < .01$) and higher ($P < .01$) beyond 31 days. Relative maturing rates were higher ($P < .01$) in M16 throughout the growth period. The correlated responses, expressed in standard deviation units, were larger in M16 than in H_6 throughout the maturing cycle.

Correlated responses in average direct genetic effects differed for the two selected populations, as measured by the (H_6-C_2) - (M16-ICR) contrast. H_6 exhibited a lower ($P < .01$) correlated response than M16 in the decrease in degree of maturity. There were also significant ($P < .01$) differential correlated responses in absolute and relative maturing rates during each age interval. For example, AMR2 increased ($P < .01$) in H_6 and decreased ($P < .01$) in M16, while RMR2 increased ($P < .01$) to a greater degree in H_6 than M16.

Correlated responses in the maturity traits due to average maternal genetic effects were generally smaller than those due to average direct genetic effects, and were manifested primarily during the preweaning and early weaning periods (birth to 21 days) in the H_6 and M16 populations. The average maternal genetic effects in H_6 increased ($P < .01$) degree of ma-

Table 7. Average maternal genetic differences in degree of maturity, absolute maturing rate, and relative maturing rate traits resulting from correlated responses and differential correlated responses to selection[a]

Trait	H_6-C_2	SD[b]	M16-ICR	SD[b]	(H_6-C_2)-(M16-ICR)
MAT1	-.07	-.12	0.16**	0.27	-.22**
MAT2	0.99**	0.33	-1.04**	-.34	2.03**
MAT3	0.11	0.02	-.27	-.06	0.37
MAT4	-.18	-.03	-.13	-.02	-.04
MAT5	-.35	-.07	-.21	-.04	-.15
AMR1	0.09**	0.39	-.10**	-.43	0.19**
AMR2	-.10**	-.34	0.09**	0.31	-.18**
AMR3	-.03	-.06	0.01	0.02	-.04
AMR4	-.02	-.04	-.01	-.02	-.01
AMR5	0.02	0.09	0.01	0.04	0.01
RMR1	0.22*	0.24	-.62**	-.68	0.84**
RMR2	-.31**	-.44	0.37**	0.53	-.68**
RMR3	0.01	0.01	0.05	0.06	-.03
RMR4	-.01	-.01	-.01	-.01	0.00
RMR5	0.02	0.07	0.01	0.04	0.01

[a] Contrasts 3, 4 and 5 have been multiplied by 100
[b] The correlated response in standard deviation units
* $P < .05$, ** $P < .01$

turity at 12 days, increased absolute ($P < .01$) and relative ($P < .05$) maturing rates between birth and 12 days, and decreased ($P < .01$) absolute and relative maturing rates between 12 and 21 days. The average maternal genetic effects of the M16 population increased ($P < .01$) degree of maturity at birth, decreased ($P < .01$) degree of maturity at 12 days, decreased ($P < .01$) absolute and relative maturing rates between birth and 12 days, and increased ($P < .01$) absolute and relative maturing rates between 12 and 21 days. The pattern of correlated responses in maturing traits was different between the two selection regimes. Correlated responses were positive for MAT2, AMR1 and RMR1 and negative for MAT1, AMR2 and RMR2 in the H_6 regime, while completely opposite correlated responses were elicited by selection in M16.

Direct and Maternal Heterotic Effects

Direct and maternal heterotic effects were evaluated within the selected and control crosses. Direct heterosis in the selected and control groups was defined as: $2[1/2[(H_6 \times M16) + (M16 \times H_6) - (H_6 + M16)]]$ and $2[1/2[(C_2 \times ICR) + (ICR \times C_2) - (C_2 + ICR)]]$, respectively. The coefficient of 2 provided the maximum expected direct heterosis since offspring were F_2 progeny. Maternal heterosis was defined similarly but without multiplication by 2, since dams were F_1 individuals. Results also were expressed in terms of percent heterosis which is the average heterosis expressed as a proportion of the midparental mean. Linear contrasts 6 and 7 accommodated a test of he-

Table 8. Direct and maternal heterosis exhibited on maturity traits[a]

	Select				Control				Select-control	
Trait	Direct heterosis	%[b]	Maternal heterosis	%[b]	Direct heterosis	%[b]	Maternal heterosis	%[b]	Direct heterosis	Maternal heterosis
MAT1	0.07	2	-.23**	-5	-.08	-1	-.14**	-3	0.15	-.09
MAT2	1.06*	4	2.24**	9	-.08	0	2.19**	8	1.14	0.05
MAT3	3.30**	8	2.28**	6	-.27	-1	2.12**	5	3.57**	0.16
MAT4	7.68**	11	1.54**	2	4.55*	6	1.22**	2	3.13*	0.31
MAT5	3.63**	4	0.87*	1	1.58**	2	0.31	0	2.05*	0.56
AMR1	0.08*	5	0.21**	13	0.00	0	0.19**	10	0.08	0.01
AMR2	0.25**	15	0.01	1	-.02	-1	-.01	-1	0.27**	0.01
AMR3	0.44**	16	-.07*	-2	0.48**	17	-.09**	-3	-.04	0.02
AMR4	-.37**	-21	-.06	-4	-.27**	-21	-.08**	-6	-.10	0.02
AMR5	-.17**	-25	-.04*	-6	-.08**	-14	-.01	-2	-.10*	-.03
RMR1	0.19	1	1.23**	9	0.11	1	0.84**	6	0.08	0.39**
RMR2	0.35**	7	-.37**	-7	-.04	-1	-.32**	-6	0.39**	-.05
RMR3	0.24*	5	-.35**	-6	0.72**	15	-.29**	-6	-.48**	-.06
RMR4	-.66**	-29	-.12*	-5	-.44**	-27	-.13**	-8	-.21	0.01
RMR5	-.21**	-29	-.05*	-7	-.09**	-15	-.02	-3	-.12*	-.03

[a] Contrasts 6, 7 and 8 have been multiplied by 100 for each trait
[b] Percent heterosis
* $P < .05$, ** $P < .01$

Table 9. Correlations among body weight and degree of maturity traits[a, b, c]

Trait	MAT1	MAT2	MAT3	MAT4	MAT5
WTB	.60	.20	.19	.11	.03
WT12	.18	.36	.23	.15	.04
WT21	.05	.08	.38	.25	.12
WT31	-.18	-.19	-.01	.53	.21
WT42	-.41	-.48	-.34	.02	.23
WT63	-.58	-.69	-.63	-.42	-.44

[a] Correlation $\geq |.058|$ is significantly different from zero at $P < .05$
[b] Correlation $\geq |.077|$ is significantly different from zero at $P < .01$
[c] 1124 degrees of freedom

terotic effects, while contrast 8 was used to determine whether selection had altered the degree of heterosis. Results are presented in Table 8.

Direct heterotic effects increased degree of maturity from 12 to 42 days in crosses of the selected populations. The selected crosses had higher absolute and relative maturing rates than the selected parent populations between birth and 31 days, while the purebred progeny matured at greater rates from 31 to 63 days. Direct heterotic effects increased degree of maturity at 31 ($P < .05$) and 42 ($P < .01$) days among control crosses. Direct heterosis for absolute and relative maturing rates between birth and 21 days was not evident, while between 21 and 31 days crossbreds matured more ($P < .01$) rapidly. From 31 days to maturity, direct heterotic effects decreased absolute and relative maturity rates in control crosses. Direct heterotic effects had a similar directional influence among selected crosses compared with the controls. However, the magnitude of direct heterosis was significantly greater for MAT3, MAT4, MAT5, AMR2, AMR5, RMR2 and RMR5 in selected crosses.

Maternal heterosis was evident in both the selected and control crosses. When compared with purebred dams, mice nursed by the selected and control crossbred dams were less ($P < .01$) mature at birth and more ($P < .01$) mature at 12, 21 and 31 days of age. By 42 days, maternal heterosis was only exhibited in the selected group, with the crossbred maternal influence increasing degree of maturity. Maternal heterosis for maturing rate traits was similar for the selected and control crosses. Absolute and relative maturing rates were greater ($P < .01$) among progeny nursed by crossbred dams birth to 12 days. Maternal heterosis decreased absolute maturing rates from 21 to 63 days as well as relative maturing rates between 12 and 63 days in the selected group. Maternal heterosis among control dams decreased ($P < .01$) absolute maturing rates between 12 and 31 days and relative maturing rates between 12 and 42 days. Selection had very little effect on changing maternal heterosis. The only significance was found for relative maturing rates between birth and twelve days ($P < .01$), with greater heterosis shown by the selected dams. For all maturing rate measures in both the selected and control crosses, the magnitude of maternal heterosis decreased with age.

Reciprocal Crosses

The reciprocal crossbreds should have received similar autosomal chromosomal contributions from either male or female parents. Cytoplasmic differences peculiar to the egg and sex-linked effects, as well as sampling of dams, are sources of reciprocal differences. Contrasts 9 and 10 were designed to test average direct and average maternal reciprocal differences between selected crossbreds and between control crossbreds, respectively. Only a small number of significant differences was observed, indicating that the contributions of cytoplasmic or sex-linked effects are of little relative influence on maturing traits.

Correlation Analysis

Approximate phenotypic correlations between body weights and degrees of maturity measured at the same age were positive (Table 9). Larger mice at earlier preweaning ages tended to be more mature at all ages, although the correlations decreased with age. Heavier individuals in the postweaning stages were less mature during the early growth periods. Correlations between 63-day body weight and degree of maturity at each age were negative.

Phenotypic correlations among degrees of maturity and abolsute and relative maturing rates are given in Table 10. Correlations among degrees of maturity at different ages were positive, decreasing as the age

Table 10. Correlations among degree of maturity, absolute maturing rate, and relative maturing rate traits[a, b, c]

	MAT2	MAT3	MAT4	MAT5	AMR1	AMR2	AMR3	AMR4	AMR5	RMR1	RMR2	RMR3	RMR4	RMR5
MAT1	.75	.68	.41	.33	.63	.30	.02	-.21	-.33	-.56	-.16	-.28	-.24	-.32
MAT2		.81	.51	.41	.99	.26	.04	-.26	-.41	.10	-.35	-.32	-.31	-.39
MAT3			.63	.50	.79	.78	.06	-.32	-.50	-.01	.25	-.37	-.40	-.49
MAT4				.64	.49	.50	.81	-.66	-.64	.01	.17	.48	-.78	-.63
MAT5					.39	.39	.44	.16	-1[d]	0	.12	.18	-.03	-1[d]
AMR1						.23	.04	-.25	-.39	.26	-.37	-.30	-.31	-.38
AMR2							.05	-.25	-.39	-.12	.79	-.27	-.32	-.39
AMR3								-.61	-.44	.03	.03	.89	-.70	-.44
AMR4									-.16	-.02	-.10	-.43	.97	-.16
AMR5										0	-.12	-.18	.03	1[d]
RMR1											-.19	.04	-.05	.01
RMR2												-.06	-.13	-.13
RMR3													-.50	-.19
RMR4														.23

[a] Correlation $\geq |.058|$ is significantly different from zero at $P < .05$
[b] Correlation $\geq |.077|$ is significantly different from zero at $P < .01$
[c] 1124 degrees of freedom
[d] Expected values of plus or minus 1

differences increased. Correlations among absolute maturing rates in different age intervals indicated that more rapidly maturing animals in early stages of growth matured less rapidly in later stages. To some extent, this pattern was also true for relative maturing rates. Greater absolute maturing rates in an age interval were associated with increased relative maturing rates during the same period, while the association was negative for different age periods. The correlations between degree of maturity and absolute maturing rates suggested that individuals maturing more rapidly at younger ages were more mature at every age, while those individuals maturing more quickly after 31 days were less mature at younger ages. Degree of maturity at each age was negatively correlated with relative maturing rates during the later growth intervals.

Discussion

Substantial differences among 8 mouse populations due to direct and maternal genetic effects were found for degree of maturity and absolute and relative maturing rates measured at several intervals from birth to 63 days of age. These maturity traits, aside from their intrinsic value in interpreting growth relative to mature size, have application to animal breeding situations where specific growth patterns are desirable for specialized breeding systems (Fitzhugh 1976). Considerable genetic variation in maturity traits exists among and within lines of beef cattle (Fitzhugh and Taylor 1971; Smith et al. 1976a,b) and Fitzhugh (1976) has emphasized the value of incorporating several maturity traits into selection indexes.

Selection for rapid growth rate in the H_6 and M16 populations has led to significant correlated responses in the maturity traits. Two points are worthy of emphasis. Average direct genetic correlated responses in these maturing traits generally were greater than average maternal genetic correlated responses and the magnitude of the correlated responses were much larger in M16 compared to H_6. These populations exhibited similar trends in comparisons of correlated responses for body weight, feed efficiency and body composition (Nagai et al. 1976b; Eisen et al. 1977).

Selection for rapid growth rate yielded positive average direct correlated responses in relative maturing (growth) rates. This result agrees with positive genetic correlations found between 3-to-6-week relative growth rate and 6-week body weight and 3-to-6-week postweaning gain, respectively, in the ICR population (Eisen 1977). In beef cattle, relative growth rate exhibited positive genetic correlations with absolute growth rates and mean body weights in the same age interval (Smith et al. 1976a).

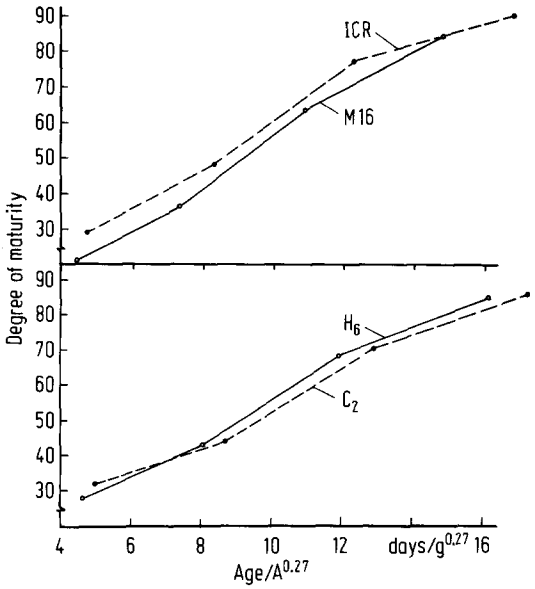

Fig.3. Degree of maturity plotted against age/$A^{.27}$ for the control and selected populations (A = mature weight estimated by 63-day body weight)

Average direct correlated responses for absolute maturing rate in M16 were negative at early ages and positive from 31 to 63 days. In general terms, a similar but less pronounced pattern was observed in H_6. The correlated response in absolute maturing rate in the age interval nearest to the criterion of selection in each population (AMR4) was positive. While no genetic correlation was available from the base population for comparison, genetic correlations observed in beef cattle between body weight or absolute growth rate and relative growth rate in the same age interval tended to be positive (Fitzhugh and Taylor 1971; Smith et al. 1976a).

Correlated responses involving average direct genetic effects for degree of maturity were positive. Again, no genetic correlations among degree of maturity and the selection criteria of 6-week body weight and 3-to-6-week postweaning gain are presently available in mice. Genetic correlations estimated from beef cattle would suggest that genetically heavier individuals tended to be more mature during that phase of growth (Fitzhugh and Taylor 1971; Smith et al. 1976a). However, when several straightbred and crossbred cattle populations were ranked for means of body weight and degree of maturity at a fixed age, the relationship was quite variable, particularly at earlier ages (Smith et al. 1976b).

The observed reduction in degree of maturity at a given age as a result of selection for rapid growth rate may be related to the fact that 63-day body weight was used as a measure of mature size, although growth is expected to continue beyond this age (Fig.1). For a given population, this will overestimate degree of maturity and absolute maturing rate, but have no effect on relative maturing rate. Comparing two populations that differ in degree of maturity at a given age using the downwardly biased estimates of mature size may, therefore, lead to biased estimtes of population differences. In order to adjust for this bias, Hayes (1974) applied Taylor's (1965) result that degree of maturity is proportional to age at an immature stage divided by mature weight to the $.27^{th}$ power. Applying this procedure to the present data (Fig.3) suggests that the correlated response in degree of maturity is negative in M16, in agreement with the previous analysis. However, H_6 showed a positive correlated response in degree of maturity, except during early growth.

Two unpublished sets of data were available for comparison with the present results. In one study, body weights were recorded at 4, 6, 10 and 14 weeks on 30 ICR and 36 M16 male mice. Using 10-week body weights as estimates of degree of maturity yielded means of 59.1 and 46.2 ($P<.01$) and 88.6 and 80.3 ($P<.01$) for degree of maturity at 6 and 10 weeks of age in ICR and M16, respectively. Using 14-week body weights as estimates of degree of maturity yielded respective means of 55.7 and 44.7 ($P < .01$) and 83.1 and 77.7 ($P < .01$). These results verify the findings that M16 had a decreased degree of maturity as a result of selection for increased postweaning gain. In the second study, 65 C_2 and 47 H_6 male mice were weighed at 3, 6, 9 and 12 weeks of age. Using 9-week body weight as the estimated degree of maturity yielded means of 41.8 and 39.0 ($P < .01$) and 86.0 and 86.8 ($P > .05$) for degree of maturity at 3 and 6 weeks of age in C_2 and H_6, respectively. When 12-week weight was used for degree of maturity, the respective means were 38.3 and 36.3 ($P < .01$) and 78.8 and 80.9 ($P < .01$). Thus, these data suggest that degree of maturity was reduced at early ages in H_6, as noted in the previous analysis. However, at 6 weeks of age, degree of maturity was increased in H_6. This result agrees with the adjusted degree of maturity values in the previous analysis, but not with the original analysis. Thus, interpreta-

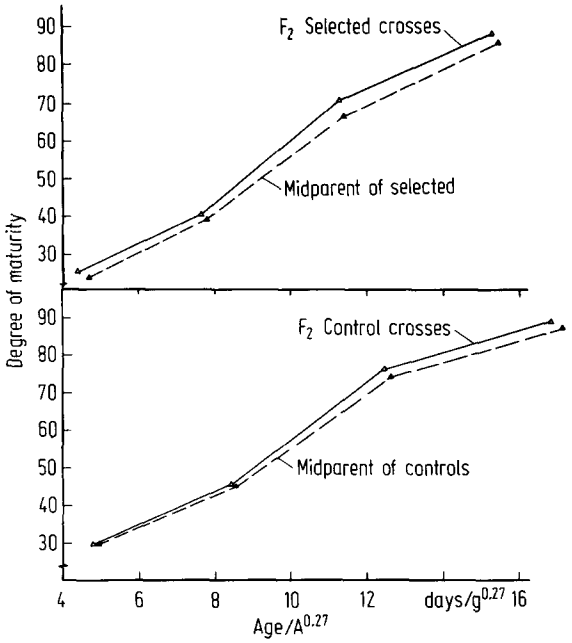

Fig.4. Degree of maturity plotted against age/$A^{.27}$ for the straightbred and crossbred populations (A = mature weight estimated by 63-day body weight)

tion of degree of maturity date must be made with caution when unbiased estimates of mature size are not available.

Non-additive genetic effects on maturing patterns were evident, based on the magnitude of direct and maternal heterosis in the selected and control crossbreds. Direct and maternal heterosis for degree of maturity was primarily positive and the former tended to be larger in the postweaning growth period. Because of the precautionary note on biases in degree of maturity mentioned above, the data were plotted against age/$A^{.27}$ (Taylor 1965), as indicated previously. The results, presented in Fig.4, verify the positive heterosis for degree of maturity in the control and selected crosses. Similar patterns of direct and maternal heterosis were observed for body weights and gains in these crosses (Nagai et al. 1976b). Positive direct heterosis for body weight and degree of maturity also has been reported in beef cattle (Smith et al. 1976b).

Reciprocal effects due to either cytoplasmic or sex-linked effects were negligible for maturity patterns, which was also the case for body weights and gains (Nagai et al. 1976b).

The results of the correlation analysis are remarkably similar to those given by Fitzhugh and Taylor (1971) and Smith et al. (1976a) for beef cattle. This is not surprising since maturity traits involve a number of part-whole relationships which will lead to predictable correlations based on the correlations among body weights at different ages and the coefficients of variation for body weights (Sutherland 1965; Eisen 1966). The main point is that the pattern of correlations are dependent on the original weights recorded. Therefore, it should be possible theoretically to devise selection indexes using body weights per se which would attain goals similar to indexes using degree of maturity and absolute and relative maturing rates. The advantages in favor of maturity traits have been reviewed by Fitzhugh (1976).

Acknowledgement

The competent technical assistance of Ms. B.J. Edwards is appreciated.

Literature

Bakker, H.; Nagai, J.; Eisen, E.J.: Average genetic and heterotic effects on growth in mice selected for large six-week body weight or rapid postweaning gain. J. Anim. Sci. 43, 1145-1155 (1976)

Brody, S.: Bioenergetics and Growth. New York: Reinhold Publishing Corp. (1945)

Dickerson, G.E.: Experimental approaches in utilizing breed resources. Anim. Br. Abstr. 37, 191-202 (1969)

Eisen, E.J.: Effect of the biometrical relationship among total milk yield, milk constituent yield, and per cent of milk constituent on response to selection. J. Dairy Sci. 10, 1230-1234 (1966)

Eisen, E.J.: Direct and maternal genetic responses resulting from selection for 12-day litter weight in mice. Can. J. Genet. Cytol. 15, 483-490 (1973)

Eisen, E.J.: Population size and selection intensity effects on long-term selection response in mice. Genetics 79, 305-323 (1975)

Eisen, E.J.: Restricted selection index: an approach to selecting for feed efficiency. J. Anim. Sci. 44, 958-972 (1977)

Eisen, E.J.; Bakker, H.; Nagai, J.: Body composition and energetic efficiency in two lines of mice selected for rapid growth rate and their F_1 crosses. Theor. Appl. Genet. 49, 21-34 (1977)

Falconer, D.S.; King, J.W.B.: A study of slection limits in the mouse. J. Genet. 51, 561-581 (1953)

Fitzhugh, H.A., Jr.: Analysis of growth curves and strategies for altering their shape. J. Anim. Sci. 42, 1036-1051 (1976)

Fitzhugh, H.A., Jr.; Taylor, St.C.S.: Genetic analysis of degree of maturity. J. Anim. Sci. 33, 717-725 (1971)

Hayes, J.F.: A genetic study of growth curves and carcass composition in selected lines of mice. M.S. Thesis, Univ. College Library, Dublin, Ireland (1974)

LaSalle, T.J.; White, J.M.: Characterization of response to selection for growth and maternal ability in laboratory mice. J. Anim. Sci. 48, 48-52(1975)
Legates, J.E.: Direct and correlated responses to selection in mice. In: Genetics Lectures, Vol. 1 (ed., R. Bogart), pp. 149-165. Corvallis: Oregon State U. Press 1969
Nagai, J.; Bakker, H.; Eisen, E.J.: Genetic analysis of nurse dams selected for six-week body weight or postweaning gain in mice. Can. J. Genet. Cytol. 4, 611-623 (1976a)
Nagai, J.; Bakker, H.; Eisen, E.J.: Partitioning average and heterotic components of direct and maternal genetic effects on growth in mice using crossfostering techniques. Genetics 84, 113-124 (1976b)
Smith, G.M.; Fitzhugh, H.A., Jr.; Cundiff, L.V.; Cartwright, T.C.; Gregory, K.E.: A genetic analysis of maturing patterns in straightbred and crossbred Hereford, Angus and Shorthorn cattle. J. Anim. Sci. 43, 389-395 (1976a)
Smith, G.M.; Fitzhugh, H.A., Jr.; Cundiff, L.V.; Cartwright, T.C.; Gregory, K.E.: Heterosis for maturing patterns in Hereford, Angus and Shorthorn cattle. J. Anim. Sci. 43, 380-388 (1976b)
Sutherland, T.M.: The correlation between feed efficiency and rate of gain, a ratio and its denominator. Biometrics 21, 739-749 (1965)
Taylor, St.C.S.: A relation between mature weight and time taken to mature in mammals. Anim. Prod. 7, 203-220 (1965)
White, J.M.; Legates, J.E.; Eisen, E.J.: Maternal effects among lines of mice selected for body weight. Genetics 60, 395-408 (1968)
Williams, W.R.: Partitioning average and heterotic components of direct and maternal genetic effects on body weight maturing patterns in mice using crossfostering techniques. Unpublished M.S. Thesis, North Carolina State University Library, Raleigh, N.C. (1976)

Received April 22, 1977
Communicated by H. Abplanalp

W.R. Williams
E.J. Eisen
J. Nagai
H. Bakker
Department of Animal Science
North Carolina State University
Raleigh, North Carolina
(USA)