

# AN EXPERIMENTAL EVALUATION OF GENETIC CORRELATION<sup>1</sup>

J. J. RUTLEDGE<sup>2</sup>, E. J. EISEN AND J. E. LEGATES

*Department of Animal Science, North Carolina State University,  
Raleigh, North Carolina 27607*

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## ABSTRACT

Heritability and genetic correlations realized from both single-trait and antagonistic index selection were compared with paternal half-sib estimates. Primary attention was focused on the genetic correlation between six-week body weight and six-week tail length. Parameters realized from single-trait selection were in excellent agreement with paternal half-sib estimates. However, the realized genetic correlation between six-week body weight and six-week tail length obtained from index selection was significantly greater than the other estimates. Differential inbreeding levels and realized selection intensities were considered and rejected as being causative factors for these results. Linkage disequilibrium probably was not a factor either, as the base population had been randomly mated and randomly selected with a large effective population size for many generations. It was concluded that with antagonistic index selection, the pleiotropic effects of genes may be more powerful in retarding response in aggregate genotype than current theory would suggest. Replication of all selected and control lines allowed the use of between-line estimators of sampling variances of realized genetic parameters in the above comparisons. Generally, standard errors of realized genetic parameters were much smaller than corresponding paternal half-sib standard errors. Thus, selection was an efficient method of estimation.

IN economic species the value of a potential replacement individual is usually a function of several quantitative characters. Those characters which determine aggregate breeding value may differ in their degree of genetic determination and may be either positively or negatively correlated, genetically and phenotypically. A key parameter in a multiple-objective breeding program is the genetic correlation. However, there is a paucity of experimental results involving simultaneous selection for more than one metric character, especially in mammals. The nature of the genetic correlation is therefore poorly understood. Theoretical evidence suggests that changes in gene frequency have more effect on genetic covariances than they do on genetic variances (BOHREN, HILL and ROBERTSON 1966), that a transient genetic correlation may be due to linkage disequilibrium rather than pleiotropy (COCKERHAM 1956) and that the genetic covariance may change sign as a consequence of selection (LERNER 1958). Apart from

<sup>1</sup> Paper No. 4047 of the Journal Series of the North Carolina State University Agricultural Experiment Station, Raleigh, North Carolina 27607.

<sup>2</sup> Present address: Department of Meat and Animal Science, University of Wisconsin, Madison, Wisconsin 53706.

genetic improvement of plants and animals, the genetic correlation is of interest in paleontological studies of evolution (HALDANE 1955). In addition, it is the genetic correlation of a quantitative character with fitness that determines the genetic properties of that character in a natural population.

The objective of this study was to test the hypothesis of no differences between genetic parameters estimated from the covariances among relatives and those realized from single-trait and/or antagonistic index selection.

#### MATERIALS AND METHODS

*Genetic stock:* The ICR stock of mice used had been maintained by random selection and random mating for 19 generations. Because of its long history of random mating and no intended selection, linkage equilibrium was assumed. Equilibrium is important since linkage can bias estimates of genetic parameters. Since it was established in the Mouse Genetics Laboratory at North Carolina State University, the stock has been maintained by mating at least 24 males each to 2 females in each generation. Male and female replacements were randomly selected within half- and full-sib families, respectively. The harmonic mean of the effective population size was about 111. HANRAHAN and EISEN (1973) give a more complete description.

*Experimental design:* Eight selected lines were initiated by randomly (avoiding full- or half-sib matings) pair mating a sample of generation 20 virgin female progeny to contemporary males. Hereafter, generation 20 will be coded as zero. Selection treatments are shown in Table 1. Each replicate was founded with 13 litters except  $W^{\circ}T^+_{i}$  with 12 litters.

Single-trait selection for increased 6-week body weight (WK 6) and increased 6-week tail length (TAIL) was conducted in the  $W+T^{\circ}_{i}$  and  $W^{\circ}T^+_{i}$  lines, respectively. In the  $W+T^{\circ}_{i}$  lines, selection was based on an antagonistic selection index derived by using economic weights of 0.39 and  $-1.83$ , respectively, for WK 6 and TAIL. The sign of the economic weights was reversed in the  $W-T^+_{i}$  lines. Absolute values of the economic weights for each trait were calculated as the reciprocal of the respective phenotypic standard deviation.

The ICR stock served as the control for generation 1. Thereafter replicate randomly selected lines ( $W^{\circ}T^{\circ}_{i}$ ) sampled from generation 1 of the ICR stock were used. The initial effective population sizes for  $W^{\circ}T^{\circ}_{i}$  and the lines shown in Table 1 were approximately 26. These lines were then maintained by mating ten males each to two females in each generation. Male selection was restricted such that at least eight full-sib families were represented; female selection was strictly on the basis of individual performance. Selected mates were mated at random, avoiding full- or half-sibbing. The restriction on male selection and avoidance of sibbing were attempts to curtail the rate of inbreeding. Seven generations of selection are reported in the present study.

Selected males were joined with selected females in all lines on the same day, except in the

TABLE 1  
Selection criteria\*

Designation†	Selection criteria	
	WK 6	TAIL
$W+T^{\circ}_{i}$	1	0
$W^{\circ}T^+_{i}$	0	1
$W+T^-_{i}$	0.2079	-1.0437
$W-T^+_{i}$	-0.2079	1.0437

\* WK 6 and TAIL, respectively, refer to six-week body weight and six-week tail length.

† For all criteria,  $i = 1, 2$ .

TABLE 2

Sources of variation, degrees of freedom and expected mean squares for paternal half-sib analyses

Source	d.f.	E(MS)
GL*	22	Not applicable
Sires/GL	326	$\sigma^2 + 7.47 \sigma_d^2 + 13.34 \sigma_s^2$
Dams/Sires/GL	285	$\sigma^2 + 7.26 \sigma_d^2$
Within	4043	$\sigma^2$

\* GL = generation—line subclasses.

stock which was not required as a control after generation 1. Breeders varied from eight to ten weeks of age when joined. After 17 days in the mating cages, males were destroyed and females were individually caged and placed on a high-energy lactation diet. The litters were randomly standardized to eight pups at five days. An attempt was made to have a sex ratio of one:one. Those pups added when standardizing a litter were discarded at weaning. At 12 days, the pups were individually identified by toe-clipping. The pups were weighed and weaned onto Purina Laboratory Chow at three weeks. After weaning, four mice of the same sex, usually representing two or three litters, were caged together. At six weeks, tail lengths to the nearest 0.1 cm and body weights to the nearest 0.1 g were recorded. Tap water and feed were supplied *ad libitum*, and the colony room was maintained at  $22 \pm 1^\circ$ . Relative humidity varied from 50% to 70%.

*Statistical analyses:* Body weight and tail length data were adjusted for sex effects by the ratio method of FALCONER and KING (1953).

Genetic parameters were estimated within generation and line from the covariance of paternal half sibs ( $C_{phs}$ ). Only the  $W^0T_1^0$  and the ICR stock populations were used in these analyses. Sources of variation, degrees of freedom and expected mean squares are shown in Table 2. Heritability was estimated by  $4\sigma_s^2/(\sigma_s^2 + \sigma_d^2 + \sigma^2)$ , and the standard error was calculated by the method of OSBORNE and PATERSON (1952). The ratio of the sire components of covariance to the geometric mean of the sire components of variance was used to estimate genetic correlations. Standard errors were calculated by the method of TALLIS (1959).

Sire-offspring covariances ( $C_{so}$ ) were estimated within generation and line. This covariance contains one-quarter of the additive direct-maternal genetic covariance ( $\sigma_{A_oA_m}$ ) plus one-half of the additive direct genetic variance ( $\sigma_{A_o}^2$ ). Thus, an estimate of the additive direct-maternal genetic covariance was obtained by the equation

$$\sigma_{A_oA_m} = 4(C_{so} - 2C_{phs}). \quad (1)$$

No attempt was made to estimate the standard error of the estimate since  $C_{so}$  and  $C_{phs}$  have an unknown covariance when estimated from the same data set.

Realized heritability from single-trait selection was estimated from the regression of generation means as deviations from control means on cumulative realized selection differential. Replicate line means within selection treatments were deviated from control line means of the same replicate number to avoid introducing correlations between replicates. Genetic regressions were calculated as the regression of correlated response means on direct response means, both expressed as deviations from control. Realized genetic correlations were estimated using the following formulas:

$$r_{g_x g_y} = [(b_{CR_y, DR_x})(b_{CR_x, DR_y})]^{1/2} \quad (2)$$

and

$$r_{g_x g_y} = b_{CR_y, DR_x} (h_x \sigma_{p_x} / h_y \sigma_{p_y}) \quad (3)$$

where  $r_{g_x g_y}$  = realized genetic correlation,  $b_{CR_y, DR_x}$  = regression of the correlated response in  $y$  on the direct response in  $x$ ,  $h_x$  = square root of heritability of  $x$  and  $\sigma_{p_x}$  = phenotypic standard

deviation of  $x$ . Values used for the terms inside the parentheses of equation (3) were estimated from the paternal half-sib analyses. Although these estimates have sampling variances, for the present purposes they were assumed to be parameter values. Two independent estimates of realized heritability were available since the direct responses were taken as deviations from separate control line means. Average realized heritability from single-trait selection and its standard error were calculated as the mean and standard error of the mean of independent replicate estimates. Average realized genetic correlations and their standard errors were calculated by the same procedure. Note that equation (2) requires three lines for an estimate of the genetic correlation—i.e., a control line and two single-trait-selected lines. On the other hand, equation (3) requires only one selected line and a control.

Genetic parameters realized from index selection were estimated by the method of BERGER and HARVEY (1971). Consider a pair of index-selected lines with selection indexes  $I_1 = b_1 p_x + b_2 p_y$  and  $I_2 = b_3 p_x + b_4 p_y$ , where the  $p_i$  are phenotypic measures and the  $b_i$  are partial regression coefficients which maximize the correlation between aggregate genotype and index. The response in  $p_x$  per unit of standardized selection differential, when selection is based on  $I_1$  is

$$\Delta G_{x.I_1} = b_{g_x I_1} \sigma_{I_1}, \quad (4)$$

where  $b_{g_x I_1}$  is the regression of the breeding value for trait  $x$  on  $I_1$  and  $\sigma_{I_1}$  is the phenotypic standard deviation of  $I_1$ . Equation (4) can be expressed as

$$\begin{aligned} \Delta G_{x.I_1} &= \frac{b_1 h_x^2 \sigma_{p_x}^2 + b_2 h_x h_y r_{g_x g_y} \sigma_{p_x} \sigma_{p_y}}{b_1^2 \sigma_{p_x}^2 + b_2^2 \sigma_{p_y}^2 + 2b_1 b_2 r_{p_x p_y} \sigma_{p_x} \sigma_{p_y}} (\sigma_{I_1}) \\ &= \frac{b_1 \sigma_{g_x}^2 + b_2 \sigma_{g_x g_y}}{\sigma_{I_1}}, \end{aligned} \quad (5)$$

where  $r_{p_x p_y}$  is the phenotypic correlation,  $\sigma_{g_x}^2$  is the additive genetic variance for trait  $x$  and  $\sigma_{g_x g_y}$  is the additive genetic covariance. Similarly,

$$\Delta G_{y.I_1} = \frac{b_1 \sigma_{g_x g_y} + b_2 \sigma_{g_y}^2}{\sigma_{I_1}} \quad (6)$$

The selection responses to  $I_2$  follow the same pattern.

Combining the expected responses from the two lines yields

$$\begin{bmatrix} b_1 & b_2 & 0 \\ 0 & b_1 & b_2 \\ b_3 & b_4 & 0 \\ 0 & b_3 & b_4 \end{bmatrix} \begin{bmatrix} \sigma_{g_x}^2 \\ \sigma_{g_x g_y} \\ \sigma_{g_y}^2 \end{bmatrix} = \begin{bmatrix} \Delta G_{x.I_1} & \sigma_{I_1} \\ \Delta G_{y.I_1} & \sigma_{I_1} \\ \Delta G_{x.I_2} & \sigma_{I_2} \\ \Delta G_{y.I_2} & \sigma_{I_2} \end{bmatrix} \quad (7)$$

or in matrix notation,  $X\beta$  and  $Y$ . With correlation of less than unity between  $I_1$  and  $I_2$ , this system

of equations may be solved by least squares to yield  $\hat{\beta} = (X'X)^{-1}X'Y$ . The elements of  $X$  were replaced with realized index weights ( $w_i$ ) by using the index in retrospect technique of DICKERSON *et al.* (1954). The elements of the response vector ( $Y$ ) of equation (7) were calculated as  $n b_{X_i T} \left( \frac{\sigma_{I_i}}{CSD_i} \right)$ , where  $n$  is the number of generations,  $b_{X_i T}$  is the regression of generation means for the  $i^{th}$  trait as deviations from control on generation number, and  $CSD_i$  is the cumulative realized selection differential for the  $i^{th}$  index. Realized heritability was calculated as the ratio of  $\sigma_g^2$  to  $\sigma_p^2$ , and the realized genetic correlation was estimated as the ratio of the realized genetic covariance to the geometric mean of the realized genetic variances.

As with genetic parameters realized from single trait selection, the mean and variance of independent estimates were taken as the appropriate values for the mean and variance of genetic parameters realized from index selection.

## RESULTS AND DISCUSSION

*Genetic and phenotypic statistics:* Genetic and phenotypic parameters estimated from the covariance between paternal half-sibs using the randomly selected lines are shown in Table 3. Heritability estimates of WK 3, WK 6 and GAIN are lower than paternal half-sib estimates reported by HANRAHAN and EISEN (1973). Their study utilized earlier generations of the same population in the same colony, and estimates were calculated within sexes. In the above order and averaged over sexes their estimates were 0.40, 0.45 and 0.34. The differences were due primarily to changes in the magnitude of the sire components of variance rather than to increases in either the dam or within full-sib family components of variance. It is possible that adjusting for sex removed some of the genetic differences but this does not seem likely. Heritability of TAIL was estimated to be  $0.44 \pm .15$ . FALCONER (1954) reported a realized heritability for six-week tail length of  $0.60 \pm .08$  in his stock of mice. Genetic correlation estimates involving WK 3 are scarcely interpretable. However, the point estimates do not suggest any genetic antagonism. The estimated genetic correlation between WK 6 and GAIN was  $1.10 \pm .03$ ; HANRAHAN and EISEN (1973) reported estimates of about 0.75. The estimated genetic and phenotypic correlations between WK 6 and TAIL were  $0.29 \pm .09$  and 0.45, respectively. FALCONER (1954) reported a realized genetic correlation between these two traits of about 0.60. BAKER and COCKREM (1970) obtained a realized genetic correlation, averaged over sexes, of 1.10 in their medium-environmental-temperature-selected line.

Covariances among relatives and direct-maternal genetic covariances estimated by equation (1) are given in Table 4. Fiducial limits for these direct-maternal genetic covariances would be large, but the point estimates suggest antagonism between direct and maternal genetic effects and substantiate similar findings by

TABLE 3

*Within generation and line estimates of genetic and phenotypic parameters in randombred ICR mice\**

Trait†	WK 3	WK 6	TAIL	GAIN
WK 3	$0.01 \pm .16$	$2.84 \pm 3.50$	$1.94 \pm 2.33$	$4.35 \pm 5.72$
WK 6	0.49	$0.36 \pm .10$	$0.29 \pm .09$	$1.10 \pm .03$
TAIL	0.48	0.45	$0.44 \pm .15$	$0.13 \pm .12$
GAIN	-.21	0.75	0.14	$0.18 \pm .10$
Mean	13.2	28.7	8.2	15.5
Phenotypic variance	2.81	6.37	0.28	5.07

\* Heritabilities on diagonal, genetic correlations above and phenotypic correlations below diagonal.

† WK 3 = three-week body weight, WK 6 = six-week body weight, TAIL = six-week tail length and GAIN = WK 6 minus WK 3.

TABLE 4

*Sire-offspring ( $C_{so}$ ) and paternal half-sib ( $C_{phs}$ ) covariances and estimates of direct-maternal genetic covariance ( $\sigma_{A_oA_m}$ )*

Trait	$C_{so}$	$C_{phs}$	$\sigma_{A_oA_m}$
WK 3	-.0723	0.0069	-.34
WK 6	0.4927	0.5814	-.67
TAIL	0.0524	0.0321	-.01
GAIN	0.5387	0.2289	0.08

HANRAHAN and EISEN (1973). In contrast, RUTLEDGE *et al.* (1972) found small positive estimates of  $\sigma_{A_oA_m}$  in this stock for body weight.

*Selection differentials and inbreeding:* Realized cumulative selection differentials and selection intensities are given in Table 5. All of the realized selection intensities were below the expected value of 1.46. This was due chiefly to the restriction on male selection and the fact that census numbers were smaller than optimum (160). The mean number of mice scored per generation (alive at six weeks) is a measure of survival and relative reproductive success (fitness) of the various lines. The well-known deleterious effect of selection for a metric character on fitness is evident. There were small differences in mean inbreeding level at generation eight among the selected lines. However, inbreeding in the selected lines did exceed that in the controls as ROBERTSON (1961) predicted.

*Single-trait-selected lines:* Mean responses of  $W+T^0$  lines are plotted against the realized cumulative selection differential in Figure 1. A positive trend is apparent in all traits. Non-linearity of these responses was investigated by sequentially fitting linear and quadratic regressions of generation mean deviations on generation number. These analyses are shown in Table 6. Generally, the responses were significant and linear. Exceptions were significant quadratic regression coefficients found for WK 3 and TAIL in  $W+T^0_1$ .

TABLE 5

*Realized cumulative selection differentials (CSD), realized selection intensities (i) mean number of animals surviving to six-weeks (N) and mean generation eight inbreeding levels (F)*

Line	CSD	i	N	F
$W+T^0_1$	21.63 g	1.22	119	0.11
$W+T^0_2$	21.08 g	1.19	116	0.14
$W^0T^+_1$	3.58 cm	0.97	125	0.14
$W^0T^+_2$	3.77 cm	1.02	130	0.13
$W+T^-_1$	4.00 index units	1.02	124	0.11
$W+T^-_2$	3.59 index units	0.92	98	0.16
$W-T^+_1$	4.13 index units	1.06	129	0.11
$W-T^+_2$	4.05 index units	1.04	131	0.13
$W^0T^0_1$	*	*	136	0.07
$W^0T^0_2$	*	*	133	0.06

\* Not applicable.

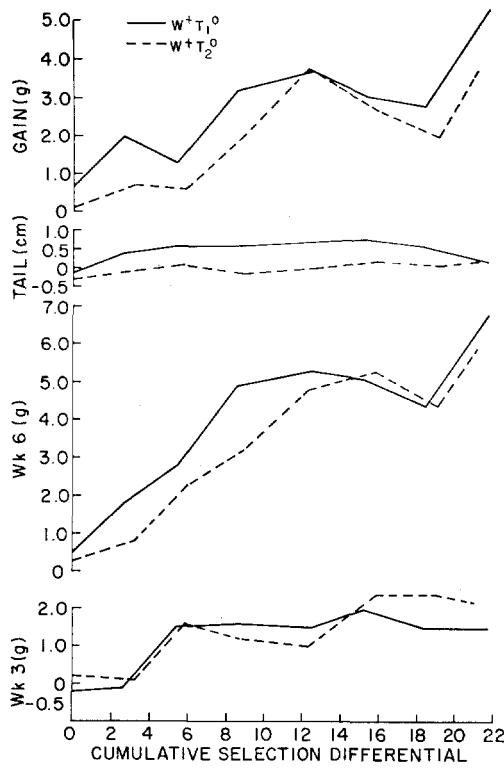


FIGURE 1.—Responses to single-trait selection for WK 6.

TABLE 6

*Regression coefficients and coefficients of determination for linear and quadratic regressions of generation means as deviation from control on generation number for  $W+T^0$  lines*

Line	Model		WK 3	WK 6	TAIL	GAIN
$W+T_1^0$	Linear	$b_0$	0.021	0.500	0.271	0.543
		$b_L$	0.254*	0.767**	0.045	0.499**
		$R^2$	0.56*	0.82**	0.14	0.71**
	Quadratic	$b_0$	-1.363*	-1.054	-0.532*	0.373
		$b_L$	1.084**	1.699*	0.527**	0.601
		$b_Q$	-0.092*	-0.104	-0.054**	-0.011
	$R^2$	0.86**	0.88**	0.92**	0.71*	
$W+T_2^0$	Linear	$b_0$	-0.096	-0.286	-0.250*	-0.182
		$b_L$	0.330**	0.811**	0.058*	0.474*
		$R^2$	0.76**	0.90**	0.68*	0.68*
	Quadratic	$b_0$	-0.427	-1.527	-0.348	-1.039
		$b_L$	0.528	1.555*	0.117	0.988
		$b_Q$	-0.022	-0.083	-0.007	-0.057
	$R^2$	0.77*	0.93**	0.72*	0.72*	

\*  $P < .05$ , \*\*  $P < .01$ .

TABLE 7

*Regression coefficients and coefficients of determination for linear regression of generation means as deviation from control on cumulative realized selection differential for W+T<sup>0</sup> lines*

Line		WK 3	WK 6	TAIL	GAIN
W+T <sup>0</sup> <sub>1</sub>	$b_o$	0.34(.379)†	1.42(.617)	0.33(.187)	1.13(.532)
	$b_L$	0.08*(.030)	0.24**(.049)	0.01(.015)	0.16**(.042)
	$R^2$	0.54*	0.81**	0.12	0.70**
W+T <sup>0</sup> <sub>2</sub>	$b_o$	0.23(.319)	0.54(.484)	-.19(.068)	0.30(.567)
	$b_L$	0.11**(.025)	0.26**(.037)	0.02*(.005)	0.15*(.044)
	$R^2$	0.76**	0.89**	0.68*	0.67*

\*  $P < 0.5$ , \*\*  $P < .01$ .

† Standard errors of regression coefficients given in parentheses.

Regression coefficients and coefficients of determination for mean responses on realized cumulative selection differential are shown in Table 7. Significant direct and correlated responses per unit of WK 6 selection differential were obtained, except for the correlated response of TAIL in replicate 1. Realized heritability estimates of WK 6 were in excellent agreement for the replicate lines, giving a mean value of  $0.25 \pm .01$ . This estimate was not significantly different from the paternal half-sib estimate ( $0.36 \pm .10$ ). The regression coefficients for correlated responses were also similar between replicates.

Mean responses of W<sup>0</sup>T<sup>+</sup> lines are plotted against the realized cumulative selection differential in Figure 2. The correlated responses appear positive but show greater dispersion than the correlated responses for WK 6. Tests for non-linearity are shown in Table 8. Significant quadratic regressions were found for WK 3 and TAIL in W<sup>0</sup>T<sup>+</sup><sub>1</sub>. However, for TAIL the linear term alone accounts for 85% of

TABLE 8

*Regression coefficients and coefficients of determination for linear and quadratic regressions of generation means as deviation from control on generation number for W<sup>0</sup>T<sup>+</sup> lines*

Line	Model		WK 3	WK 6	TAIL	GAIN
W <sup>0</sup> T <sup>+</sup> <sub>1</sub>	Linear	$b_o$	-.375	-.654	-.257	-.207
		$b_L$	0.183	0.320*	0.207**	0.116
		$R^2$	0.41	0.70*	0.85**	0.18
	Quadratic	$b_o$	-1.643*	-.805	-.882**	1.052
		$b_L$	0.944*	0.411	0.582**	-.640
		$b_Q$	-.085*	-.010	-.042**	0.084
	$R^2$	0.75*	0.70	0.99**	0.56	
W <sup>0</sup> T <sup>+</sup> <sub>2</sub>	Linear	$b_o$	0.193	-.114	-.257	-.239
		$b_L$	0.182	0.381*	0.240**	0.181
		$R^2$	0.46	0.55*	0.87**	0.21
	Quadratic	$b_o$	-.513	-1.954	-.721	-1.293
		$b_L$	0.605	1.485*	0.519*	0.813
		$b_Q$	-.047	-.123	-.031	-.070
	$R^2$	0.58	0.78*	0.93**	0.34	

\*  $P < 0.5$ , \*\*  $P < .01$ .



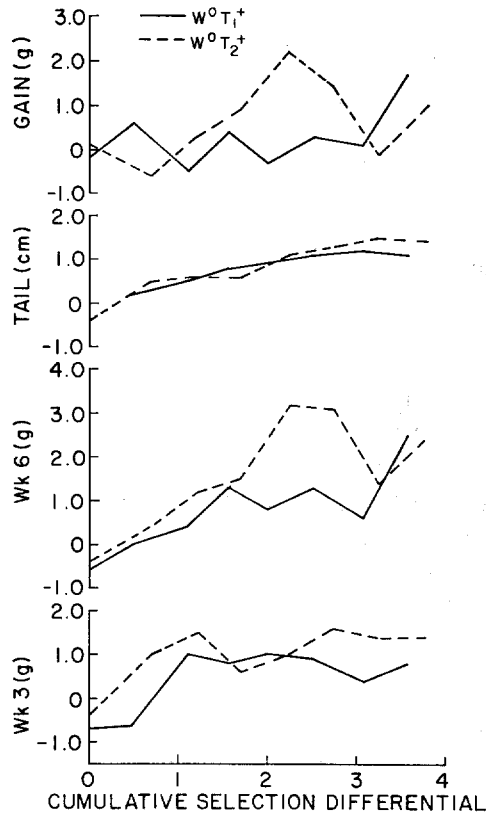


FIGURE 2.—Responses to single-trait selection for TAIL.

the variance. Significant and positive correlated responses in WK 6 were found in both replicates. The correlated responses in GAIN were positive but not significant.

Linear regressions of responses on cumulative realized selection differentials for the  $W^0T^+$  lines are shown in Table 9. Good agreement between replicates was

TABLE 9

*Regression coefficients and coefficients of determination for linear regression of generation means as deviation from control on cumulative realized selection differential for  $W^0T^+$  lines*

Line		WK 3	WK 6	TAIL	GAIN
$W^0T^+_{1}$	$b_0$	-.21 (.377)†	-.35 (.361)	-.06 (.147)	-.09 (.426)
	$b_L$	0.37 (.176)	0.63** (.169)	0.41** (.069)	0.22 (.199)
	$R^2$	0.42	0.70**	0.86**	0.17
$W^0T^+_{2}$	$b_0$	0.30 (.341)	0.15 (.600)	-.08 (.150)	-.10 (.620)
	$b_L$	0.36* (.148)	0.74** (.261)	0.46** (.065)	0.34 (.270)
	$R^2$	0.50*	0.57**	0.89**	0.21

\*  $P < 0.5$ , \*\*  $P < .01$ .

† Standard errors of regression coefficients given in parentheses.

TABLE 10

*Genetic regressions for single trait selected lines*

Line	WK 3	WK 6	TAIL	GAIN
W+T <sub>1</sub> <sup>0</sup>	0.36**	...	0.09	0.68**
W+T <sub>2</sub> <sup>0</sup>	0.36**	...	0.05*	0.61**
W <sup>0</sup> T <sub>1</sub> <sup>+</sup>	1.00**	1.40**	...	0.22
W <sup>0</sup> T <sub>2</sub> <sup>+</sup>	0.89**	1.89**	...	0.62

\* P &lt; 0.5,    \*\* P &lt; .01.

found; realized heritability estimates were 0.41 and 0.46 with a mean value of  $0.44 \pm .03$ . The paternal half-sib estimate of  $0.44 \pm .15$  was in excellent agreement with realized heritability.

Genetic regression coefficients for the single-trait-selected lines are shown in Table 10. There was little evidence for heterogeneity between replicate estimates. The genetic regression for TAIL in W+T<sub>1</sub><sup>0</sup> approached statistical significance (P < .08). The genetic correlations of WK 6 and TAIL with WK 3 presented in Table 3 and realized genetic correlations to be presented later are of little value as they are inflated by the small heritability estimate obtained from WK 3. Genetic regression coefficients involving WK 3, however, clearly indicate positive additive genetic covariances with WK 6 and TAIL.

Realized genetic correlations estimated by equation (3) are given in Table 11. The genetic correlation between TAIL and GAIN realized from selection for TAIL ( $0.16 \pm .08$ ) agreed well with the paternal half-sib estimate ( $0.13 \pm .12$ ). The realized genetic correlation between WK 6 and GAIN ( $1.04 \pm .05$ ) was comparable with the paternal half-sib estimate ( $1.10 \pm .03$ ). The genetic correlation between WK 6 and TAIL realized from selection for WK 6 ( $0.31 \pm .09$ ) was consistent with that realized from selection for TAIL ( $0.38 \pm .06$ ). With no evidence for asymmetry of correlated responses, the geometric mean of the genetic regressions (equation [2]) was used to estimate this genetic correlation. Estimates of 0.35 and 0.31 for replicates 1 and 2, respectively, resulted in a mean value of  $0.33 \pm .02$ . All realized estimates of the genetic correlation between WK 6 and TAIL were in accord with the paternal half-sib estimate ( $0.29 \pm .09$ ).

TABLE 11

*Genetic correlations realized from single trait selection\**

Line	WK 3	WK 6	TAIL	GAIN
W+T <sub>1</sub> <sup>0</sup>	3.24	...	0.39	1.09
W+T <sub>2</sub> <sup>0</sup>	3.24	...	0.22	0.98
Mean	$3.24 \pm .00$	...	$0.31 \pm .09$	$1.04 \pm .05$
W <sup>0</sup> T <sub>1</sub> <sup>+</sup>	2.08	0.32	...	0.08
W <sup>0</sup> T <sub>2</sub> <sup>+</sup>	1.85	0.43	...	0.23
Mean	$1.97 \pm .12$	$0.38 \pm .06$	...	$0.16 \pm .08$

\* Genetic correlations of traits with WK 6 are given above the line while those below are genetic correlations with TAIL.

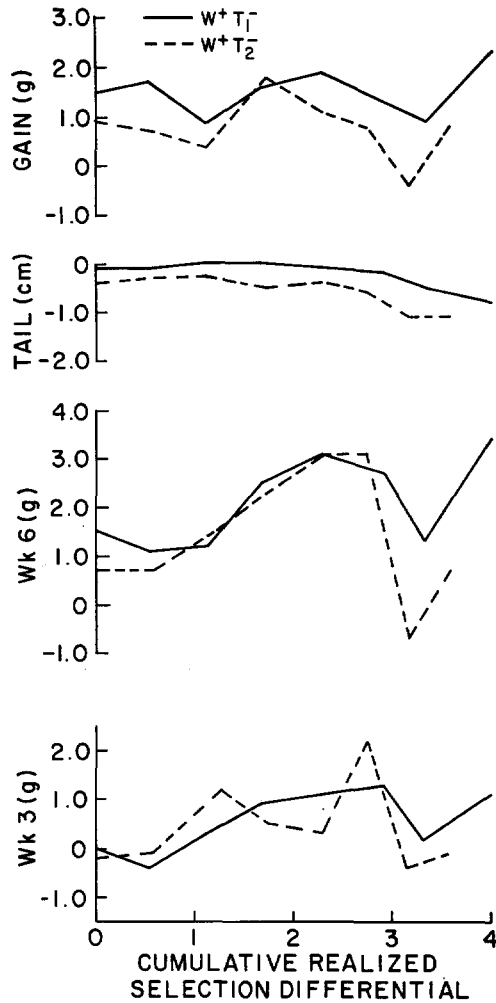


FIGURE 3.—Responses to antagonistic index selection for increased WK 6 and decreased TAIL.

*Antagonistic index-selected lines:* Mean responses of  $W^+T^-$  are plotted against the realized cumulative selection differential in Figure 3. Replicate 2 had an outbreak of severe juvenile diarrhea in generation 7. The effect on WK 6 is apparent with a drop of mean WK 6 of about 3.5 g. Using the guidelines suggested by SNEDECOR and COCHRAN (1967), it was decided to make no use of the data for generations 7 and 8 of  $W^+T_2^-$ . Tests for responses are shown in Table 12. Aggregate genotype (AG) responded significantly in each replicate. Both replicates increased in WK 6 and decreased in TAIL, but the responses were not always statistically significant. There was no significant genetic change in WK 3 or GAIN. The only evidence for non-linearity was the significant quadratic regression for TAIL in  $W^+T_1^-$ .

Figure 4 gives the mean deviated responses of  $W-T^+$ , and the regression results

TABLE 12

*Regression coefficients and coefficients of determination for linear and quadratic regression of generation means as deviation from control on generation number for W<sup>+</sup>T<sup>-</sup> lines*

Line	Model		WK 3	WK 6	TAIL	GAIN	AG
W <sup>+</sup> T <sup>-</sup> <sub>1</sub>	Linear	$b_o$	-.221	1.061	0.182	1.346*	0.025
		$b_L$	0.171	0.231	-.091*	0.037	0.270*
		$R^2$	0.43	0.37	0.62*	0.04	0.69*
	Quadratic	$b_o$	-.882	0.798	-.336**	1.802	0.880
		$b_L$	0.568	0.392	0.220	-.236	-.232
		$b_Q$	-.044	-.018	-.035**	0.030	0.055
W <sup>+</sup> T <sup>-</sup> <sub>2</sub>	Linear	$b_o$	-.600	-.073	-.267*	0.740	0.433
		$b_L$	0.357	0.569**	-.043	0.060	0.306**
		$R^2$	0.54	0.94**	0.47	0.06	0.90**
	Quadratic	$b_o$	-.100	-.140	-.450	0.390	0.710
		$b_L$	-.018	0.619	0.095	0.323	0.098
		$b_Q$	0.054	-.007	-.020	-.038	0.030
	$R^2$	0.56	0.94*	0.68	0.10	0.93*	

\* P < 0.5, \*\* P < .01.

are shown in Table 13. Response in AG was significant in both replicates. Both replicates decreased in WK 3, WK 6 and GAIN, but the responses were not always significant. The increase in TAIL was significant in only one replicate. There were significant quadratic response curves for four of the ten responses measured.

Realized index weights ( $w_i$ ) for the four index lines are shown in Table 14. Also shown are the intended weights and the ratio of absolute values of the real-

TABLE 13

*Regression coefficients and coefficients of determination for linear and quadratic regressions of generation means as deviation from control on generation number for W<sup>-</sup>T<sup>+</sup> lines*

Line	Model		WK 3	WK 6	TAIL	GAIN	AG
W <sup>-</sup> T <sup>+</sup> <sub>1</sub>	Linear	$b_o$	0.486	1.761*	0.375	1.293	-.870
		$b_L$	-.144	-.752**	0.067	-.618*	0.493**
		$R^2$	0.27	0.90**	0.21	0.81**	0.78**
	Quadratic	$b_o$	-.934	1.850	-.304	2.784*	-1.233
		$b_L$	0.708	-.806	0.474	-1.513*	1.164*
		$b_Q$	-.095*	0.006	-.045	0.099	-.083*
W <sup>-</sup> T <sup>+</sup> <sub>2</sub>	Linear	$b_o$	0.296	1.471*	-.111	1.175	-.757
		$b_L$	-.155*	-.638**	0.111**	-.483**	0.448**
		$R^2$	0.65*	0.86**	0.73**	0.78**	0.94**
	Quadratic	$b_o$	-.150	-.064	-.530*	0.086	-.902
		$b_L$	0.113	0.283	0.363**	0.170	0.535*
		$b_Q$	-.030	-.102*	-.028*	-.073	-.010
	$R^2$	0.75*	0.95**	0.92**	0.85**	0.96**	

\* P < 0.5, \*\* P < .01.

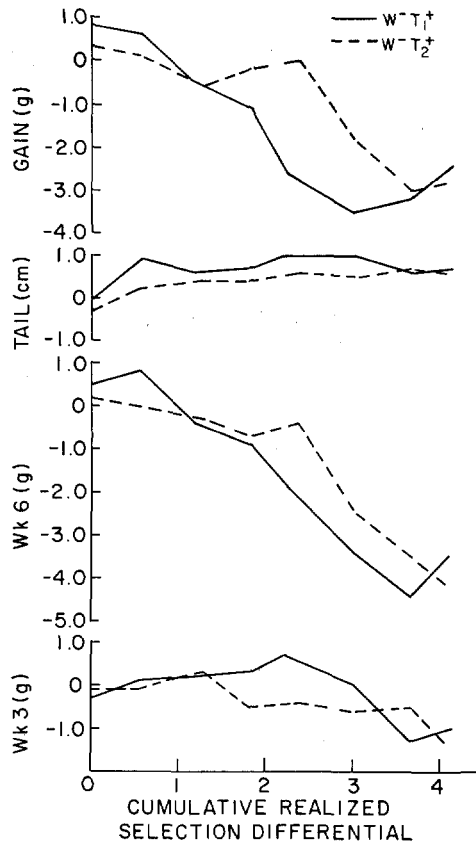


FIGURE 4.—Responses to antagonistic index selection for decreased WK 6 and increased TAIL.

ized and attempted index weights. These ratios, rather than the actual values of index weights, should be used to judge departures from the intended index. Small differences in the attempted and realized ratios were found. There was a suggestion that the  $W^+T^-$  treatment had slightly more emphasis on TAIL than did  $W^-T^+$ .

A random pairing of the four index lines was made; ( $W^+T^-_1$ ,  $W^-T^+_1$ ) and

TABLE 14  
*Realized index weights*

Line	Ratio of absolute value of weights	Emphasis on	
		WK 6	TAIL
$W^+T^-_1$	5.69	0.4327	-2.4626
$W^+T^-_2$	4.87	0.4227	-2.0573
$W^-T^+_1$	4.85	-.5191	2.5182
$W^-T^+_2$	4.56	-.5789	2.6377
Attempted	5.02	0.2079*	1.0437*

\* Absolute value.

TABLE 15

*Genetic parameters realized from index selection by pair and pooled values*

Parameter	Pair 1	Pair 2	Pooled
Realized heritability			
WK 6	0.39	0.33	0.36 ± .03
TAIL	0.34	0.38	0.36 ± .02
Realized genetic correlation	0.82	1.19	1.00 ± .19

( $W^+T_2^-$ ,  $W^-T_2^+$ ) were designated pairs 1 and 2, respectively. Solutions for realized genetic parameters from index selection were obtained as outlined previously and are given in Table 15. Realized heritability of WK 6 from index selection was  $0.36 \pm .03$ . This estimate was significantly different from realized heritability from single-trait selection ( $0.25 \pm .01$ ), but exactly the value found from the covariances among relatives ( $0.36 \pm .10$ ). Realized heritability of TAIL from index selection ( $0.36 \pm .02$ ) was significantly different from that realized from single-trait selection ( $0.44 \pm .03$ ) but was not significantly different from that estimated from the covariances among relatives ( $0.44 \pm .15$ ). It was concluded that the realized heritability estimates obtained from antagonistic index selection by the method of BERGER and HARVEY (1971) were in fair agreement with those obtained from single-trait selection.

A disturbing feature of these data, however, was the marked difference in estimates of the realized genetic correlation. The mean genetic correlation ( $1.00 \pm .19$ ) realized from index selection was significantly different from the other estimates. It was recognized that there were several difficulties with the procedure used. First, estimation of three parameters with only four observations is not desirable and the estimates obtained, although unbiased, may be unrealistic. Second, there was a perfect correlation between the  $W^+T^-$  and  $W^-T^+$  treatments in terms of the attempted index. The procedure of using realized index weights allows a solution but may result in an ill-conditioned  $X'X$  matrix. The point estimate of the realized genetic correlation is not consistent with the observed responses in WK 6 and TAIL (Tables 12 and 13). Both estimates from index selection (0.82 and 1.19), however, were consistent in suggesting a rather large realized genetic correlation. When all four index-selected lines were included in the same analysis, the estimate of the realized genetic correlation was 0.70. This point estimate of the realized genetic correlation from index selection may be most useful. However, no reasonable method is available for obtaining the standard error.

On a mean basis after seven generations, the  $W^+T^-$  lines diverged from control about 1.1 and  $-0.9$  phenotypic standard deviations in WK 6 and TAIL, respectively. Corresponding values for  $W^-T^+$  were  $-1.9$  and  $1.4$ . The expected response in aggregate genotype per unit of standardized selection differential is the phenotypic standard deviation of the index (PIRCHNER 1969). Expected and observed per-generation responses in aggregate genotype are given in Table 16. Expected responses vary because of slightly different realized cumulative selec-

TABLE 16

*Expected and observed per-generation response in aggregate genotype for the index-selected lines*

Line	Observed	Expected	Observed/expected
W+T <sup>-</sup> <sub>1</sub>	0.26	0.57	0.46
W+T <sup>-</sup> <sub>2</sub>	0.30	0.55	0.55
W-T <sup>+</sup> <sub>1</sub>	0.42	0.59	0.71
W-T <sup>+</sup> <sub>2</sub>	0.45	0.58	0.78

tion differentials. There was good agreement between replicates for observed response. The W+T<sup>-</sup> lines' mean response was about 50% of expected while the W-T<sup>+</sup> lines' mean response was about 75% of expected. Different selection intensities and/or differential inbreeding levels (Table 5) are insufficient to account for asymmetry of this magnitude. The failure of expected and observed responses to agree is consistent with the conclusion that the realized genetic correlation from index selection was larger than the genetic correlation computed from the covariance among paternal half-sibs. It is of interest to note that for each treatment, the line having the larger divergence for one component trait had the smaller divergence for the other component trait (Tables 12 and 13).

A plot of standardized selection responses in WK 6 and TAIL for the four selection treatments is shown in Figure 5. Observed responses are generation means

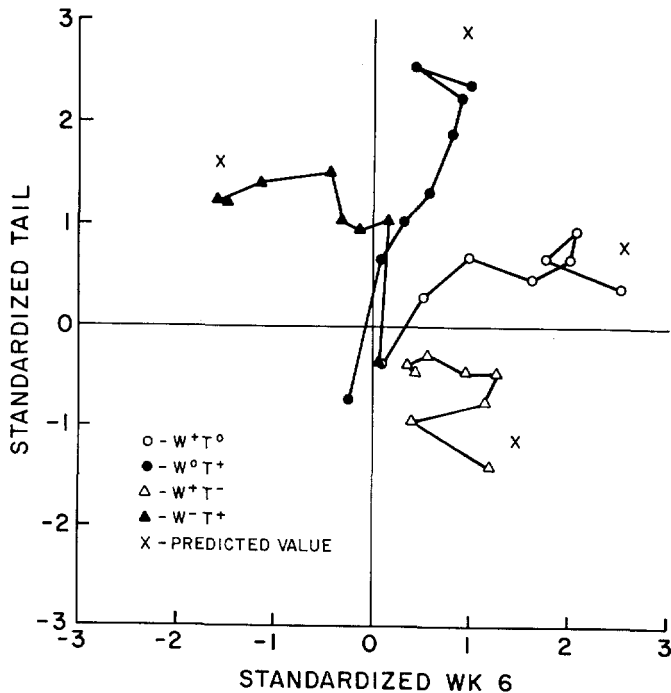


FIGURE 5.—Standardized responses of TAIL plotted against WK 6 for the four selection treatments.

averaged over replicates minus the mean of the control replicates and then standardized. Also shown are values for generation eight estimated from the linear regression of response on generation number, pooled over replicates. Generally, these values lie in the neighborhood of the observed generation responses, as they should. The divergence of a particular treatment from control (0,0) in this Cartesian plane can be calculated as the length of the directed line segment (vector) from (0,0) to the estimated generation eight coordinates. It is obvious from Figure 5 that the single-trait-selection lines had greater divergence from control than the index lines. This is consistent with a positive genetic correlation between WK 6 and TAIL, since such a correlation would enhance the divergence of the single-trait lines and inhibit the divergence of antagonistic index lines. The vector lengths were 2.67, 3.09, 1.83 and 2.25, respectively, for  $W^+T^0$ ,  $W^0T^+$ ,  $W^+T^-$  and  $W^-T^+$ . It is also of interest to note the patterns of selection response in the index lines. For example,  $W^+T^-$  had little response in TAIL but increased in WK 6 for the first four generations and then had little response in WK 6 but decreased in TAIL for the next three generations. After an initial increase in TAIL for  $W^-T^+$ , there was little increase for the subsequent six generations, so that improvement in aggregate genotype subsequent to the initial surge was due almost solely to decreases in WK 6.

#### GENERAL DISCUSSION AND CONCLUSIONS

Direct and correlated responses to single-trait selection were adequately predicted from paternal half-sib parameter estimates. Thus, these results offer an empirical verification of current selection theory. Several studies have suggested that estimates of realized genetic correlations may vary depending upon which of the traits is the selection criterion (ABPLANALP, OGASAWARA and ASMUNDSON 1962; BAKER and COCKREM 1970; BERGER and HARVEY 1971). Only the latter authors based the suggestion on analyses of selection responses in lines originating from a single base; the others used data from two experiments conducted at different times and at different locations with different base populations (species for the first study) as the basis for this suggestion. The present report and that of FALCONER (1954) do not support this suggestion, at least for short-term responses.

In contrast to single-trait-selection responses, the responses to index selection were not consistent with current theory. This finding differs from that of BERGER and HARVEY (1971). They obtained realized genetic correlations from index selection which were roughly equivalent to paternal half-sib estimates. Our results indicate that in the dynamic situation of antagonistic selection, the genetic correlation may be more powerful in impeding component responses than predicted from presently available theory. It can be argued that LERNER's (1958) theory suggests a change in magnitude of genetic covariance with simultaneous selection of two traits and that this change was measured in the present experiment. This seems doubtful, however, since the duration of selection was relatively short (seven generations), and the correlation measured was an average correlation over that period. In addition, there was little indication of cessation of linear re-



sponse in aggregate genotype, as only one of the four index lines had a significant quadratic response curve.

BAKER and COCKREM (1970) concluded from their selection experiment that it would not be wise to place much weight on estimates of the genetic correlation when selection plans are being formulated. An unknown bias due to linkage relationships and a lack of replication, however, hampers an interpretation of their results. The present study, especially the single-trait-selection portion, clearly indicates that estimates of genetic parameters of complex characters such as body weight and tail length are useful in predicting direct and correlated responses to selection. Further, it appears that these responses are repeatable at least for short-term responses. Correlated responses were more variable than direct responses, as expected from the study of BOHREN, HILL and ROBERTSON (1966). However, mean responses in all correlated traits were in the direction suggested by the genetic correlation.

COCKREM's (1959) demonstration that antagonistic selection can be successful was confirmed. In addition, the design of the present study permitted a test for symmetry of response. Although some asymmetry was observed, response in the intended direction was made in both component traits in all replicates. When compared with other laboratory mouse strains, the ICR population can be characterized as being larger than most with a proportionately shorter tail. The mean six-week body weight and tail length in randombred ICR stock is about 28.7 g and 8.2 cm, respectively. COCKREM's (1959) base population averaged 19.1 g and 8.5 cm while FALCONER's (1954) base population averaged about 21 g and 8.7 cm. This observation is relevant in light of the observed asymmetry. The W-T<sup>+</sup> lines may have been selected back towards, and the W<sup>+</sup>T<sup>-</sup> away from, the population norm. FALCONER (1955) reported that the rate of selection response depended on the direction of selection and on the initial level.

This study offers some information on the desirability of replication in selection work and the precision of different methods of estimating heritability and genetic correlation. The use of within-line variability to estimate between-line variability, as was done by HILL (1971) in deriving a standard error of realized heritability, is logically defensible only with a number of simplifying assumptions. The extension of his results to realized genetic correlations requires further assumptions. If the experimenter is unwilling to make the necessary assumptions, replication is essential for estimating experimental error. Estimating experimental error on the basis of two observations, as was done in the present study, reflects minimal replication. However, the standard errors obtained were unbiased, unencumbered by assumption, and small. Each heritability estimate reported herein was based on over 4,000 observations. The standard errors of heritability realized from single-trait selection for WK 6 and TAIL were about one-tenth and about one-fifth the standard errors of the corresponding paternal half-sib estimates. Optimal distribution of full-sib families of size eight within sire families would not have reduced the paternal half-sib standard errors to the magnitude obtained by selection. Thus, selection furnished the best linear unbiased estimators.

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## LITERATURE CITED

- ABPLANALP, H., F. X. OGASAWARA and V. S. ASMUNDSON, 1962 Influence of selection for body weight at different ages on growth of turkeys. *Brit. Poul. Sci.* **4**: 71-82.
- BAKER, R. L. and F. R. M. COCKREM, 1970 Selection for body weight in the mouse at three temperatures and the correlated response in tail length. *Genetics* **65**: 505-523.
- BERGER, P. J. and W. R. HARVEY, 1971 Simultaneous two trait selection in mice. *J. Animal Sci.* **33**: 196 (Abstr.).
- BOHREN, B. B., W. G. HILL and A. ROBERTSON, 1966 Some observations on asymmetrical correlated responses to selection. *Genet. Res.* **7**: 44-57.
- COCKERHAM, C. CLARK, 1956 Effects of linkage on the covariances between relatives. *Genetics* **41**: 138-141.
- COCKREM, F., 1959 Selection for relationships opposite to those predicted by the genetic correlation between two traits in the house mouse (*Mus musculus*). *Nature* **183**: 342-343.
- DICKERSON, G. E., S. T. BLUNN, A. B. CHAPMAN, R. M. KOTTMAN, J. L. KRIDER, E. J. WARWICK, J. A. WHATLEY, JR., M. L. BAKER, J. L. LUSH and L. M. WINTERS, 1954 Evaluation of selection in developing inbred lines of swine. *Mo. Agr. Exp. Sta. Res. Bull.* **551**.
- FALCONER, D. S., 1954 Validity of the theory of genetic correlation. *J. Hered.* **45**: 42-44. —, 1955 Patterns of response in selection experiments with mice. *Cold Spring Harbor. Symp. Quant. Biol.* **20**: 178-196.
- FALCONER, D. S. and J. W. B. KING, 1953 A study of selection limits in mice. *J. Genetics* **51**: 561-581.
- HALDANE, J. B. S., 1955 The relation between density regulation and natural selection. *Proc. Roy. Soc. London B* **145**: 306-308.
- HANRAHAN, J. P. and E. J. EISEN, 1973 Sexual dimorphism and direct and maternal genetic effects on body weight in mice. *Theor. Appl. Genetics* **43**: 39-45.
- HILL, W. G., 1971 Design and efficiency of selection experiments for estimating genetic parameters. *Biometrics* **27**: 293-311.
- LERNER, I. M., 1958 *The Genetic Basis of Selection*. John Wiley and Sons, Inc., N. Y.
- OSBORNE, R. and W. S. B. PATERSON, 1952 On the sampling variance of heritability estimates derived from variance analyses. *Proc. Roy. Soc. Edinburgh B* **64**: 456-461.
- PIRCHNER, F., 1969 *Population Genetics in Animal Breeding*. W. H. Freeman Co., San Francisco.
- ROBERTSON, A., 1961 Inbreeding in artificial selection programmes. *Genet. Res.* **2**: 189-194.
- RUTLEDGE, J. J., O. W. ROBISON, E. J. EISEN and J. E. LEGATES, 1972 Dynamics of genetic and maternal effects in mice. *J. Animal Sci.* **35**: 911-918.
- SNEDECOR, G. W. and W. G. COCHRAN, 1967 *Statistical Methods*. Sixth Ed. The Iowa State University Press, Ames.
- TALLIS, G. M., 1959 Sampling errors of genetic correlation coefficients calculated from analyses of variance and covariance. *Aust. J. Stat.* **1**: 35-43.

Corresponding editor: R. ALLARD