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Maturing patterns of organ weights in mice selected for rapid postweaning gain*

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Summary. Correlated responses to selection for increased 3–6 week postweaning gain in male mice were estimated for seven internal organs (testes, spleen, liver, kidneys, heart, small intestine (S intest) and stomach) weighed at specific degrees of maturity in body weight (37.5, 50.0, 62.5, 75.0, 87.5 and 100%). Correlated responses in organ weights were generally large, but the magnitude and direction of response depended upon whether 1) comparisons were made at the same age, degree of maturity or body weight and 2) absolute or proportional organ weights were used. The selected line (M16) weighed more and had larger organ weights than controls (ICR) when compared at either the same degree of maturity or the same age, indicating positive genetic correlations between body weight and the respective organ weights. Positive correlated responses were found in spleen weight/body weight at all degrees of maturity and in liver and S intest weights as a proportion of body weight at some degrees of maturity. Testes, kidneys, heart and stomach weights as a proportion of body weight had negative correlated responses, though this was consistent only for kidneys across all degrees of maturity. Correlated responses in organ weights adjusted for body weight by covariance analysis were positive for spleen, S intest and stomach and negative for testes and kidneys. Based on the constrained quadratic model, degree of maturity in organ weight relative to degree of maturity in body weight responded positively for testes, kidneys and S intest and negatively for spleen and liver. Selection for increased growth caused negative correlated responses in allometric growth of testes, kidneys, S intest and stomach.

Key words: Mice – Correlated responses – Organ growth – Degree of maturity – Allometry

Introduction

Selection in mice for increased growth rate generally results in large positive correlated responses of muscle (Byrne et al. 1973), adipose tissue (Eisen and Leatherwood 1978; Allen and McCarthy 1980) and bone (Hooper 1977). Less data is available on correlated responses of internal organs. Selection for increased growth rate in mice causes positive correlated responses of both cell size and cell number of several internal organs measured at similar ages (Robinson and Bradford 1969; Eisen et al. 1978; Falconer et al. 1978). Information on correlated responses in the growth of internal organs following selection for rapid body weight gain in mammals is of value in understanding the quantitative genetics of growth and development. Correlated responses provide data on the magnitude of pleiotropic effects between body size and organ size. Knowledge of the correlated responses in ontogenetic growth of internal organs is essential for understanding evolutionary allometry (Atchley 1984). Furthermore, the magnitude of correlated responses in organ weights may affect protein synthesis and maintenance requirements. Fractional rates of protein synthesis are higher in visceral organs than in skeletal muscle (Garlick et al. 1976). Internal organs contribute more to maintenance requirements than skeletal muscle (Baldwin et al. 1980; Tess et al. 1984).

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The present study reports the effects of selecting mice for rapid postweaning body weight gain on different internal organ weights either at a specific degree of maturity in body weight or at a specific body weight.

Materials and methods

Mice were sampled from an unselected control line (ICR) whose progenitors were obtained from the Institute for Cancer Research, Philadelphia, PA, USA and a line (M16) derived from ICR by long-term selection for high postweaning gain from 3 to 6 weeks of age (Eisen 1975).

The experimental design and laboratory procedure were reported in a study of maturing patterns of fat depots in the selected and control lines (Eisen 1987). Briefly, male mice from each line were assigned randomly to be killed at one of the following degrees of mature body weight: 37.5, 50.0, 62.5, 75.0, 87.5 or 100%. The use of males only assumes the absence of line by sex interaction. Mature body weights were 38 and 65 g for ICR and M16, respectively, as estimated from growth curves of these mice (Eisen and Leatherwood 1978). No selection was practiced in M16 in the intervening period, and no evidence of mean change in body weight over generations was found.

Each mouse was killed by cervical dislocation when it was within ± 1 g of its designated degree of maturity. After the abdominal cavity was opened, the mouse was partially immersed in physiological saline to prevent dessication of organs. The following organs were dissected and weighed immediately: testes, spleen, liver, kidneys, heart, small intestine (S intest) and stomach. Stomach and S intest were flushed with water and blotted prior to being weighed. Paired organs were weighed together.

Least-squares procedures for unequal subclass numbers (Harvey 1979) were used to estimate the means of absolute organ weights and organ weights as a percentage of body weight. The statistical model included fixed effects of line, degree of maturity for body weight and line by degree of maturity interaction and a random error term.

Degree of maturity traits were defined as follows (Taylor 1980a):

$u_y = y/A_y$ = degree of maturity for organ weight (y) where A_y is mature organ weight,

$u_x = x/A_x$ = degree of maturity for body weight (x) where A_x is mature body weight.

A_y was estimated as the mean organ weight of mice killed at $A_x = 38$ g in ICR and $A_x = 65$ g in M16.

Several methods have been proposed to describe development of a body component to maturity relative to development of body weight to maturity (Taylor 1980b; Butterfield et al. 1983a; Parks 1983). Two of these methods were used in the present study. Butterfield et al. (1983a) proposed the constrained quadratic curve which passes through the origin (0, 0) and point (1, 1) giving

$$u_y = q\,u_x + (1-q)\,u_x^2 \qquad (1)$$

where q and 1−q are linear and quadratic partial regression coefficients. When $q = 1$, the equation describes a body component which matures at the same rate as the whole body. When $q < 1$, the equation represents a late maturing component, and when $q > 1$, it represents an early maturing component. A second method of analysis is based on the standardized allometric equation (Taylor 1980b)

$$u_y = u_x^b \qquad (2)$$

or in natural logarithmic form

$$\ln u_y = b \ln u_x \qquad (3)$$

where b is the slope of the regression equation fitted through the origin. Interpretation of maturing rate for $b = 1$ is identical to that for $q = 1$, but interpretation for $b \neq 1$ is opposite to that of q in the constrained quadratic; i.e., for $b > 1$ the component is slow maturing, and for $b < 1$ the component is fast maturing.

Formula (1) can be rearranged to predict proportional organ weight (y/x) at any fixed degree of maturity in body weight (Butterfield et al. 1983a) as

$$y/x = q\,(A_y/A_x) + (1-q)\,(A_y/A_x)\,u_x. \qquad (4)$$

Similarly, (2) can be modified to predict proportional organ weight as

$$y/x = (A_y/A_x)^{b-1}. \qquad (5)$$

Note that (4) gives a linear prediction of proportional weight whereas (5) is curvilinear. The adequacy of equations (4) and (5) for predicting proportional organ weight in the present data was evaluated.

Bivariate allometry relating organ weight (y) to body weight (x) was analyzed by Huxley's (1932) allometric equation

$$y = a\,x^k$$

transformed to natural logarithms

$$\ln y = \ln a + k \ln x \qquad (6)$$

where ln a is the intercept and k is the regression coefficient. The logarithms of organ weights and body weight were also analyzed by principal components using the covariance matrix (Morrison 1976). The principal components analysis was used to find the multivariate analogues of the bivariate regression coefficients (Jolicoeur 1963a, b). A principal components analysis was then completed on the combined data of both lines in order to determine growth and shape differences (Shea 1985).

Least-squares procedures were used to fit the models in (1), (3) and (6) for each line, and the line regression coefficients were tested for homogeneity.

Results

Body weight means were close to the intended means for each degree of maturity (Table 1). M16 mice were consistently older ($P < 0.01$) than ICR mice at the same degree of maturity. Thus, selection for rapid growth resulted in M16 mice maturing more slowly than ICR mice.

Mean organ weights at each degree of maturity in body weight are presented in Table 2. Organ weights generally increased with increased degree of maturity in body weight. An exception was spleen weight which showed no significant change from 75 to 100% maturity in ICR and from 62.5 to 87.5% maturity in M16. In contrast, Webster and Liljegren (1955) found no diminution of spleen growth in mice in the body weight range of 10 to 46 g. At each degree of maturity in body weight, organ weights in M16 were larger ($P < 0.01$) than in ICR.

The design of the present experiment permitted organ weights in M16 vs ICR to be compared at three similar ages (24.3 vs 25.1 d, 30.1 vs 28.8 d and 34.4 vs 33.8 d), which corresponded to the following degrees of maturity: 37.5 vs 50.0%, 50.0 vs 62.5% and 62.5 vs 75.0% (Table 1). The M16 mice had larger organ weights than ICR mice at each age (Table 2).

Regression coefficients relating degree of maturity for each organ weight to degree of maturity for body weight were estimated by the constrained quadratic (1) and standardized allometric (2) equations (Table 3). Both equations gave similar results for each organ regarding 1) rate of maturity and 2) line differences in rate of maturity. Therefore, plots of the predicted degree of maturity for organ weights in each line are given only for the standardized allometric equation (Fig. 1 A–G).

Table 1. Means of body weight and age at each degree of maturity

Degree of maturity %	Line	No. of mice	Body wt mean (g)	Age mean ±SE (d)[a]
37.5	ICR	20	14.1	20.3±0.3
	M16	19	24.1	24.3±0.5
50.0	ICR	20	19.1	25.1±0.5
	M16	19	33.2	30.1±0.6
62.5	ICR	20	24.0	28.8±0.5
	M16	20	41.1	34.4±0.3
75.0	ICR	20	28.8	33.8±0.8
	M16	19	49.1	44.9±1.8
87.5	ICR	16	32.9	42.1±1.1
	M16	16	57.1	54.7±1.2
100.0	ICR	20	38.0	71.0±3.3
	M16	20	65.2	82.9±2.6

[a] All line differences were significant ($P<0.01$) within each degree of maturity

In ICR mice, testes and kidneys were slow-maturing organs relative to body weight ($q < 1$, $b > 1$), heart matured at approximately the same rate as the whole body ($q=b=1$), and the four remaining organs matured more rapidly than the whole body ($q > 1$, $b < 1$). Selection for rapid postweaning gain in M16 mice resulted in positive correlated responses in degree of maturity of testes, kidneys and S intest weights relative to degree of maturity in body weight. Negative correlated responses were found for spleen and liver. Selection for rapid growth caused testes to be modified from a slow- to a fast-maturing organ while liver was modified from a fast-maturing organ to one that matured at the same rate as body weight.

Organ weights as a percentage of body weight are plotted against degree of maturity for body weight in Fig. 2 A–G. Line by degree of maturity interactions were significant ($P < 0.05$) for all organ percentages except stomach. Interactions for proportional weights of spleen and kidney were the result of changes in magnitude of line differences at each degree of maturity, but the direction of line differences was not

Table 2. Least-squares mean ±SE for organ weights (mg) at each degree of maturity in body weight[a]

Line	Degree of maturity (%)					
	37.5	50.0	62.5	75.0	87.5	100.0
Testes						
ICR	64± 2	99± 4	138± 4	164± 4	208± 6	232± 8
M16	120± 3	172± 4	220± 5	262± 6	280± 7	300± 6
Spleen						
ICR	109± 5	103± 5	133± 5	147± 5	143± 11	138± 6
M16	213± 14	278± 13	313± 12	303± 20	309± 14	337± 13
Liver						
ICR	917± 18	1,405± 21	1,650± 21	2,104± 32	2,393± 51	2,508± 50
M16	1,713± 37	2,371±131	3,131±166	3,884± 73	4,528± 91	4,898± 82
Kidneys						
ICR	238± 5	335± 9	440± 9	545± 12	660± 21	784± 16
M16	364± 8	480± 9	636± 8	806± 16	922± 17	1,066± 20
Heart						
ICR	94± 1	112± 2	136± 4	157± 5	202± 8	230± 9
M16	142± 4	173± 4	227± 8	276± 9	332± 11	356± 15
S intest						
ICR	991± 20	1,472± 37	1,998± 49	2,192± 61	2,441±108	2,663± 95
M16	2,151±104	3,367± 98	3,576±131	3,792±135	4,159±144	4,587±145
Stomach						
ICR	107± 2	148± 3	172± 4	206± 5	237± 7	259± 6
M16	190± 5	258± 8	294± 8	328± 7	382± 9	435± 15

[a] Line differences were significant ($P<0.01$) for all organ weights at each degree of maturity

Table 3. Regression coefficients ±SE relating degree of maturity for each organ weight to degree of maturity for body weight

Organ	Line	$\hat{q} \pm SE^{a,c}$	$\hat{b} \pm SE^{b,c}$
Testes	ICR	0.693±0.054	1.272±0.024
	M16	1.295±0.048**	0.850±0.020**
Spleen	ICR	2.444±0.097	0.268±0.038
	M16	2.120±0.093*	0.415±0.038**
Liver	ICR	1.136±0.040	0.936±0.017
	M16	0.967±0.057*	1.088±0.054**
Kidneys	ICR	0.700±0.041	1.228±0.018
	M16	0.847±0.032**	1.112±0.014**
Heart	ICR	0.951±0.064	0.997±0.025
	M16	1.018±0.067	0.974±0.024
S intest	ICR	1.226±0.065	0.907±0.024
	M16	1.639±0.073**	0.671±0.030**
Stomach	ICR	1.204±0.044	0.870±0.017
	M16	1.250±0.054	0.839±0.020

* Line regression coefficients were different ($P < 0.05$)
** Line regression coefficients were different ($P < 0.01$)
[a] Estimated from the constrained quadratic model
[b] Estimated from the logarithmic form of the standardized allometric model
[c] All regression coefficients were different from one ($P < 0.01$) except liver in M16 and heart in M16 and ICR which were not different from one ($P > 0.05$)

changed. Interactions for the other organ percentages, for the most part, were caused by significant line differences in one direction at certain degrees of maturity and not at others.

Testes weight as a percentage of body weight increased in ICR and M16 from 37.5 to 50.0% degree of maturity, but from 75.0 to 100% maturity ICR increased and M16 decreased. Spleen weight/body weight decreased with degree of maturity in both lines, with M16 consistently exceeding ICR. Liver weight/body weight increased from 37.5 to 87.5% maturity in M16, after which it declined, whereas no trend was evident in ICR. Kidney weight as a percentage of body weight increased with degree of maturity at a higher rate in ICR than in M16, and kidney proportional weights of ICR were consistently larger than M16. Heart percentages were larger in ICR than in M16 at early and late degrees of maturity with no differences apparent at intermediate points. S intest weight/body weight was much larger in M16 than in ICR at 37.5 and 50.0% maturity, but no differences were found at subsequent degrees of maturity. In both lines, S intest percentage initially increased and then decreased sharply with degree of maturity. Stomach percentage decreased and then tended to level off in ICR and M16, with ICR exceeding M16 at 75.0 and 87.5% maturity.

Butterfield et al. (1983 a) showed that equation (4), derived from the constrained quadratic, can be used to predict proportional organ weight at a specific degree

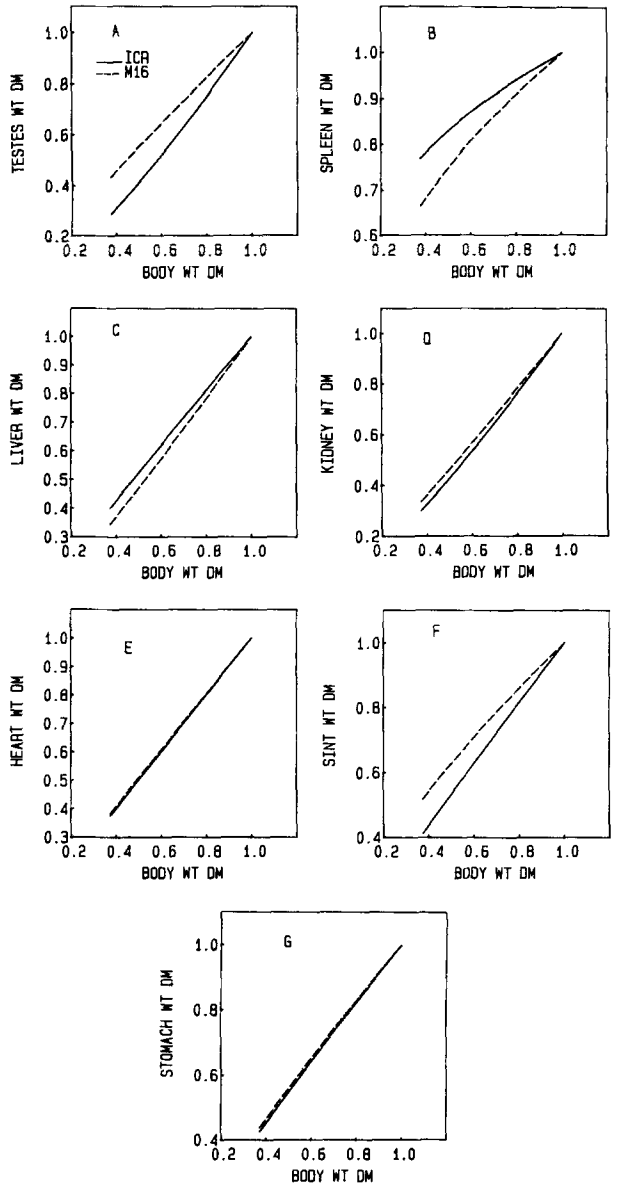

Fig. 1A–G. Predicted degree of maturity (DM) for organ weights based on degree of maturity (DM) for body weight using the standardized allometric model: **A** testes; **B** spleen; **C** liver; **D** kidneys; **E** Heart; **F** S intest; **G** stomach

of maturity. If data on degree of maturity are fitted by the standardized allometric equation, then equation (5) can be used. If q (or b) differs among lines or treatment levels, then each mean should be predicted by using an estimate of q from each line, and inferences about line differences in proportional organ weight are valid only for the specific degree of maturity.

Use of equations (4) or (5) is of questionable value for prediction of proportional organ weights that change nonlinearly with degree of maturity because the predicted means may deviate considerably from observed means. In the present data, only kidney weight/

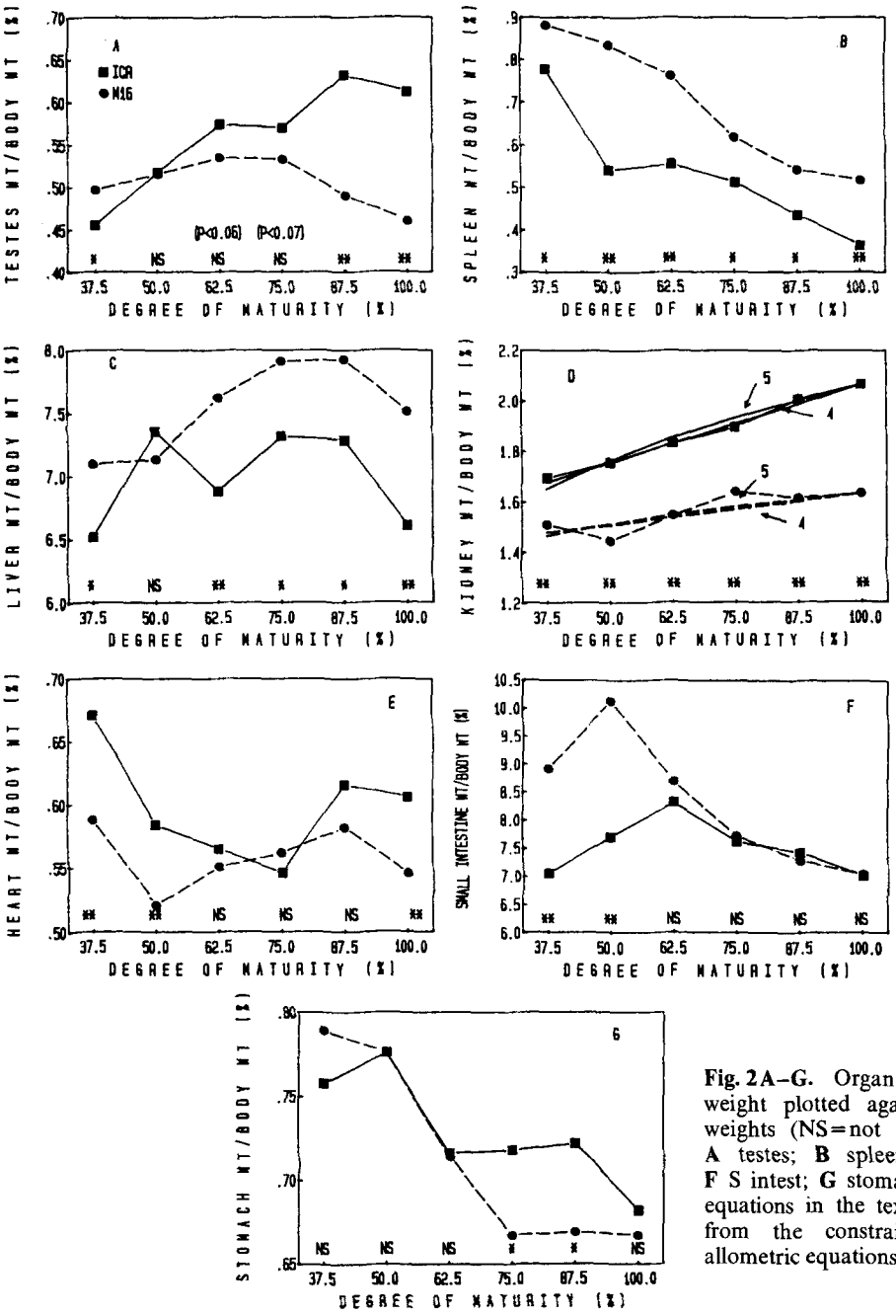

Fig. 2A–G. Organ weights as a percentage of body weight plotted against degree of maturity for body weights (NS=not significant; $*P < 0.05$; $**P < 0.01$): **A** testes; **B** spleen; **C** liver; **C** kidneys; **E** heart; **F** S intest; **G** stomach. In **D**, plots (4) and (5) refer to equations in the text used to predict organ percentages from the constrained quadratic and standardized allometric equations, respectively

body weight showed a linear relationship with degree of maturity in body weight, and equations (4) and (5) appeared to give equally good predictions (Fig. 2 D).

Regression coefficients of ln organ weights on ln body weight indicated that M16 had significant negative correlated responses in growth of testes, kidneys, S intest and stomach relative to whole body growth (Table 4, Fig. 3 A–G). The qualitative types of allometry (positive, $k > 1$; isometric, $k = 1$; negative, $k < 1$) observed for each organ in the control and selected lines were compared to determine if selection for increased postweaning growth not only had caused quantitative correlated responses in allometry, but also qualitative changes, e.g., positive allometry to isometry. In ICR mice, testes and kidneys showed positive allometry; spleen, heart and stomach negative allometry; and liver and S intest isometry. Selection for increased growth in M16 mice led to the following qualitative allometric changes compared with ICR mice: from positive to isometric (testes), from isometric to positive (liver), from negative to isometric (heart) and from isometric to negative (S intest).

Table 4. Intercept and regression coefficient ± SE relating ln organ weights to ln body weight and multivariate coefficient

Organ	Line	ln â[a]	k̂ ± SE[a]	Multivariate[b]
Testes	ICR	−8.381	1.314 ± 0.035[2]	1.340
	M16	−4.666	0.941 ± 0.035**	0.962
Spleen	ICR	1.434	0.336 ± 0.061[2]	0.337
	M16	1.077	0.429 ± 0.062[2]	0.464
Liver	ICR	−2.939	1.027 ± 0.064	1.046
	M16	−3.966	1.127 ± 0.065[1]	1.268
Kidneys	ICR	−6.022	1.201 ± 0.026[2]	1.223
	M16	−5.375	1.114 ± 0.026*,[2]	1.131
Heart	ICR	−4.081	0.896 ± 0.039[1]	0.923
	M16	−4.944	0.976 ± 0.040	1.005
S intest	ICR	−2.437	0.984 ± 0.044	1.006
	M16	0.753	0.694 ± 0.045**,[2]	0.708
Stomach	ICR	−3.804	0.889 ± 0.030[2]	0.897
	M16	−2.825	0.801 ± 0.030*,[2]	0.804

* Line regression coefficients were different ($P < 0.05$)
** Line regression coefficients were different ($P < 0.01$)
[1] Regression coefficients were different from one ($P < 0.05$)
[2] Regression coefficients were different from one ($P < 0.01$)
[a] Estimated from the logarithmic form of the allometric model
[b] Direction cosines in the eigenvector of the first principal component associated with each ln organ weight divided by the direction cosine in the eigenvector associated with ln body weight

Comparisons of line mean organ weights, adjusted for body weight by covariance analysis, are strictly valid only when the regression coefficients are homogeneous as was true in the present study for spleen, liver and heart (Table 4). When regression coefficients are heterogeneous, the line mean organ weight contrasts will depend upon the adjusted body weight used. Nevertheless, contrasts also were made for the organ weights with heterogeneous regression coefficients (testes, kidneys, S intest and stomach) because, for the most part, the regression lines for these organs did not intersect (Fig. 3). The model used to obtain adjusted means in the case of heterogeneous slopes included the overall regression coefficient and the line regression coefficient deviated from the overall regression coefficient. The present design also permitted organ weights for ICR and M16 to be recorded at two similar body weights, approximately 24 and 33 g (Table 1). Results are presented in Table 5.

The covariance analysis indicated that line differences in liver and heart weights were not significant at a constant body weight. ICR mice had larger ($P < 0.01$) testes and kidneys and smaller ($P < 0.01$) spleen, S intest and stomach than M16 mice when adjusted for body weight. The observed organ weight

Table 5. Organ weight means (mg) adjusted by covariance analysis to mean body weight (32.2 g) and organ weight means recorded at constant body weights of ~24 and ~33 g, respectively

Organ	Line	Covariance adjusted body wt[a]	Observed body wt[b]	
		32.2 g (10.38)	~24 g (10.08)	~33 g (10.40)
Testes	ICR	192	138 ± 4	208 ± 6
	M16	164**	120 ± 3**	172 ± 4**
Spleen	ICR	138	133 ± 5	143 ± 11
	M16	255**	213 ± 14**	278 ± 13**
Liver	ICR	2,276	1,650 ± 21	2,393 ± 51
	M16	2,298	1,713 ± 37	2,371 ± 131
Kidneys	ICR	631	440 ± 9	660 ± 21
	M16	485**	364 ± 8**	480 ± 9**
Heart	ICR	187	136 ± 4	202 ± 8
	M16	181	142 ± 4	173 ± 4**
S intest	ICR	2,387	1,998 ± 49	2,441 ± 108
	M16	2,855**	2,151 ± 104	3,367 ± 98**
Stomach	ICR	226	172 ± 4	237 ± 7
	M16	241**	190 ± 5**	258 ± 8*

* Line difference ($P < 0.05$)
** Line difference ($P < 0.01$)
[a] Tests of significance were based on data transformed to natural logarithms, and ln organ weights were adjusted to an overall logarithmic mean body weight (mg) of 10.38; line slopes for testes, kidneys, S intest and stomach were heterogeneous (see text for explanation). The logarithmic means were converted to arithmetic means for presentation
[b] Observed body weight of ~24 g (~33 g) was recorded at 62.5 (87.5) and 37.5 (50.0) % degrees of maturity in body weight in ICR and M16, respectively; values in parentheses are logarithms of arithmetic means

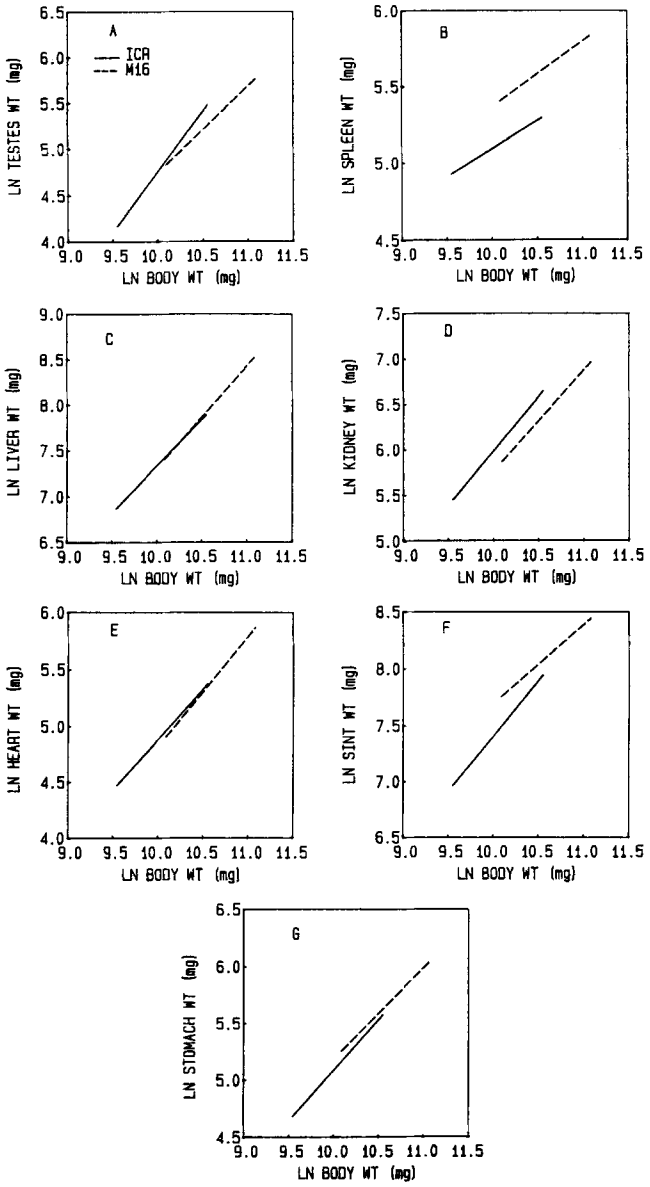

Fig. 3A–G. Regression lines of ln organ weights on ln body weight. **A** testes; **B** spleen; **C** liver; **D** kidneys; **E** heart; **F** S intest; **G** stomach

means recorded at body weights of approximately 24 and 33 g were in general agreement with the covariance analysis, with the exception of heart weight at 33 g.

The first two principal components accounted for 93.3 and 89.0% of the variance in ICR and M16, respectively (Table 6). The first principal component is interpreted as accounting for variation in size, and the second is associated with shape variation (Jolicoeur 1963b). The direction cosines of the first principal component for ICR and M16 were all positive (Table 6), indicating a simultaneous increase in all organ weights with body weight. The second principal component contained positive and negative direction

Table 6. Direction cosines of first two principal components (PC1, PC2)

Trait	ICR		M16	
	PC1	PC2	PC1	PC2
Body wt	0.350	0.011	0.373	0.124
Testes	0.469	−0.302	0.359	0.134
Spleen	0.118	0.941	0.173	0.128
Liver	0.366	0.039	0.473	−0.854
Kidneys	0.428	0.013	0.422	0.127
Heart	0.323	−0.087	0.375	0.226
S intest	0.352	0.119	0.264	0.334
Stomach	0.314	−0.022	0.300	0.203
Eigenvalue[a]	88.2	5.1	79.8	9.2

[a] Expressed as a percentage of total variance

cosines which differ for ICR and M16. If all organs grow at the same rate, all the direction cosines of the first principal component are expected to be equal to $1/\sqrt{p}$ where $p=8$, the number of variables (Jolicoeur 1963a). A test of this hypothesis (Morrison 1976) yielded χ^2 (d.f.$=7$)$=267.97$ ($P < 0.01$) and χ^2 (d.f.$=7$)$=124.06$ ($P < 0.01$) for ICR and M16, respectively. The conclusion based on this analysis is that the rate of growth differed among the organs, which agrees with the conclusion reached from the bivariate allometry analysis.

Jolicoeur (1963a, b) has generalized the bivariate allometric relationship to the multivariate case based on principal components analysis. The ratio of the direction cosine of each ln organ weight to the direction cosine of ln body weight (multivariate coefficient) for the first principal component is expected to be proportional to the regression (allometry) coefficient (k) in the bivariate model (6). The multivariate and bivariate coefficients within each line (Table 4) were in close agreement ($r=0.994$; $P < 0.01$), the multivariate coefficient being slightly larger than k in every case.

A third principal components analysis was conducted on the combined ICR and M16 data. A plot of means of the first and second principal components showed a pattern that distinguished the two lines and the six degrees of maturity (Fig. 4).

Discussion

The correlated responses in organ growth is summarized in Table 7. Selection in M16 for increased post-weaning growth over a constant age interval resulted in sizable positive correlated responses in weights of testes, spleen, liver, kidneys, heart, S intest and stomach when compared with ICR controls at either a constant

Table 7. Summary of correlated responses in organ growth[a]

Organ	Mean organ wt			Mean organ wt/body wt	Slope	
	Same degree of maturity	Same age	Same body wt	Same degree of maturity[b]	Degree of maturity (q)	Allometry coefficient (k)
Testes	+	+	–	–	+	–
Spleen	+	+	+	+	–	0
Liver	+	+	0	+	–	0
Kidneys	+	+	–	–	+	–
Heart	+	+	0	–	0	0
S intest	+	+	+	+	+	–
Stomach	+	+	+	–	0	–

[a] Correlated response: "+" = positive, "–" = negative, "0" = no change
[b] Line by degree of maturity interaction was significant for most organs; only the major trend is indicated

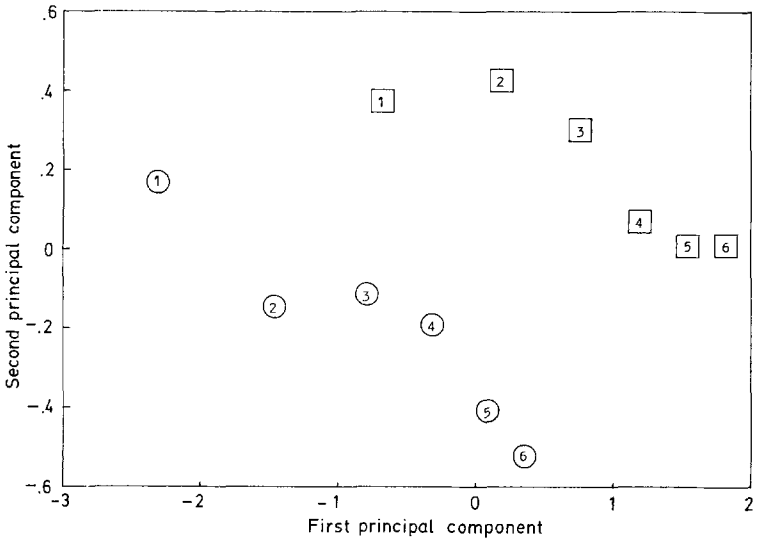

Fig. 4. Plot of means of first against second principal components from analysis based on the covariance matrix involving ln organ weights and ln body weight. The circles and squares represent means of ICR and M16, respectively, and numbers 1 to 6 represents 37.5, 50.0, 62.5, 75.0, 87.5 and 100% maturity, respectively

degree of maturity in body weight or a constant age. Based on these results, it was concluded that the genetic correlations between body weight and the respective organ weights were moderately high when measured at the same age or the same degree of maturity in body weight, at least during postweaning growth. Evidence from other selection studies supports this conclusion. Selection for increased 6-week body weight resulted in a positive correlated response in testes weight; the realized genetic correlation between body weight and testes weight was 0.6 (Eisen and Johnson 1981). Bünger et al. (1985) reported positive correlated responses in weights of heart, liver and kidneys in 6-week-old mice selected for large 6-week body weight. Nash and Lodgson (1978) found larger weights of liver, spleen, kidneys, heart and lungs at 60 days of age in a line selected for increased 60-day body weight compared with a randombred control line. Contrasted to these results were small paternal half-sib estimates of genetic correlations between 60-day body weight and heart, liver, spleen and kidney weights (Shibata 1965). However, these genetic correlations were probably biased by linkage disequilibrium effects because they were based on F_1 progeny of a cross between two inbred lines.

Because the M16 and ICR lines differed in body weight at the same age, comparing line means based on organ weights as a percentage of body weight does not, in general, provide an appropriate adjustment for body weight (Gould 1966). Two methods of adjustment for body weight were made. The first method was to compare organ weights as a percentage of body weight at the same degree of maturity in body weight (Butterfield et al. 1983 a). The second method used to adjust organ weights for body weight was the standard covariance analysis. The two methods give differences in correlated responses for some organs (Table 7), which is

not surprising since one method uses proportional weight and the other uses absolute weight.

Comparisons between breeds or species made at the same degree of maturity in body weight reduce the influence of body weight considerably (Taylor 1985). Line × degree of maturity interactions indicated that line differences in organ weights as a percentage of body weight varied with degree of maturity. However, a pattern of correlated responses did emerge. Positive correlated responses were found in M16 for spleen weight/body weight at all degrees of maturity, and in liver and S intest weights as a proportion of body weight at some degrees of maturity. In contrast, testes, kidneys, heart and stomach weights as a percentage of body weight had negative correlated responses, though this was consistent only for kidneys across all degrees of maturity. The conclusion from these results is that proportinal organ weights at the same degree of maturity have been modified by selection for rapid growth, but the magnitude of the change for each organ depends upon the degree of maturity.

Butterfield et al. (1983 b) compared percentage organ weight at the same degree of maturity (62%) for six alimentary tract organs and eight major internal organs in a large and small line of Merino sheep. The assumption was made that line by degree of maturity interactions were zero. The large strain had significantly larger small intestine and smaller kidney weights as percentages of body weight.

Correlated responses in organ weights adjusted to the same body weight by covariance analyses were positive for spleen, S intest and stomach and negative for testes and kidneys, whereas liver and heart showed no significant correlated responses (Table 7). The larger stomach and S intest of M16 mice compared with ICR mice when adjusted to the same body weight indicate that selection for rapid growth in M16 has increased the capacity of the alimentary tract. The M16 mice consume more food per unit metabolic body size than ICR mice (Eisen and Leatherwood 1978). The lack of correlated responses in weights of liver and heart after adjustment for body weight suggests that any physiological function of these vital organs which may have been modified by selection for increased growth did not lead to an increase in organ weight at a specific body weight. Falconer et al. (1978) found no differences between large, small and intermediate body size lines of mice in cell size and cell number and hence cell mass of liver, lungs, kidneys and spleen when adjusted for body weight; however, this conclusion was based on a plot of the data and not a statistical comparison. The results from the present data concur with conclusions of Falconer et al. (1978) for liver but not for spleen and kidney which showed positive and negative correlated responses, respectively.

Dynamics of organ growth can be studied by comparing the degree of maturity in organ weight relative to the degree of maturity in body weight (Taylor 1980 b). Selection for rapid postweaning growth resulted in significant correlated responses in maturing patterns of five of the seven organs investigated. Maturity coefficients based on the standardized allometric (constrained quadratic) model responded positively (negatively) for testes, kidneys and S intest and negatively (positively) for spleen and liver (Table 7). The heart and stomach showed no significant correlated responses. Butterfield et al. (1983 b) compared maturity coefficients from the constrained quadratic model in large and small strains of Merino sheep for omasum, abomasum, ruminoreticulum, small intestine, large intestine, liver, kidneys, spleen and heart; only the omasum showed a strain difference, being larger in the small strain.

The allometric coefficient (Huxley 1932) is an alternative approach to measuring organ growth relative to body growth. Both quantitative and qualitative allometric correlated responses were found. The quantitative correlated responses in the allometric coefficients were negative for testes, kidneys, S intest and stomach. Qualitative correlated responses in allometric coefficients were detected for testes, liver, heart and S intest.

The maturity coefficients and allometry coefficients are closely associated (Taylor 1980 b; Butterfield et al. 1983 a) and were expected to yield similar results. Although the tests of significance between lines for the two coefficients did not agree for spleen, liver and stomach, the expected direction of the correlated responses were in agreement, and the correlation between q and k was high ($r = -0.96$; $P < 0.01$). The disagreements regarding tests of significance for these organs may be the result of an inadequacy of the models to describe the data. There is no question, however, that selection has modified the rate of organ growth relative to body growth in several major internal organs. These correlated responses may reflect physiological changes in organ metabolism associated with the dynamics of the growth process.

Organ growth relative to body growth has been studied in other mammals. In rats (Trieb et al. 1976), sheep (Butterfield et al. 1983 b) and pigs (Doornenbal and Tong 1981; Tess et al. 1986), the allometry coefficients which were measured are less than one for spleen, liver, kidneys, heart, small intestine and stomach. In the baboon, the coefficients are less than one for liver, heart and kidneys of males, and equal to one for spleen and kidneys of females (Larson 1985). The allometric coefficients for spleen, liver, kidneys and heart in five macaque species vary from less than one to one (Larson 1985). The high frequency of allometry coefficients less than one for the major internal organs across mammalian species is consistent with the hypothesis that these organs are early maturing because they are essential for future growth of the whole body (Butterfield et al. 1983 b). Larson (1985) speculated that the similar allometric coefficients found for the heart, kidneys, liver and spleen in macaques and baboons are associated with these organs having a common function in the

processing of blood. The present data with mice does not support this hypothesis completely; kidneys of ICR and M16 mice and livers of M16 mice had allometry coefficients greater than one. The physiological basis for these differences remains to be determined.

An allometric coefficient greater than one for testes in ICR mice agrees with results in macaques and baboons (Larson 1985), but the coefficient was not different from one in rats (Trieb et al. 1976). The increased testes growth associated with puberty in males accounts for the positive allometric growth of testes. However, selection for increased growth in M16 caused a decrease in testes growth relative to whole body growth, and consequently negative allometry for testes growth.

The multivariate and bivariate allometry coefficients were in very close agreement as predicted from theory (Jolicoeur 1963a, b). A comparison of the two coefficients for fat depots from the same data did not agree nearly as well; this result was associated with nonlinearity among the variables in the ln–ln covariance matrix (Eisen 1987). Analysis of growth allometry in chimpanzees and gorillas (Shea 1985), rhesus monkeys (Cochard 1985) and cockroaches (Brown and Davies 1972; Davies and Brown 1972) indicated good agreement between the bivariate and multivariate allometry coefficients.

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