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Long-term Selection for a Quantitative Character in Large Replicate Populations of *Drosophila melanogaster*

Part 3: The Nature of Residual Genetic Variability

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Summary. Six replicate lines of *Drosophila melanogaster*, which had been selected for increased abdominal bristle number for more than 85 generations, were assayed by hierarchical analysis of variance and offspring on parent regression immediately after selection ceased, and by single-generation realised heritability after more than 25 generations of subsequent relaxed selection.

Half-sib estimates of heritability in 5 lines were as high as in the base population and much higher than observed genetic gains would suggest, excluding lack of sufficient additive genetic variance as a cause of ineffective selection in these lines. Also, there was considerable diversity among the six lines in composition of phenotypic variability: in addition to differences in the additive genetic component, one or more of the components due to dominance, epistasis, sex-linkage or genotype-environment interaction appeared to be important in different lines.

Even after relaxed selection, single-generation realised heritabilities in four lines were as high as in the base population. As a large proportion of total genetic gain must have been made by fixation of favourable alleles, the compensatory increase of genetic variability has been sought in a genetic model involving genes at low initial frequencies, enhancement of gene effects during selection and/or new mutations.

Key words: Long-term selection – Residual genetic variability – Heritability – Abdominal bristle number – *Drosophila melanogaster*

Introduction

The genetic properties of long-term selection lines, when either at or approaching selection limits, have been shown to be diverse and often perplexingly complex. The first step in analysing such lines should be to investigate the presence of residual genetic variability by observing responses to reverse or relaxed selection (e.g. Frankham et al. 1968) or to systematic inbreeding (Falconer 1971), or by estimating genetic components of phenotypic variance.

Although theory predicts loss of additive genetic variability with continuous selection through fixation of favourable alleles and random genetic drift (Robertson 1960), the experimental results of long-term selection do not always conform to this expectation. When rapid inbreeding is inevitable due to small population size, the genetic variability is usually exhausted soon after selection is started (Tantawy 1956). But, when populations are reasonably large, selection limits may be reached in spite of considerable residual genetic variability, a large portion of which is presumably additive genetic (Lerner and Dempster 1951; Reeve and Robertson 1953; Dickerson 1955; Clayton and Robertson 1957; Eisen 1972). However, study on the magnitude and the kind of residual genetic variability has been limited because of the difficulties involved in analysing long-term selection lines, although the information from such a study is a desideratum in any attempt to overcome the selection limit.

This paper reports the results of genetic analyses in six replicate long-term selection lines of *Drosophila melanogaster* (Yoo 1980a) at the end of the selection experiment and after more than 25 generations of subsequent relaxed selection.

Materials and Methods

Three separate experiments were carried out with six replicate selection lines described by Yoo (1980a). Briefly, these lines were derived from a cage population of the *sc* Canberra outbred strain of *Drosophila melanogaster* and selected upward for bristle number on one abdominal sternite, the fourth in males and the fifth in females. Each generation, 50 pairs were selected out of 250 scored, and selection was continued for 86-89 generations. Three lines (Ua, Ub and CRa) appeared to have reached selection pla-

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teaux, while the other three (CRb, CCa and CCb) were still responding when selection was terminated. Thereafter each line was maintained by 50 pairs of parents taken at random for a further 32-35 generations. Experiment 1 was designed to study the genetic and environmental components of phenotypic variability in the lines still under selection pressure using intraclass correlation and parent-offspring regression methods. The aim was to sample 120 males and 600 females from the progeny of the last selected parents, each male being mated to 5 females and 5 offspring of each sex scored from each of 3 dams per sire. However, except for CCa, poor fertility and fecundity made it necessary to score all the available progeny (to a maximum of 10 in each sex) from all dams. Details of the data structure are given in Table 1. The parents were mated for 2-3 days and then bristle number on both the fourth and the fifth sternite was scored in survivors of both sexes; subsequently females were allowed to lay eggs in separate vials for 4-5 days. The females which were sterile or died during the egg laying period were recorded. Female fertility was determined by the trace of larval working in the medium; when all the females mated to one male were sterile, the male was assumed to be sterile. Experiment 2 was carried out to facilitate the comparison between Experiments 1 and 3, hence in parallel with Experiment 3, but using the procedures of Experiment 1 except that males (parents and offspring) only were scored for the fourth abdominal bristle number. Two lines (Ub and CRa) were chosen for this purpose on the basis of fitness and ease of scoring. In Experiment 3, the residual genetic variability after 26-29 generations of relaxed selection was estimated by single-generation realised heritability; this lapse of time should have been sufficient to eliminate most of the lethals which appeared to be the major source of the unusual heritability estimates in Experiment 1. In generation (G) 115, single-generation realised heritabilities were obtained in each line using 5 replicate sublines each of 10 pairs of parents selected at an intensity of 20% and 5 corresponding unselected controls. Fifty pairs of progeny from each subline or control were scored in the same way as for the previous selection. The same procedures were repeated in the next generation using the progeny in the controls. The realised heritability from a pair of subline and corresponding control was treated as the statistical unit in a 6 (lines) X2 (sexes) X2 (generations) factorial analysis with 5 replicates within each line. In Experiments 1 and 2, 2.5 X 7.6 cm vials were used for mating of parents and for single-female cultures, while ten pairs of parents were mated in cream jars (142 ml) in Experiment 3. Flies were cultured on a dead yeast fortified medium (Medium F of Claringbold and Barker 1961) at 25 ± 0.5°C and 65-70% relative humidity. The results of Experiments 1 and 2 were analysed following the general model for hierarchical analysis of variance given by Gates and Shiue (1962). Phenotypic variance was then divided into observational components by the methods given by Hammond and Nicholas (1972), and heritabilities were estimated from sire and from dam components in the usual way (Falconer 1960). Standard errors for heritability estimates were approximated using the formulae given by Becker (1964). Also, heritabilities were estimated from offspring on sire and intra-sire offspring on dam regression following the standard procedures. More details of statistical analyses may be found in Hammond et al. (1972). In Experiment 1, all heritability estimates were computed separately for the fourth and for the fifth abdominal bristle number, and arithmetic means were calculated over the two sternites. Standard error for a mean estimate was calculated on the assumption that the original estimates were not correlated, although they were usually positively correlated to some extent. Therefore, the standard errors given here might have been underestimated at most by a factor of 0.7.

Results

Selection Response in the Last Period of Selection

In spite of intense selection for more than 85 generations, some of the selection lines were still responding to selection when Experiment 1 was started. The rate of response (Table 2) was calculated as regression coefficients of cumulated standardised response on cumulated standardised selection differential in the last period of about ten generations; phenotypic standard deviation of current generation was used in standardisation. The standard errors given in Table 2 were based on deviations from the regression lines. There was little response in Ub and CRa, while Ua tended to move in the opposite direction to the selection. CRb and CCb were still responding to selection at a considerable rate and CCa at a lower, non-significant rate.

Mean and Phenotypic Variance

Population mean and phenotypic variance in the last generation of selection (parents) and in the next generation

Table 1. Total number of sires, average number of dams per sire and average number of offspring per dam, in male (M) and female (F) analyses of Experiment 1

	Total no. of sires		No. of dams/sire		No. of offspring/dam	
Line	M	F	M	F	M	F
Ua	105	103	2.4	2.2	4.2	4.4
Ub	81	81	3.0	3.0	6.8	6.2
CRa	106	100	3.1	2.9	7.0	5.5
CRb	83	83	2.9	2.7	3.8	3.4
CCa	101	99	2.8	2.6	4.0	4.0
CCb	75	75	2.7	2.8	3.8	3.7

Table 2. Regression of cumulated standardised selection response on cumulated standardised selection differential during the last period of selection (averaged over the sexes)

Line	Generations included	Regression coeff. ± S.E.
Ua	76-86	−0.018 ± 0.013
Ub	77-87	0.004 ± 0.008
CRa	75-87	0.003 ± 0.005
CRb	77-89	0.033[a] ± 0.006
CCa	78-86	0.019 ± 0.011
CCb	78-89	0.050[a] ± 0.008

[a] Significantly different from zero at $P < 0.01$

(progeny) are given in Table 3. The parents represent the offspring of the last selected individuals, while the progeny were obtained in effect after one generation of relaxed selection. Except for Ua, the means of progeny were on average about two bristles below those of parents. This is well anticipated as the regression of population mean towards the base was very rapid during the first few generations of relaxed selection (Yoo 1980a). But phenotypic variance did not change in a consistent way, although there was a slight increase on average. Experiments 2 and 3 were started when decline in population mean had almost ceased after a long period of relaxed selection. Table 4 summarises means and phenotypic variances in Experiment 3. The proportion of total response lost during the period was large and very variable, from 7% in Ua to 50% in CRb. The decrease in phenotypic variance was more drastic, apart from the relatively small change in Ua, and closely associated with that in population mean.

Table 3. Mean and phenotypic variance (σ_p^2) of the parents used in Experiment 1 and of their progeny (average of the fourth and the fifth sternite)

		Parents		Progeny	
Line	Sex	Mean	σ_p^2	Mean	σ_p^2
Ua	♂	22.5	6.5	22.4	5.4
	♀	34.3	7.6	33.9	8.0
Ub	♂	26.8	11.7	24.8	11.8
	♀	35.5	24.9	32.7	28.2
CRa	♂	28.2	19.3	26.0	17.9
	♀	34.3	28.8	31.9	25.9
CRb	♂	33.9	20.2	30.7	26.1
	♀	42.6	46.7	39.2	48.7
CCa	♂	31.4	18.0	30.2	18.3
	♀	42.2	28.5	40.2	27.0
CCb	♂	30.6	10.9	29.5	13.3
	♀	41.0	20.5	39.9	23.6
Base[a]	♂	7.3	2.2		
	♀	10.1	3.0		

[a] From Hammond (1973)

Table 4. Mean and phenotypic variance (σ_p^2) of the fourth abdominal bristle number in males and of the fifth in females in Experiment 3

	4th in males		5th in females	
Line	Mean	σ_p^2	Mean	σ_p^2
Ua	21.3	4.4	33.0	7.1
Ub	19.6	3.6	24.2	5.2
CRa	20.9	6.3	25.1	8.2
CRb	20.6	4.2	26.1	5.0
CCa	26.4	6.5	36.3	10.8
CCb	21.5	4.1	30.1	6.2

Heritability Estimates in Experiment 1

The half-sib estimates of heritability (Table 5) are all significantly positive and in general quite large. Apart from the extremely large estimates of CRb and the rather small ones of CRa, they are comparable, within the limit of standard errors, to the base estimates (Hammond 1973). In CCb, the considerably larger half-sister than the half-brother estimate suggests the importance of sex-linkage, which however was not supported by the offspring-parent regression estimates. The full-sib estimates also are given in Table 5. The difference between full-sib and half-sib estimates (FS-HS) was large and positive in CRa. The large, negative difference in CRb was rather unexpected. Table 6 summarises heritability estimates from regression of offspring on one parent. The estimates in CRb have been corrected for the unexpected correlation between sire and dam (0.11-0.17) as suggested by Lush (1948). Within any one line, the estimates from different relatives were reasonably consistent except for a few odd values. The average of the four different estimates was much higher in all but one (Ua) selection line than in the base population. In Ub and CRa, the dam-daughter estimates were significantly larger than the sire-son estimates. A significant difference was found also in Ua, but the difference was in the opposite direction.

The comparison of half-sib estimate (averaged over the sexes) with regression estimate (averaged over the relatives) shows an interesting contrast: half-sib estimates were significantly larger than regression estimates in Ua and CRb, while the reverse was true in Ub, CRa and CCa; CCb showed little difference between them.

Table 5. Heritability estimates and their standard errors for the number of bristles on one abdominal sternite from sib analysis (Experiment 1)

Line	Sex	Half-sib estimate	Full-sib estimate	Difference (FS – HS)
Ua	♂	0.26 ± 0.08	0.15 ± 0.10	–0.11
	♀	0.18 ± 0.08	0.24 ± 0.11	0.06
Ub	♂	0.30 ± 0.07	0.39 ± 0.07	0.09
	♀	0.28 ± 0.07	0.48 ± 0.08	0.20
CRa	♂	0.12 ± 0.04	0.35 ± 0.06	0.23
	♀	0.13 ± 0.06	0.48 ± 0.09	0.35
CRb	♂	0.60 ± 0.11	0.14 ± 0.09	–0.46
	♀	0.61 ± 0.12	0.23 ± 0.12	–0.38
CCa	♂	0.22 ± 0.08	0.41 ± 0.10	0.19
	♀	0.25 ± 0.08	0.38 ± 0.10	0.13
CCb	♂	0.28 ± 0.10	0.43 ± 0.13	0.15
	♀	0.47 ± 0.11	0.28 ± 0.11	–0.19
Base[a]	♂	0.20 ± 0.02	0.35 ± 0.03	0.15
	♀	0.34 ± 0.03	0.35 ± 0.03	0.01

[a] Adapted from Hammond (1973)

Table 6. Heritability estimates and their standard errors from offspring-parent regression for the number of bristles on one abdominal sternite (Experiment 1)

Line	Relatives				Average
	Sire-son	Dam-son	Sire-daughter	Dam-daughter	
Ua	0.17 ± 0.04	0.03 ± 0.06	0.16 ± 0.04	−0.06 ± 0.07	0.08
Ub	0.41 ± 0.04	0.58 ± 0.04	0.39 ± 0.04	0.55 ± 0.05	0.48
CRa	0.25 ± 0.03	0.39 ± 0.03	0.33 ± 0.04	0.45 ± 0.04	0.35
CRb[a]	0.48 ± 0.04	0.19 ± 0.06	0.54 ± 0.05	0.52 ± 0.07	0.43
CCa	0.33 ± 0.04	0.40 ± 0.05	0.42 ± 0.04	0.39 ± 0.05	0.39
CCb	0.38 ± 0.06	0.40 ± 0.06	0.47 ± 0.06	0.27 ± 0.06	0.38
Base[b]	0.17 ± 0.02	0.25 ± 0.02	0.19 ± 0.01	0.27 ± 0.02	0.22

[a] Corrected for phenotypic correlation between mates
[b] From Hammond (1973)

The Influence of High-frequency Lethals in Experiment 1

Lethals affecting a quantitative character may cause inconsistencies in heritability estimates by disrupting the normal Mendelian segregation ratios. However, it would be possible to separate that part of the genetic variability contributed by the lethals, if we knew their frequencies, heterozygous effects on the quantitative character and on reproductive fitness, and linkage relations between them. The contribution of lethals to the statistics commonly used in estimating heritability has been derived for independently segregating lethals and a completely balanced lethal system (Appendix). Four lines (Ub, CRa, CCa and CCb) carried one or more high-frequency lethals segregating more or less independently (Yoo 1980b). Heritabilities were recalculated in these lines after expected contributions of the lethals had been subtracted on the basis of lethal frequencies at G 79 and their effects on abdominal bristle number estimated directly (Yoo 1980b) or inferred from their frequencies (Hollingdale 1971). Fertility and viability were assumed to be the same for lethal carriers and non-carriers. The new estimates (Table 7) indicate some reductions in half-sib and offspring on parent regression estimates (more in the latter), and increases in full-sib estimates (except in CCb). This clearly shows that the nature of residual genetic variability may not be correctly inferred from the original heritabilities and that only a part of the residual genetic variability in these lines can be explained in terms of segregation of high-frequency lethals.

CRb was segregating for two closely linked lethals on the third chromosome which formed an incomplete balanced lethal system before G 79 (Yoo 1980b). The expected contributions of these lethals were calculated over the likely range of map distance between them ($2t$) in two different ways: (1) using the formulae given in the Appendix, assuming that the balanced lethal system had been brought to completeness by G 89, and (2) by a numerical method, regarding the frequency at G 79 of the chromosome free of either lethal as an equilibrium frequency under the incomplete balanced lethal system. Table 8 summarises the heritabilities recalculated after deducting these contributions. This attempt to remedy the anomalous estimates of heritability was apparently unsuccessful, leading to the suggestion that the two lethals might not have been responsible for the anomalies.

Table 7. Heritability estimates in Experiment 1 recalculated after deducting contributions of the high-frequency lethals. Original estimates are given in parentheses

Line	Half-sib estimate[a]	Full-sib estimate[a]	O-P regression estimate[b]
Ub	0.25 (0.29)	0.58 (0.44)	0.26 (0.48)
CRa	−0.08 (0.12)	0.52 (0.42)	0.16 (0.35)
CCa	0.21 (0.24)	0.42 (0.39)	0.27 (0.39)
CCb	0.37 (0.37)	0.20 (0.35)	0.10 (0.38)

[a] Averaged over the sexes
[b] Average of 4 different estimates

Natural Selection Among Parents in Experiment 1

The females that died during the egg laying period, 9-29 out of about 400 in each line, were not significantly different in bristle number from the rest. Sterility was quite high (5-27% in males and 15-40% in females) and significantly ($P < 0.05$) associated with high bristle number in CRa males and females, and CRb females, and with low bristle number in CCb females. The difference in bristle number between the sterile and the fertile groups was equivalent to a selection differential resulting from culling by truncation of 2, 8, 6 (of right tail) and 4% (of left tail),

Table 8. Heritability estimates for CRb in Experiment 1, recalculated after deducting the contributions of the balanced lethal system. Original estimates are the average over the sexes

Assumptions for deduction	Half-sib	Full-sib	Sire-offspring	Dam-offspring
Original estimates	0.61	0.19	0.51	0.35
Complete bal. leth. syst.				
$t^a = 0.01$	0.53	0.14	0.50	0.34
0.05	0.59	0.08	0.46	0.29
0.10	0.75	0.17	0.45	0.29
Incomplete bal. leth. syst.[b]				
$t^a = 0.01$	0.53	−0.34	0.31	0.02
0.05	0.41	−0.44	0.33	0.07
0.16	0.90	−0.03	0.37	0.22

[a] The probability of crossing-over between the two loci forming the balanced lethal system is $2t$ in females and zero in males

[b] See text for details

respectively. Hence, the selection superficially appeared to be mild, and its effect on heritability estimates was unlikely to be large, although without knowing the genetic causes underlying the association, the bias in heritability cannot be properly assessed. There was also significant ($P < 0.05$) negative regression of the number of offspring scored on dam bristle number in CRb which might have influenced the full-sib estimates of heritability.

Experiment 2

Table 9 gives the summary of heritability estimates. Compared to those in Experiment 1, the low half-sib estimate in Ub indicates that additive genetic variance had been proportionately more reduced than other components during relaxed selection, while the reverse might have happened in CRa. For non-additive genetic components, the small difference between half-sib and regression estimates of Ub, together with the large full-sib estimate, suggests presence of dominance, sex-linkage and/or common environmental effects, but little additive × additive epistasis. In CRa, however, additive × additive epistasis seems to have been important also.

Table 9. Heritability estimates for the fourth abdominal bristle number in males (Experiment 2)

Estimates	Ub	CRa
Sib analysis		
Half-sib estimate	0.07 ± 0.10	0.29 ± 0.11
Full-sib estimate	0.88 ± 0.16	0.67 ± 0.13
Difference (FS − HS)	0.81	0.38
Sire-son regression	0.07 ± 0.07	0.37 ± 0.06

Experiment 3

The single-generation realised heritabilities were firstly subjected to an analysis of variance with three main factors (sex, line and generation) and with all the two- and three-factor interactions in the model. Selection line was the only significant source of variation. Individual lines were then separately analysed using generation, sex and replicate as main factors. In CRa, generation and replicate were the two main factors of significance, while two-factor interactions were significant only when sex was involved. Replicate was the only significant source of variation in Ua, the realised heritability being significantly positive in one replicate and significantly negative in another. In the rest of the lines, none of the sources of variation was significant.

For each line, realised heritabilities were averaged over replicates, generations and sexes, and the standard error of the average was calculated from the observed variance (Table 10). These standard errors were reasonably close to those expected from the theory (Hill 1972). In Ub and CRa, the realised heritability was in fair agreement with the half-sib and sire-son regression estimates in Experiment 2. Thus, it might be reasonable to assume for all lines that the realised heritabilities are estimates of largely the additive genetic component.

Although the significant replicate variation in Ua suggests the presence of genetic variability, little seems to be utilisable in selection. The heritability has been considerably reduced in Ub during relaxed selection, but it was still significantly positive, indicating a moderate amount of residual genetic variability. In the other selection lines, realised heritabilities were somewhat smaller than the regression estimates of heritability under selection (Table 6), but they were nevertheless as large as in the base population.

Table 10. Single generation realised heritability (h_r^2) for the number of bristles on one abdominal sternite, averaged over the replicates, generations and sexes (Experiment 3). Expected standard errors from Hill's (1972) theory, E(S.E.), are also given for comparison

Line	h_r^2 ± S.E.	E(S.E.)	Comment
Ua	−0.05 ± 0.04	0.03	Heterogeneous[a]
Ub	0.13 ± 0.06	0.04	
CRa	0.24 ± 0.05	0.05	Heterogeneous[a]
CRb	0.20 ± 0.05	0.04	
CCa	0.21 ± 0.05	0.04	
CCb	0.25 ± 0.04	0.05	
Base[b]	0.20 ± 0.01		

[a] Heterogeneous among the replicates
[b] From Hammond (1973), realised heritability over 11 generations in treatment 50-50

Discussion

The High Level of Residual Genetic Variability

The half-sib estimates of heritability in Experiment 1 indicate that in all lines except perhaps in CRa, the residual additive genetic component, apart from that due to major lethals, was probably as large as in the base population and much larger than would be indicated by the rates of genetic gain in the immediately preceding generations (Table 2). In other words, there is no evidence to suggest lack of sufficient additive genetic variance as a cause of selection plateaux or sluggish responses in those lines. It has already been argued that the attenuation of selection intensity due to selection for lethals appeared to be one of the major causes (Yoo 1980b).

It is rather surprising that the realised heritability (Experiment 3), after most of the grossly detrimental genes had been eliminated, was at least in four lines as high as in the base population, because a large part of total selection response must have been made through fixation of favourable genes (Yoo 1974). Then, what would be the source of additional genetic variability compensating for the loss incurred during selection? There seem to be two main avenues by which the additional genetic variability might have originated, viz. selection for genes initially at low frequency and enhancement of gene effects during selection (Reeve and Robertson 1953). Jones et al. (1968) also suggested the presence of rare genes with large effects for a different reason. In both cases, the genes involved may not have been able to reach fixation because of either their own deleterious effects on reproductive fitness or the attenuation of selection intensity mentioned above. Further, a large proportion of the genetic variability due to such genes appeared to remain in the relaxed lines, perhaps implying that some of them had not been strongly selected against under culture conditions of low competation. It is noteworthy that the large population size used in the selection experiment might have been important in retaining rare genes and appropriate modifiers required for the above models.

Spontaneous mutation has been suggested as a likely source of high-frequency lethals (Yoo 1980b). Similarly, mutations in the broad sense might have contributed to the residual genetic variability, although the experiments to evaluate induced mutations have produced conflicting results (Hollingdale and Barker 1971; references therein).

The Diversity of Replicate Selection Lines

The nature of residual genetic variability inferred in each line from different heritability estimates was quite different among the six replicate lines not only in the additive genetic component and contribution of lethals, but in other causal components, as summarised in the following.

Ua: This line carried no major lethals and showed little sign of accelerated response. The large sib estimates of heritability (Table 5) and the significant replicate variation in single-generation heritability indicated some additive genetic variance remaining in this line, but other evidence showed that this apparent variance could not be utilised by mass selection. To interpret the conflicting results a few simple genetic models have been considered, and found to be unsatisfactory. For want of a simple explanation, a special type of genotype-environment interaction is suggested which makes superior genotypes more susceptible to unfavourable environments. This model is similar to that postulated in Abplanalp's (1962) feed shock experiment to break selection limits in poultry.

Ub: Dominance, presumably due to favourable but non-fixable recessives at high frequency, seems to be an important non-additive genetic component.

CRa: The deduction of lethal contributions probably was not adequate for the incomplete lethal interacting with genetic background (Yoo 1980b). Experiments 2 and 3 suggest additive × additive epistasis and sex-linkage to be important. Regression of offspring on parent was significantly non-linear in Experiment 2.

CRb: The anomalous estimates in Experiment 1 cannot be explained, but three sources of bias need to be mentioned, viz. positive assortative mating, directional selection of dams through fertility and negative regression of the number of offspring on dam's bristle number.

CCa: The heritability estimates in Experiment 1, after adjustments were made for the lethals, indicate that the additive × additive epistatic component might have been important, as often suggested for long-term selection lines (Lush 1948; Lerner 1958).

CCb: This line probably carried mostly additive genetic and little non-additive variance. If we take only the last 6 generations of selection (instead of 12 as in Table 2), during which there was an indication of accelerated response, and exclude the part of phenotypic variance caused by the lethals, the realised heritability becomes 0.26, much closer to the heritability estimates in Experiment 1.

A number of assumptions were made in the above to get an insight into the genetic properties of the lines while still under selection pressure. For instance, the lines were assumed to be in gene frequency, and gametic phase equilibrium, although this must not have been the case. Also, in some cases, transmitted maternal and common environmental effects were assumed to be absent, which was probably true in the base population (Hammond 1973). It seems more serious that natural selection violating the basic assumptions of the analysis could not be dealt with properly. In spite of these inherent problems, the general picture was reasonably clear: additive genetic variability apparently was hardly diminished in most of the lines, although the rates of genetic gain at the final stage of selection were very low or almost zero, and the nature of residual genetic variability was quite different among the replicate lines.

These results confirm that genetic variability is not necessarily exhausted in a selection line at or near the plateau. Similar conclusions were drawn in many experiments with *Drosophila* (Reeve and Robertson 1953; Robertson 1955, long thorax lines; Clayton and Robertson 1957), mice (Roberts 1966, small line; Wilson et al. 1971; Eisen 1972) and poultry (Lerner and Dempster 1951; Dickerson 1955), while long-term selection did deplete the additive genetic variance in some cases (Robertson 1955, short thorax lines; Yamada et al. 1958; Brown and Bell 1961; Roberts 1966, large line).

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Appendix

The Contribution of Lethal Genes to Variance Components in Sib Analysis and to Covariance Between Parent and Offspring

The expected contribution of lethal genes to various statistics commonly used in estimating heritability has been derived by constructing mating matrices for a hierarchically structured population, i.e. a large number of sires are each mated to several dams, and an equal number of offspring from each dam is scored. The fertility and viability of lethal heterozygotes are assumed to be the same as those of lethal-free individuals.

Independently segregating lethals: Let the frequency of a recessive lethal in parental generation be q, and the heterozygous effect on the selected character a. Then this gene would contribute to various statistics as follows:

(1) Variance of parents	$2a^2q(1-2q)$
(2) Variance of offspring	$2a^2q(3-2q)(3-6q+4q^2)/9$
(3) Between-sire component of variance	$a^2q(1-2q)(3-4q)^2/18$
(4) Between-dam, within sires component	$a^2q(1-2q)(9-16q)/18$
(5) Offspring-sire covariance	$a^2q(1-2q)(1-4q/3)$
(6) Intra-sire offspring-dam covariance	$a^2q(1-2q)(1-4q/3)$

Two closely-linked lethals forming a balanced lethal system: For simplicity, the balanced lethal system is assumed to be complete, i.e. selected individuals are all repulsion heterozygotes. From the progeny of the selected individuals, a random sample is taken to be used as parents in the statistical analysis. Let us assume the probability of crossing-over between the two loci to be $2t$ in females and zero in males, and heterozygous effect on the selected character of the two lethals a and b respectively. When approximation (approx.) is made in the following formulae, t^3 or higher order terms are deleted. The contributions of the balanced lethal system to the statistics (as above) are then:

(1)	$(a^2+b^2)t-(a+b)^2t^2$
(2)	$7(a^2+b^2)t/3-82a^2+53ab+82b^2)t^2/9$ (approx.)
(3)	$2(a+b)^2t/9-14(a+b)^2t^2/9$ (approx.)
(4)	$2(a+b)^2t/9-(31a^2+78ab+31b^2)t^2/18$ (approx.)
(5)	$(a+b)^2t/3-(5a^2+26ab+5b^2)t^2/6$ (approx.)
(6)	$(a+b)^2t/3-(9a^2+26ab+9b^2)t^2/6$ (approx.)

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