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The effects of population size and selection intensity in selection for a quantitative character in *Drosophila*

III. Analyses of the lines

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1. INTRODUCTION

Jones, Frankham & Barker (1968) described the results of long-term response to selection for abdominal bristle number. Although some lines were still showing appreciable responses after 50 generations of selection, progress had slowed down in most lines. In general, response increased as both population size and selection intensity increased, but several lines gave irregular responses.

Analyses have been carried out on these lines in an attempt to explain peculiarities in their behaviour, to determine the nature of the genetic variation responsible for selection response, and to detect the forces limiting response to selection.

Jones *et al.* (1968) suggested that genes (or gene combinations) with large effects may have caused the irregular response patterns. Lethal analyses were done on each line to assess the importance of one class of genes of large effect, viz. recessive lethals with a pleiotropic effect on bristle number. Genes with fairly large effects on the selected trait and at intermediate frequencies in the base population should be fixed in lines in which a large number of individuals were scored. Differences between such lines would be due to genes either with small effects or at low initial frequencies. The response to selection in lines formed as crosses between these lines would indicate if there were appreciable genetic differences between them. Crosses between pairs of the three highest lines were selected to detect such differences and to see if the response of these lines was near the maximum possible for the character in this population.

Decline in additive genetic variation is the simplest reason for reduced selection response. Thus, the heritability of the selected trait was estimated in each line between the tenth and twentieth generation of selection, and at generation 40, reverse selection lines were taken from the lines to determine whether any genetic variation remained. Further, natural selection opposing artificial selection is likely to be an important factor limiting response to selection (James, 1962), and its importance can be assessed by relaxing selection periodically. However, Griffing

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(1960) showed that selection response due to epistatic variance is also lost on relaxation. Relaxed lines were taken off regularly from each selection line to detect if these factors were important. Culture conditions, selection régimes and the codes used to designate each line were described by Frankham, Jones & Barker (1968).

2. METHODS AND RESULTS

(i) *Heritabilities*

For each line, heritabilities were estimated from an analysis of variance of full and half-sib families using an hierarchal design of 33 sires, each with three dams, and five pairs of offspring per dam. In 10(10%)c and 20(10%)b only 29 and 32 sires respectively were used, while 40(10%) was analysed on a slightly larger scale (59 sires and 167 dams), with each sire being mated to two or three dams. Bristle numbers of fourth and fifth abdominal segments of males, and fifth and sixth of females were scored.

Treatments were not analysed contemporaneously, the smaller population sizes being done first. Treatments 10(10%), 10(20%), 10(40%) and 10(C) were analysed at generation (G) 10, G.11, G.12, and G.14 respectively, the 20 pair lines at G.15 (20(10%) and 20(20%)) and G.16 (20(40%) and 20(C)), and all 40 pair lines at G.20.

Sire and dam variance component heritability estimates were obtained for each segment in both males and females. Standard errors of these estimates were approximately 0·20. Consequently, there was large variation between estimates for individual segments within lines. Treatment averages for sire and dam component estimates averaged over sexes and segments are shown in Table 1.

Table 1. *Treatment means of sire* (h_S^2) *and dam* (h_D^2) *component estimates of heritability for one abdominal segment*

		Selection intensity									
		10%		20%		40%		Control		Mean	
		h_S^2	h_D^2	h_S^2	h_D^2	h_S^2	h_D^2	h_S^2	h_D^2	h_S^2	h_D^2
Population size	10	0·25	0·19	0·10	0·27	0·22	0·18	0·12	0·30	0·17	0·24
(pairs of parents)	20	0·10	0·28	0·10	0·28	0·24	0·23	0·27	0·38	0·18	0·29
	40	0·17	0·36	0·16	0·27	0·15	0·26	0·23	0·32	0·18	0·30
	Mean	0·17	0·28	0·12	0·28	0·20	0·22	0·21	0·33	0·18	0·28
Base population		0·16	0·37	—	—	—	—	—	—	—	—

Dam component estimates were generally higher than sire component estimates (except for treatments 10(10%), 10(40%), and 20(40%)). Selection treatments averaged 0·17 for the sire component estimate and 0·26 for the dam component estimate, while the corresponding averages for the controls were 0·21 and 0·33. Dam component estimates contain slightly more sex-linkage than sire-component estimates and are biased by sire × dam interaction and common environmental

effects. In the base population, the dam component estimate was higher than the sire component estimate due to both sex-linkage and epistasis (Sheridan *et al.* 1968). From the data of Sheridan *et al.* (1968), single segment heritabilities comparable to these here were estimated, but were not presented. These estimates were 0·34 and 0·55 in Expt 1, and 0·16 and 0·37 in Expt 2, for the average sire and the average dam heritability estimates respectively. The Expt 2 estimates were more precise so they are used for comparisons in this paper.

Table 2. *Mean of sire and dam component estimates of heritability* (h^2), *phenotypic correlation* (r_P) *between bristle numbers of the two segments, realized heritability* (*over the 10 generations subsequent to the heritability estimations*), *and mean female bristle numbers* ($\bar{x}$) *at the generation of estimation for each line.*

Line	h^2	r_p	Realized h^2	$\bar{x}$	Line	h^2	r_p	Realized h^2	$\bar{x}$
10(10%)a	0·19	0·36	0·04	30·20	20(10%)a	0·12	0·18	0·06	31·82
b	0·32	0·51	0·07	28·18	b	0·25	0·25	0·15	28·09
c	0·23	0·23	0·04	27·63	20(20%)a	0·24	0·50	0·07	32·18
d	0·15	0·24	0·04	27·57	b	0·17	0·21	0·13	29·11
10(20%)a	0·16	0·30	0·11	25·76	c	0·17	0·28	0·04	29·82
b	0·20	0·19	0·08	26·82	20(40%)a	0·37	0·45	0·18	27·80
c	0·16	0·23	0·05	26·00	b	0·13	0·14	0·04	27.20
d	0·16	0·15	0·10	27·08	c	0·21	0·29	0·09	28·68
e	0·27	0·27	0·09	28·74	20(C) a	0·27	0·21	—	21·80
10(40%)a	0·34	0·29	0·14	25·04	b	0·27	0·29	—	24·45
b	0·18	0·31	0·10	25·04	c	0·44	0·37	—	22·00
c	0·22	0·24	0·16	26·60	40(10%)	0·26	0·74	0·11	37·82
d	0·10	0·12	0·04	23·52	40(20%)a	0·27	0·33	0·13	31·29
e	0·14	0·20	0·04	27·24	b	0·16	0·24	0·12	32·76
10(C) a	0·20	0·33	—	23·30	40(40%)a	0·15	0·20	0·16	29·11
b	0·27	0·33	—	23·90	b	0·26	0·31	0·13	28·80
c	0·28	0·28	—	21·70	40(C) a	0·27	0·31	—	23·30
d	0·20	0·17	—	22·50	b	0·27	0·32	—	23·15
e	0·10	0·23	—	22·60					

The average sire component estimate of heritability of the selected lines (0·17) was similar to that of the controls (0·21) and of the base population (0·16), but the dam component estimate (0·26) was less than that of the controls (0·33) and the base population (0·37). The over-all effect of selection on heritability has been rather small, but this conclusion must be taken cautiously due to the large differences between replicate lines and the large standard errors. Little consistent effect of selection intensity and population size on heritability was evident.

The average of sire and dam component estimates for each line is shown in Table 2. In 10(10%)b, 10(40%)a, 20(40%)a and 20(C)c the heritability was somewhat higher than the base population average (0·27), while in 10(10%)d, 10(20%)a, 10(20%)c, 10(20%)d, 10(40%)b, 10(40%)d, 10(40%)e, 10(C)e, 20(10%)a, 20(20%)b, 20(20%)c, 20(40%)b, 40(20%)b and 40(40%)a it was appreciably lower. As there were large differences between sire and dam estimates

within some lines, these averages may not be very reliable. However, the phenotypic correlation between bristle numbers of the two segments provides a more accurate measure of genetic variation. The phenotypic (r_P), total hereditary (r_H) and environmental (r_E) correlations are related as follows

$$r_P = h_x h_y r_H + \sqrt{(1-h_x^2)}\sqrt{(1-h_y^2)} r_E \text{ (modified from Falconer, 1960),}$$

where h_x^2 and h_y^2 are the broad sense heritabilities of the two traits. As the environmental correlation was effectively zero and the total hereditary correlation effectively unity in the base population, the phenotypic correlation provides an estimate of one segment heritability. This estimate contains all genetic variance (additive, non-additive and sex-linked) and is related to the variance of the difference between segments as used by Clayton & Robertson (1957). The genetic correlation between the segments in all lines at the time of heritability estimation remained not significantly different from unity, but we have no evidence whether the environmental correlation has changed from the base population value of zero. Provided it has not changed appreciably, there should be little bias in the phenotypic correlation estimate of heritability. Standard errors of the phenotypic correlations were 0·01 to 0·02. The average of the female and male phenotypic correlation estimates for each line is shown in Table 2. In general, the correlation was similar in both sexes, the averages over all lines being 0·30 in females and 0·28 in males. The averages of the selected lines (0·29) and the controls (0·29) were the same, but were lower than that in the base population (0·36). There were large increases in the phenotypic correlation in 10(10%)b, 20(20%)a, 20(40%)a and 40(10%), while in 10(20%)b, 10(20%)d, 10(40%)d, 10(C)d, 20(10%)a and 20(40%)b the phenotypic correlation had fallen appreciably ($< 0{\cdot}20$).

It is important to know whether heritability estimates in selection lines will allow prediction of their subsequent response to selection. Realized heritabilities were estimated for each line by the regression of abdominal bristle number on cumulative selection differential over the 10 generations subsequent to heritability estimation (Table 2). The average of these realized heritabilities (0·085) was much less than the average heritability estimate from the sire or dam components, or from the phenotypic correlation. There was little relationship between estimated and realized heritabilities in individual lines.

(ii) *Relaxed lines*

Every five generations, relaxed lines were taken from each line. These were maintained in crowded cultures with approximately 30 pairs of parents transferred each generation. At the first, second and fifth generations, 25 pairs were scored, taken from two cultures set up the previous generation with five pairs of parents each.

The declines in the average of male and female bristle number after five generations of relaxation, of lines split from the selection lines at generations 5, 10, . . . , 45 are shown in Fig. 1. As there was little change in bristle number in the first two generations, these results are not included. The effect of relaxation has been plotted

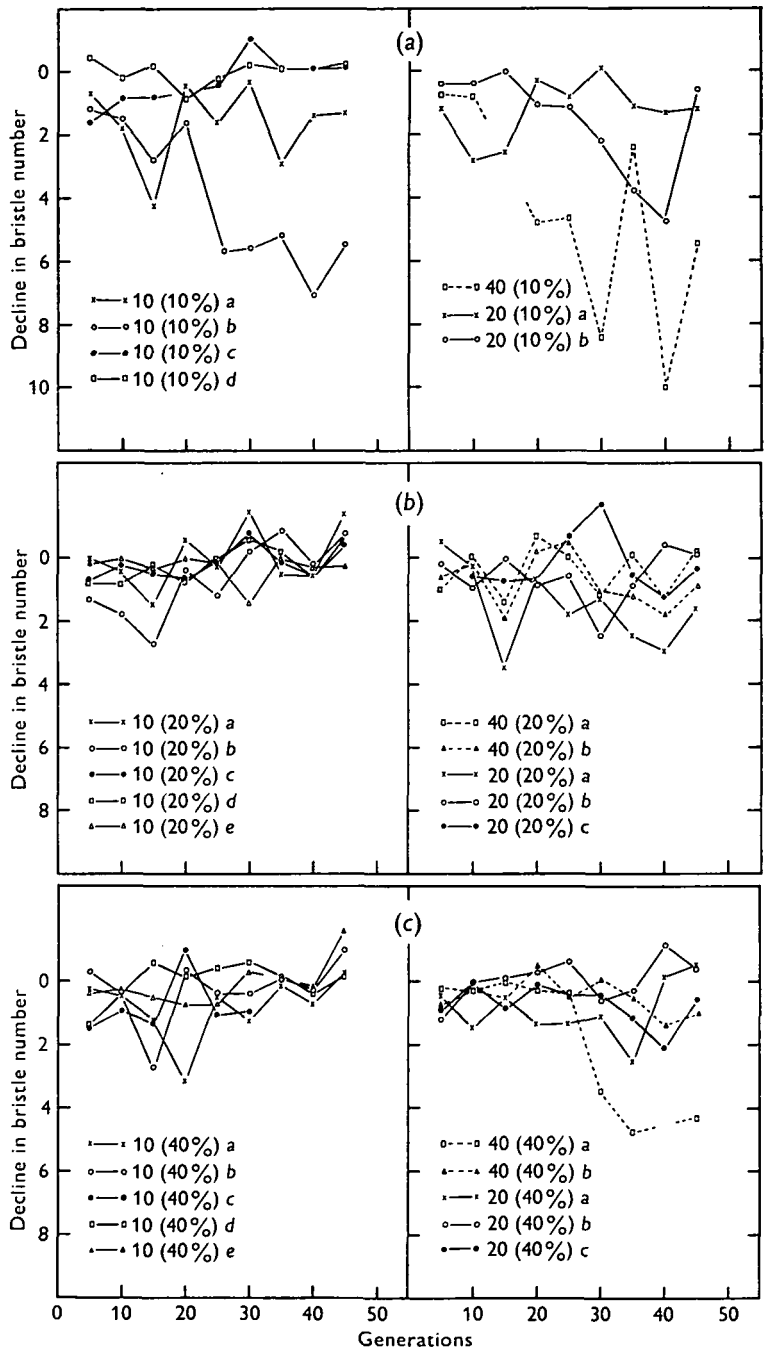

Fig. 1. The decline in bristle number of the individual lines after 5 generations of relaxation from generations 5, 10, . . . 45. (*a*) 10 % lines, (*b*) 20 % lines, (*c*) 40 % lines.

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as the decline in bristle number rather than the change in absolute value, to allow ready comparison between lines.

The mean of the line taken from 10(10%)b at generation 5 fell 1·1 bristles after five generations of relaxation. At later stages, 10(10%)b declined much further. From generation 25 onwards, it fell at least 5 bristles. Other lines which declined considerably on relaxation were 40(10%), 10(10%)a (until it was lost at generation 37 and reconstituted from its relaxed line), 20(10%)b (until generation 40), 20(20%)a, 40(20%)b and 40(40%)a. For 40(10%), 40(40%)a, and to a lesser extent 20(20%)a and 20(10%)b, this decline increased in later generations. Most of the lines fell only slightly on relaxation and this decline became less in later generations. This was true for 10(10%)c, 10(10%)d, the 20% lines (except 20(20%)a, 40(20%)b) and the 40% lines (except 40(40%)a). 20(10%)a showed a small and lessening regression on relaxation until G.30 and an increased regression thereafter. This increased regression occurred after a period of rapid response to selection in this line (Jones *et al.* 1968). 20(40%)a declined by one to two bristles until G.35, after which it did not regress. Its fitness decreased at about G.40, so that subsequent selection was generally less intense than planned.

(iii) *Lethal test*

Tests for the presence of second and third chromosome recessive lethals were carried out in all selection lines and the base population between G.21 and G.32 using a modification of the technique of Brown & Bell (1961). The first and fourth chromosomes of their tester stock were replaced by wild-type chromosomes from the Canberra strain. The stock was thus:

$$+ ; In-SMI, al^2\ Cy\ sp^2/dp\ b\ Pm\ ds^{33k}; \quad Ubx^{130}\ e^s/CSb; +$$

The *Cy* and *Ubx* chromosomes contain multiple inversions as crossover suppressors, but as they are not completely effective (MacIntyre & Wright, 1966) the frequency of lethals could be slightly underestimated. The frequencies of individual lethal genes were determined by allelism testing.

For each line approximately 60 matings (300 for base population) were set up in the first cross. The number of successful tests and the frequency of lethal chromo somes for each line are given in Table 3. Highest frequency was in 10(10%)b in which 91·9% of the second chromosomes were lethal. 10(10%)a, 20(10%)b, 20(20%)a, 20(40%)a, and 40(10%) also had fairly high lethal frequencies. 10(10%)c, 10(20%)a, 10(20%)d, 10(20%)e, 10(40%)b, 20(10%)a, 20(20%)b, 20(40%)b, 20(40%)c, and 40(20%)a all had lethal frequencies less than the base population.

Of the 13 lines with individual lethals at frequencies of over 10% (Table 4), nine contained chromosome II lethals and seven chromosome III lethals. 10(10%)a and 10(10%)b both had two chromosome II lethals while 20(10%)b, 20(40%)a and 40(10%) had one on each chromosome. 40(20%)b had four chromosome II lethals at less than 10% frequency (9·5, 7·1, 7·1 and 4·8% frequencies). Most lines had lethals present at low frequencies.

The maximum frequency of a lethal gene is expected to be 33·3% where, because of higher bristle number, only lethal heterozygotes are selected as parents. The two chromosome II lethals in 10(10%)b, the chromosome II lethals in

Table 3. *The percentage of lethal chromosomes in each line and number of individuals tested (n)*

Line	Chromosome II	Chromosome III	*n*	Line	Chromosome II	Chromosome III	*n*
10(10%)a	31·0	10·3	29	20(10%)a	1·8	0·0	54
b	91·9	0·0	37	b	22·2	22·2	36
c	5·4	0·0	37	20(20%)a	5·3	52·6	38
d	0·0	21·4	28	b	0·0	6·8	44
10(20%)a	2·2	0·0	45	c	10·9	4·3	46
b	2·0	28·0	50	20(40%)a	15·2	23·9	46
c	16·7	14·6	48	b	0·0	4·3	46
d	4·0	6·0	50	c	3·1	0·0	32
e	0·0	4·3	23	40(10%)	22·7	31·8	22
10(40%)a	7·1	7·1	28	40(20%)a	2·0	5·9	51
b	0·0	5·9	51	b	28·6	4·8	42
c	14·7	0·0	34	40(40%)a	22·2	2·2	45
d	16·0	6·0	50	b	13·7	11·8	51
e	14·3	5·7	35	Base population	9·5	14·5	221

Table 4. *The frequencies (%) of particular lethals (with frequencies greater than 10%) in the lines*

Line	Chromosome II	Chromosome III	Line	Chromosome II	Chromosome III
10(10%)a	13·8 10·3	—	20(10%)b	22·2	13·9
b	37·8 56·8	—	20(20%)a	—	36·8
d	—	17·9	c	10·9	—
10(20%)b	—	20·0	20(40%)a	13·0	10·9
c	—	14·6	40(10%)	22·7	31·8
10(40%)c	14·7	—	40(40%)a	15·6	—
d	16·0	—			

20(10%)b and 40(10%) and the chromosome III lethals in 10(20%)b, 20(20%)a and 40(10%) were at or approaching this frequency. All other lethals were half this frequency or less. Chromosome II of 10(10%)b had two lethals, one at a frequency of 56·8%, the other at 37·8%. 89·2% of the second chromosomes in this line carried one lethal, and only 2·7% carried both lethals. Thus a balanced lethal system apparently had developed in this line.

Allelism tests were carried out between lethals (which were represented at least twice) in different lines, and with two exceptions they were all non-allelic. The chromosome II lethals at frequencies of 22·7% in 40(10%) and 15·6% in 40(40%)a

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were allelic, and the chromosome III lethal at a frequency of 17·9% in 10(10%)d was allelic with one at a frequency of 8·3% in 20(10%)b.

A progeny test was carried out in 40(10%) to measure the effect of its chromosome II lethal on abdominal bristle number. Flies were scored for bristle number and test-crossed to flies heterozygous for this lethal, and for Curly. Individuals heterozygous for the lethal are expected to give a 2:1 ratio of Curly to non-Curly flies, and wild-type homozygotes a 1:1 ratio. The average difference between lethal heterozygotes and wild-type homozygotes was 4·9 bristles in females (14 and 11 individuals in the two classes), and 4·6 bristles in males (13 and 20 in the two classes). Thus this lethal had a large effect on bristle number (greater than two standard deviations).

(iv) *Reverse selection*

Sublines, with 10 pairs of parents and 40% selection intensity, were taken from all lines at G.40 (G.42 for 40(40%)b) and selected for decreased abdominal bristle number for eight generations. In Table 5 the response to selection (average of males and females) of the forward and reverse selection lines between G.40 and G.48 are shown as a deviation from the G.40 level. The regressions of mean bristle number on generations were estimated for both males and females, but are noted only where the differences between the G.40 and G.48 means do not give a clear picture of the changes in bristle number.

Table 5. *Response to selection from G.40 to G.48 of the forward and reverse selection lines, and mean female bristle number* ($\bar{x}$) *at G.40*

	Response to selection				Response to selection		
Line	Reverse	Forward	$\bar{x}$	Line	Reverse	Forward	$\bar{x}$
10(10%)a	− 3·17	1·37	36·51	20(10%)a	−10·29	1·47	41·26
b	−14·52	0·40	48·03	b	− 5·17	1·23	38·91
c	0·64	0·72	32·10	20(20%)a	− 5·04	2·10	36·24
d	− 1·50	0·14	32·61	b	− 1·40	2·20	33·95
10(20%)a	− 1·42	1·69	33·64	c	− 2·08	2·04	33·03
b	− 0·91	1·45	31·78	20(40%)a	− 1·08	0·45	36·48
c	− 0·08	0·74	29·74	b	0·16	1·48	28·38
d	− 0·75	1·51	32·06	c	− 2·39	1·15	32·84
e	− 1·64	0·74	30·50	40(10%)	−14·87	2·06	50·96
10(40%)a	− 0·08	0·62	28·08	40(20%)a	− 3·10	1·56	38·27
b	− 1·98	0·04	29·44	b	− 1·38	1·88	38·43
d	− 0·88	0·04	25·64	40(40%)a	− 5·99	1·90	36·76
e	lost	0·44	30·40	b	− 4·38	1·20	35·12

10(10%)b, 20(10%)a, and 40(10%) showed very large responses to reverse selection, while 10(10%)a, 20(10%)b, 20(20%)a, 40(20%)a, 40(40%)a and 40(40%)b showed lesser, but still large, responses. 10(10%)b, 10(10%)d, 10(40%)b and 10(40%)d showed significant response only in the reverse direction, i.e. they appear to have plateaued to forward selection while still retaining genetic variation. All other lines except 10(10%)c, 10(20%)c, 10(40%)a and 20(40%)b showed

small but significant reverse responses. In both 10(10%)c and 20(40%)b the regression coefficients were significant for forward selection (both 0·11 for the average of male and female regression coefficients) but non-significant for reverse selection (0·00 for 10(10%)c and 0·02 for 20(40%)b). In 10(20%)c the two sexes behaved differently. Females did not change significantly in either direction (0·04 for forward and −0·09 for reverse selection lines), while males gave significant forward

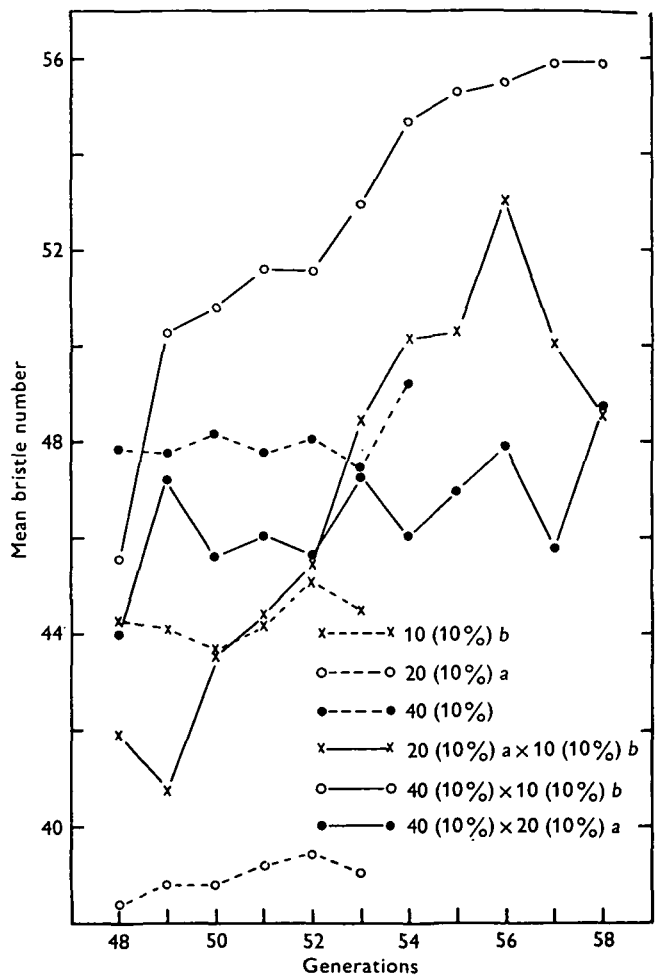

Fig. 2. Response to selection of 10(10%)b, 20(10%)a, and 40(10%), and of crosses between them.

response (0·10) and similar but non-significant reverse response (−0·08). Regression coefficients for 10(40%)a were non-significant in both directions (0·03 for forward and −0·03 for reverse selection lines). Thus, two of the lines (10(10%)c, 20(40%)b) responded only to forward selection, four (10(10%)b, 10(10%)d, 10(40%)b, 10(40%)d) only to reverse selection, one (10(20%)c) only in males, one (10(40%)a) in neither direction, and the remainder in both directions.

(v) *Selection on crosses between lines*

At G.47, the three highest lines (40(10%), 10(10%)b, 20(10%)a) were crossed to produce the three possible two-way crosses. For each pair of lines, reciprocal crosses were made using 10 pairs of parents for each cross. The highest ten out of fifty flies of each sex were selected from each reciprocal. The twenty pairs thus selected were mass-mated at random with five pairs of parents per culture. The lines were selected at an intensity of 20% until G.58. Twenty pairs of parents were used until G.50, after which only ten pairs were used. The three parent lines were selected until G.53 (G.54 for 40(10%)) with the same régime as in previous generations, i.e. a selection intensity of 10% and population sizes of 10, 20 and 40 pairs of parents for 10(10%)b, 20(10%)a and 40(10%) respectively.

The mean bristle numbers (averaged over sexes) of the parent lines and crosses are shown in Fig. 2. The means of the F_1 crosses were not significantly different from the mid-parent means. The parent lines at this stage were only responding slowly to selection.

40(10%) × 10(10%)b gave rapid response to selection and from G.49 was well above both parent lines. It continued to respond rapidly until G.54 when its rate of progress declined. 20(10%)a × 10(10%)b also responded rapidly and after G.52 was well above either parent. At G.56 its fitness was quite low and virtually no selection was made over the last two generations, so that the mean dropped rapidly. The response of 40(10%) × 20(10%)a was much less and it barely reached the level of 40(10%).

Thus, different genes had been selected in 10(10%)b than in either 40(10%) or 20(10%)a. Crossing of 10(10%)b with either of the other two lines gave further response to selection. Conversely, 20(10%)a apparently contains little genetic variation not present in 40(10%). Selection on the cross has merely restored the mean to that of 40(10%).

3. DISCUSSION

Jones *et al.* (1968) found that several lines were still responding to selection after fifty generations, but that the response in a few lines had slowed down after about 10 generations. The sire and dam component estimates of heritability indicated that little, if any, over-all decline in genetic variation had occurred after ten to twenty generations of selection. Dempster, Lerner & Lowry (1952) and Dickerson (1955) found no decline in heritability for egg production in poultry after a similar number of generations of selection, while Tantawy & Reeve (1956) and Tantawy (1956, 1957, 1959) showed that heritability for body size in *Drosophila* did not decline nearly as rapidly as expected under either random inbreeding or inbreeding with selection. Sheldon (1963) found that additive genetic variation decreased and epistatic variation increased, so that there was little change in total genetic variance after a number of generations of selection in his lines. Here, neither the mean sire nor the mean dam component estimate was much less in the selected lines than in unselected controls or base population so that no consistent change in additive

or non-additive genetic variance was indicated. The large differences among replicates in response to selection and heritability estimates indicated that the lines were genetically different and so suggestions of overall trends were of limited value.

Heritability estimates for individual lines from the sire and dam components of variance had considerably larger sampling errors than the phenotypic correlation between bristle numbers of the two segments (provided r_G and r_E did not change), so the latter is used when discussing individual lines. The phenotypic correlation had declined considerably in 10(20%)b, 10(20%)d, 10(40%)d, 20(10%)a and 20(40%)b at the time of the heritability estimations. The slowing down of progress in these lines could have been due to a decline in genetic variation. Realized heritabilities for these lines during the 10 generations subsequent to their heritability estimations ranged from 0·04 for 10(40%)d and 20(40%)b, to 0·10 for 10(20%)d. Between G.30 and G.40, 20(10%)a responded rapidly to selection. 10(20%)d and 10(40%)d gave renewed response to selection after G.30 following temporary cessation of progress (Jones *et al.* 1968). 10(10%)c, 10(10%)d, 10(20%)c and 10(40%)e showed decreased rates of progress and had lower phenotypic correlations than the unselected controls and the base population.

Realized heritabilities showed little relation to and were less (except 40(40%)a) than variance component and phenotypic correlation heritability estimates. Although standard errors were large, and the differences within lines probably not significant, the over-all trend is clear. Mean estimates were 0·21 for average sire and dam component heritability, 0·29 for phenotypic correlation, and 0·09 for realized heritability. On average then, heritability estimates after some generations of selection would here overestimate future rates of response.

Phenotypic correlations were considerably higher in 10(10%)b, 20(20%)a, 20(40%)a and 40(10%) than in the base population. The last gave most response of all the lines and the others gave more response than their replicate lines. Lethals were present at appreciable frequencies in these four lines. Much of the response in 40(10%) was probably due to the chromosome II and III lethals present as it showed a bimodal distribution, high variance, large regression on relaxation, and a large response to reverse selection. A lethal with an appreciable effect on bristle number will bias the heritability as James (1966) showed that natural selection lowers the correlation between relatives and provides a similar expectation in the analysis of variance to epistasis. However, an appreciable proportion of the response of 40(10%) was caused by non-lethal genes as crossing to 20(10%)a (which carried no lethals) and selecting indicated that both lines had changed at the same loci, but with additional loci (probably the lethal loci) involved in 40(10%).

Of the lines with individual lethals at frequencies greater than 10%, 10(10%)b, 20(10%)b, 40(10%) and 40(40%)a declined appreciably on relaxation; 10(10%)a, 10(40%)c, 20(20%)a and 20(40%)a declined to a lesser extent; and 10(10%)d, 10(20%)c, 10(40%)d and 20(20%)c showed virtually no regression. 10(20%)b showed appreciable decline to G.15, and thereafter virtually no regression. The lethals may have been selected because of heterozygote superiority for bristle

number or fitness, or because of linkage to genes affecting bristle number. The lack of regression on relaxation in 10(10%)d, 10(20%)b, 10(20%)c, 10(40%)d and 20(20%)c indicates that their lethals had little effect on bristle number, as did their small responses to reverse selection. They may have been concentrated through linkage to bristle genes and could well have been lost in later generations. The large declines on relaxation and reverse selection in 10(10%)b and 40(10%) leave little doubt that the lethals in these lines had large effects on bristle number. Assuming that all the increase in phenotypic variance during selection or decline in bristle number on relaxation was due to the lethal(s) at high frequency in any line, the maximum effect of the lethal may be estimated. Such estimates indicate effects of individual lethals of up to five standard deviations (10 bristles).

In most lines without lethals at high frequency, the regression on relaxation became less in later generations. Either natural selection or the decay of epistatic combinations will cause regression on relaxation which lessens as the genes become fixed. A number of these lines (10(20%)e, 10(40%)b, 20(10%)a, 20(40%)c, 40(20%)a) showed greater response to reverse than forward selection. A gene of large effect at a high frequency will cause such response (Latter, 1965). Much of the response in 20(10%)a between G. 30 and G. 40 may have been due to the increase in frequency of one or two genes of large effect. If at high frequencies but not fixed, they would give appreciable response to reverse selection. Two lines (10(10%)c, 20(40%)b) responded to forward selection but not to reverse selection. A similar phenomenon was found in one line by Thoday & Boam (1961). 10(10%)c did not respond to selection between G. 30 and G. 40 but gave renewed response after G. 40. This may have been due to genes at low frequency with small individual effects on bristle number but appreciable effects when combined. Thoday & Boam (1961) found that certain genes had to be utilized in a particular order under selection because of gene interactions. Linkage of a few genes in repulsion would also explain this phenomenon (Latter, 1966). If recombination occurred a few generations before the reverse selection line was split off, renewed response would be obtained (but only noticeable after a few generations) as the + + gamete increased in frequency, but the − − gamete would be eliminated. However, to obtain response to reverse selection, a new recombinant would be needed after selection was reversed.

10(40%)a was the only line in which genetic variation was apparently exhausted as it failed to respond to forward or reverse selection after G. 40. However, Frankham (1967) showed that unexpressed genetic variation was present in this line. Genetic variation was therefore present in all selection lines after 40 generations of selection.

Fraser & Hansche (1965) suggested that irregular patterns of selection response could be caused by relational balance between linked polygenes (only likely in small populations), by changes in the background genotype causing genes with initially small effects to become major genes, or by recessive genes of large effect at low initial frequencies. Latter (1966) showed that linkage between two genes of large but similar effect would cause periods of rapid response following temporary cessation of progress. Irregularities in the response patterns could, of course, be

caused by the occurrence of new mutations with large effects on the character. However, spontaneous mutations are unlikely to be very important as B. J. Hollingdale (personal communication) obtained no response to selection for abdominal bristle number in lines commenced from an inbred line of Oregon-R-C. Epistasis can also produce irregular selection responses, e.g. two genes each with small effects but a large effect when combined. In short, any event with a low probability of occurrence at any particular time, but a high probability over a number of generations, and a large effect on the character, will cause irregular responses to selection.

It is difficult to separate these possibilities without measuring the effects of particular genes and chromosomes and the interactions between them. In a few lines, particular lethal genes with large effects on bristle number were important. In general, different lines had different lethals and there were no lethals in the base population at a frequency of greater than 2%. Such genes could cause large differences between lines, because of initial sampling. The gene *scabrous*, which has a large effect on bristle number, was found in 10(40%)c and in other selection lines from the Canberra base population. Other genes of large effect may be important but we have not attempted to demonstrate their presence.

Detailed analyses of the genetic changes in selected lines are needed to determine the phenomena responsible for their behaviour. The most successful analysis with *Drosophila* has been that of Thoday & Boam's (1961) lines by Spickett & Thoday (1966). In that case, most of the response was due to three genes in one line and five in another, and important interactions were present between some of the genes. Their results and those of Robertson (1966) with *Drosophila*, and Wehrhahn & Allard (1965) and Law (1966, 1967) with wheat indicate that relatively few loci may determine much of the selection response in any particular line or population. Analyses at the chromosome level by Mather & Harrison (1949), Robertson & Reeve (1953), Robertson (1954), Breese & Mather (1957), and Scowcroft (1966) indicated that gene interactions were important.

All our data point to the genetic dissimilarity of our lines. They gave different selection responses and response patterns, contained different lethals, regressed different amounts on relaxation, showed different responses to reverse selection, gave different heritability estimates, had different variances and showed different correlated responses to selection and different sex-dimorphism ratios (Frankham, 1967).

Similarly, King & Somme (1958) showed that the response to selection in King's (1955) lines had utilized different genetic variation, while Scowcroft (1966) showed that the selection lines of Fraser *et al.* (1965) were all genetically different, even though many of them were at similar levels of response. This genetic dissimilarity of selection lines suggests that many loci are potentially capable of influencing a quantitative character, but that only a few genes are responsible for response in any particular line.

If different genes were fixed in different lines, crosses between them should give further response to selection. Genes in either parent line will be present at reason-

able frequencies in the cross. In the crosses between the three highest lines (40(10%), 10(10%)b, 20(10%)a), renewed response resulted when 10(10%)b was crossed to either of the other lines; 10(10%)b × 40(10%) exceeding the highest parent after only one generation of selection, 10(10%)b × 20(10%)a after three and both responding very rapidly. But 40(10%) × 20(10%)a had only just reached the level of 40(10%) after 10 generations of selection. This indicated that 10(10%)b was quite dissimilar to the other two lines, and that 20(10%)a contained little or no variation not present in 40(10%). If there is any evidence of genetic differences between selection lines, crosses between them may be particularly advantageous. 40(10%) and 10(10%)b contained different lethals with apparently large effects on bristle number. 10(10%)b also had a much higher scutellar bristle number than 40(10%) (Frankham, 1967). It was therefore expected that 10(10%)b contained variation not present in 40(10%), which had a higher mean bristle number. 20(10%)a (the lowest of the three) had no lethals at high frequency and had a similar scutellar bristle number to 40(10%). It was therefore not clear before selection whether it contained variation not present in either 40(10%) or 10(10%)b.

Robertson (1960) showed that if two plateaued lines, each of which had been selected with an effective population size of N_e and selection differential of $\bar{\imath}$, were crossed and selection continued from the cross population with twice the value of $N_e\bar{\imath}$, the expected limit would be the same as that of a line which had been selected from the original population with the larger value of $N_e\bar{\imath}$. Dempster (1963) suggested that this conclusion could be used to determine when $N_e\bar{\imath}$ was sufficiently large to fix most of the favourable genes. The extra gains obtained by crossing 40(10%) and 10(10%)b and reselecting showed that even with the largest population used, the total response was well below the maximum possible from the Canberra base population.

Falconer & King (1953) and Roberts (1967) obtained renewed response to selection for increased body weight in crosses between plateaued lines of mice. However, Roberts (1967) obtained little response in crosses of low lines. Roberts also found that the response of the cross of the high lines was delayed for a few generations. He suggested that much of the response of all the lines was due to the same genes, and that differences were due to linkage of genes affecting the character. Hill & Robertson (1966) showed that linkage of two loci would decrease the chance of fixation of the favoured genes at both loci. The cross could contain the favoured genes at both loci at a reasonable frequency, but response would not occur until recombination allowed breakdown of the repulsion gametes. In the crosses here there was no delay in response. Differences therefore were not due to fixation of different genes at closely linked loci in the different lines. The rapid rate of progress in the crosses involving 10(10%)b indicated that differences between this line and the others were due to only a few genes with a large effect on bristle number. Genes of large effect and at intermediate frequency in the base population would be fixed in the larger populations. It is therefore likely that the genes concerned were at low frequencies in the base population or their expression had been modified by selection. Robertson (1966) suggested that rare genes of large effect were fairly un-

important in his population as restricting the initial sample from twenty-five pairs to one pair or to three consecutive generations of single-pair mating reduced total response by only 30 and 50% respectively. However, the selection régime used (10/25 in each sex) is rather inefficient at selecting genes at low initial frequency and the responses of the lines from the large sample were only about half that possible in his population. Rare genes of large effect may be more important than he suggests.

Many of the phenomena discussed in this paper may have been due to large gene effects, linkage, gene interaction effects or a combination of these, but it was not possible to distinguish among them. However, it seems likely that all have operated to some extent.

4. SUMMARY

1. In order to determine the nature of the genetic variation causing the response to selection in our lines (Jones *et al.* 1968), various analyses were performed.

2. There was no consistent change in heritability, estimated from half-sib correlation or from the phenotypic correlation between the bristle numbers of two abdominal segments, after 10 to 20 generations of selection.

3. Realized heritabilities over the 10 generations subsequent to the heritability estimations were less than in the early generations but bore little relationship to the estimated values.

4. Six lines contained recessive lethals with appreciable effects on bristle number as indicated by high variances, large regression on relaxation and large response to reverse selection.

5. Reverse selection lines taken from the main lines at generation 40 indicated that genetic variation was still present in almost all of the lines. Only one line failed to respond to further forward or to reverse selection.

6. The three highest lines were crossed in pairs and reselected. Two of the three possible crosses gave further response, exceeding the higher parent after one and three generations, but the other cross failed to pass the highest parent line.

7. A combination of large gene effects, linkage, and gene interaction effects have been suggested as the cause of irregularities in the response of the lines. It has not been possible to determine the relative importance of these effects.

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