THE EFFECTS OF X-RAY IRRADIATION ON SELECTION RESPONSE IN *DROSOPHILA MELANOGASTER*¹⁾

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One of the most important problems in population genetics concerns how much genetic variation can be induced in the polygenic systems of various organisms by exposure to radiation, and the extent to which this variation affects the process of organic evolution. However, works dealing with spontaneous or induced mutations in polygenic systems in animals as well as in plants are rather few. Buzzati-Traverso (1953) reported in *Drosophila* that new variation induced by X-rays in polygenic systems can be utilized for natural selection under normal laboratory conditions. He has also shown that a rapid increase in fitness as measured by its main components, such as the number of eggs laid and the numbers of adult offspring, accompanies this increased mutation rate. Scossiroli (1953) reported a high efficacy of artificial selection for number of sternopleural bristles after irradiation in a strain that had previously reached a plateau under selection without irradiation. More recent works by several investigators on artificial selection for the number of bristles in *Drosophila* have shown more effective response under irradiation than under natural conditions (Clayton and Robertson, 1955, 1964; Scossiroli and Scossiroli, 1959; Tobari and Nei, 1965).

The purpose of the present experiment is to clarify the mechanism by which new genetic variability available for artificial selection is induced by X-rays, and to estimate the amount of increase of polygenic variability in abdominal bristle numbers. The main result of this work has already published in Yamada and Kitagawa (1961). The details of the selection experiments after irradiation is presented in this paper.

MATERIALS AND EXPERIMENTAL METHODS

Selection was conducted for the total number of bristles on the fourth and fifth abdominal plates of *D. melanogaster*. Two strains were used as the base populations. The P strain was the isogenic Oregon-R strain. The C strain consisted of F₂ flies from a cross between two isogenic strains, Oregon-R and Samarkand, each having been maintained by full-sib pair mating for several hundred generations.

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The high, low and non-directional selection lines in each strain were classified into five lots according to the type of selection and X-ray treatment: Lot 1 — non-directional randomly selection lines without any irradiation (P-1, P-2, C-1, and C-2), Lot 2 — neither males nor females X-rayed (P-3, P-4, C-3, C-4 high, and P-5, P-6, C-5, C-6 low selection lines), Lot 3 — only males X-rayed (P-7, P-8, C-7, C-8 high, and P-9, P-10, C-9, C-10 low selection lines), Lot 4 — only females X-rayed (P-11, P-12, C-11, C-12 high, and P-13, P-14, C-13, C-14 low selection lines), Lot 5 — both male and female flies X-rayed (P-15, P-16, C-15, C-16 high, and P-17, P-18, C-17, C-18 low selection lines). In each lot two replicated lines were set up; *e. g.*, in Lot 2, P-3 and P-4 were the high-selection replicates. Selection in each line was conducted in the following manner: — Thirty pairs of flies were scored for bristle number, and the six extreme flies from each sex were chosen as parents of the next generation, the selection intensity thus being 20 percent. In some strains of later generations, however, selection could not be performed because of low fertility due to irradiation. In such a case, the strains were maintained by random mating. Except for the untreated Lots 1 and 2, selected parents in each generation were treated with X-rays of 1,500 R intensity just before mating, under the conditions of 180KVP, 25ma. and 1mm Aluminum filtration. A description of the selection lines is given in Table 1.

The parental flies were transferred into fresh vials three times at two-day intervals. Several yeast suspension drops were added to the culture medium when the first instar

Table 1. Description of Selection Lines

The P strain			The C strain		
Symbol	Direction	Radiation treatment	Symbol	Direction	Radiation treatment
P- 1	None	None	C- 1	None	None
P- 2	"	"	C- 2	"	"
P- 3	High	"	C- 3	High	"
P- 4	"	"	C- 4	"	"
P- 5	Low	"	C- 5	Low	"
P- 6	"	"	C- 6	"	"
P- 7	High	Males	C- 7	High	Males
P- 8	"	"	C- 8	"	"
P- 9	Low	"	C- 9	Low	"
P-10	"	"	C-10	"	"
P-11	High	Females	C-11	High	Females
P-12	"	"	C-12	"	"
P-13	Low	"	C-13	Low	"
P-14	"	"	C-14	"	"
P-15	High	Both sexes	C-15	High	Both sexes
P-16	"	"	C-16	"	"
P-17	Low	"	C-17	Low	"
P-18	"	"	C-18	"	"

larvae appeared; subsequently heavy yeast solution was added several times to maintain a sufficient nutritional condition and to minimize larval competition. Discarding the first culture, male and virgin female flies to be scored were collected from the second and third cultures, and if necessary from the fourth. Usual corn-meal, molasses, agar food was used for culture medium. Flies were allowed to develop at 25°C. Abdominal bristle number of flies was counted by one person (the author) throughout this experiment.

RESULTS

Selection was carried out for twenty generations in all lots of both strains. The response to selection of the different selection lines is shown in Figures 1-5 (for the P strain), and 6-10 (for the C strain). In these figures, solid and broken lines are used to portray the bristle numbers for the generations in which selection was practiced, while dotted lines refer to the generations during which selection was suspended. Each value represents the mean number of bristles of both sexes.

The P strain

Since the base populations of this strain, which had been originated from isogenic Oregon-R, showed little genetic variation in bristle number, little response to selection in all selection lines had been expected in the early generations.

It was expected that no selection response would be observed in Lot 1 since this lot was not subjected to any directional selection. The mean number of bristles in lines 1 and 2 remained unchanged throughout the experiment.

The lines belonging to Lot 2, which received no irradiation but were selected for high and low bristle number, also showed no significant change in mean value during the course of the experiment. From this it may be concluded that selection response attributable to new variations caused by spontaneous mutation did not occur during twenty generations.

Lot 3, which involved male treated lines, showed rather striking effects of X-rays on selection response in both high and low directions. Strong responses were observed especially in P-7 and P-10 after the first four generations. In P-8 and P-9 the mean number of bristles was not affected by selection until about the 14th generation; thereafter both lines showed response.

A comparison of the results obtained in Lot 3 with those in Lot 2 suggests that the response to selection in Lot 3 was due to new variations which originated as induced mutations affecting bristle number; furthermore, some of these mutations became available in just a few generations after the start of the experiment.

In Lot 4, where female parents only had been treated with X-rays, a less-pronounced response to selection occurred. However, in high line P-12 small but continuous progress was observed from the fourth generation to the end of the experiment. In

Figure 1. Mean abdominal bristle numbers of Lot 1 of the P strain.

Figure 2. Mean abdominal bristle numbers of Lot 2 of the P strain.

Figure 3. Mean abdominal bristle numbers of Lot 3 of the P strain.

Figure 4. Mean abdominal bristle numbers of Lot 4 of the P strain.

Figure 5. Mean abdominal bristle numbers of Lot 5 of the P strain.

the low lines of Lot 4 selection response was generally rather small, but the mean number of bristles in P-13 decreased rapidly in the last few generations.

It seems reasonable to expect that response to selection in Lot 5 would exceed all other lots in the P strain, because a double dose of X-rays was used (*i. e.*, both sexes were X-rayed each generation). The results obtained in Lot 5 are, however, similar to Lot 3. This provides further support for the ineffectiveness of X-ray irradiation to females. In high line P-15 selection response was discerned in about the sixth generation. From the sixth to the ninth generation remarkable responses were observed, but during the subsequent generations selection was forced to stop twice because of high sterility, the line being maintained by mass culture. In high line P-16, the size of flies diminished with successive generations, and the mean number of bristles gradually decreased until the last generation in spite of continued selection for large number of bristles. This effect, noted only in P-16, might have been due to some physiological disorder caused by X-irradiation. The change in body size directly affected the number

of abdominal bristles (see Reeve and Robertson, 1954) apparently, no genetical changes occurred in the polygenes controlling bristle number in P-16. This line was therefore excluded from further analysis.

Response to selection in low lines P-17 and P-18 was detected in about the sixth generation. A significant effect of X-rays is again observed from the comparison between these lines and the low lines of Lot 2. In P-17 there was a rather large fluctuation in the middle of the experiment.

From the comparison with Lot 2, the un-irradiated control in the P strains, it may be concluded that the selection responses observed in Lots 3, 4 and 5 were mostly due to new variations which originated from induced mutations.

The C strain

In the C strain, a remarkable response was observed in all lines except Lot 1, showing that high genetic variability had been presented prior to selection in the base population.

Lot 1 included untreated random selection lines which served as controls. The two replicated lines were alike in general aspect. Fluctuations in mean bristle number were apparent, but the regression coefficients of bristle number on generation were close to zero.

Lot 2 serves as a control to assess the effect of irradiation, since it was subjected to directional selection without any irradiation. The effect of selection was clearly observed in both high and low lines. The progress of response slowed down after several generations, but neither line had reached a plateau by the twentieth generation.

In Lot 3 of the C strain, where only male parents were irradiated, the effect of X-ray treatment was clearly observed in high lines C-7 and C-8, and in low line C-10 by comparison with the lines of Lot 2. In C-10 a rapid decrease of mean bristle number was observed in early generations, and the response was the largest of all low selection lines near the end of the experiment.

Lines of Lot 4, which involved only female irradiation, tended to show a similar but smaller response than those of Lot 3. A significant effect of X-ray irradiation is again observed from the comparison between Lot 4 and Lot 2.

As to Lot 5, in which both sexes were irradiated just before mating, C-15 line showed the strongest response during the first seven generations. However, because of low fertility, this line had to be maintained by random mating without any artificial interference for the next two generations. After the fifteenth generation the previous maximum number of abdominal bristles was gradually recovered. In C-16 line an explosive increase took place after the thirteenth generation, following a relatively slow response in the first half of the experiment. This change was apparently caused by a major gene mutation "*scaboras (sca)*" which was fixed after several generations in the C-16 line. It is known that the *sca* causes twinning of bristles, and also eye-surface

Figure 6. Mean abdominal bristle numbers of Lot 1 of the C strain.

Figure 7. Mean abdominal bristle numbers of Lot 2 of the C strain.

Figure 8. Mean abdominal bristle numbers of Lot 3 of the C strain.

Figure 9. Mean abdominal bristle numbers of Lot 4 of the C strain.

Figure 10. Mean abdominal bristle numbers of Lot 5 of the C strain.

abnormality. The mutant flies obtained from C-16 show both characteristics. It is of great interest that such mutant flies appeared in other similar selection experiments for bristle numbers (McBride and Robertson, 1963; Clayton and Robertson, 1964). Our *sca* line in comparison with Clayton and Robertson's line is completely fertile even in homozygous condition, and has been kept as a mutant stock in our laboratory for more than eight years. Therefore, the data of C-16 were discarded in subsequent analyses. A comparison of C-15 and C-16 with the high lines of Lot 2 clearly shows that X-ray treatment is effective in producing new genetic variability which can be utilized for

artificial selection. The low lines C-17 and C-18 also showed a significant effect of irradiation by comparison with Lot 2, but the response to selection gradually diminished in later generations.

VARIABILITY IN THE SELECTION LINES

Variability in different selection lines is shown in Figures 11 and 12 in terms of the coefficient of variation. In Figures 11 and 12, the thin lines of all types show the generation at which selection was suspended. From a comparison of selection responses in Lot 2 it has already been shown that the genetic variation of the base population of the C strain was larger than that of the P strain. It may also be noted in Figures 11-1 and 12-1 that the C strain surpassed the P strain in coefficient of variation at the beginning of the experiment.

In both the P and the C strains gradual increase of coefficient of variation is found in many of the lines belonging to Lots 3, 4 and 5, whereas the lines of Lot 2 show little change with successive generations. It seems reasonable to ascribe this increased variability to the effect of X-irradiation. The changes in coefficient of variation in successive generations closely corresponded to those in the mean values of bristle number one generation later; *i.e.*, the larger the coefficient of variation in number of bristles in a given generation, the more the selection progress in the next generation. This can be seen in the graphs of C-15, C-14, C-10, P-7, P-8 and P-10. Larger coefficients of variation were found for Lots 3 and 5 than for Lot 4 in both strains. This complements the larger selection response in 3 and 5 mentioned earlier. This strongly suggests that the major cause of increased variability can be ascribed to new mutations arising from X-ray irradiation of males.

A sudden increase in coefficient of variation was observed in C-16 in the fifteenth and sixteenth generations. As mentioned previously, it is likely that this was due to the presence of some homozygous *sca* mutant flies which had extremely large numbers of bristles. Thereafter variability in C-16 line returned to the previous level, because of the fixation of the *sca* gene in this line.

ANALYSIS OF DATA AND RESPONSIVENESS TO X-RAY IRRADIATION

If there were little fluctuation from generation to generation, the information from the last generation should be sufficient for the analysis of the responses to the selection experiments. In order to decide how many generations could most effectively be used for analysis of response to X-rays repeatability values were computed for each generation, taking deviations of response from the respective mean values of Lot 1. Repeatability based on components obtained from the variance analysis of the above deviations is written as,

$$\frac{\sigma_L^2}{\sigma_L^2 + \sigma_G^2 + \sigma_{G \times L}^2 + \sigma_E^2}$$

where σ_L^2 , σ_G^2 , σ_E^2 and $\sigma_{G \times L}^2$ stand, respectively, for variance between lots, generations,

Figure 11-1~4. Variabilities in different selection lines, in terms of coefficient of variation, of the P strain.

Figure 12-1~4. Variabilities in different selection lines, in terms of coefficient of variation, of the C strain.

Table 2. Amount of response to selection in the selected lines of the P, C and combined strains. Each value is the mean deviation per generation from Lot 1 in the last five generations

Lot	The P strain	The C strain	Both combined
2	0.1925	4.7125	2.4524
3	3.3600	6.0350	4.6975
4	1.7975	5.5275	3.6625
5	3.1300	6.6300	4.8801

Least significant difference is 0.8605 for each strain.

Least significant difference is 0.6085 for combined strain.

replicated lines, and the first order interaction. Repeatabilities calculated from the data of the last seven generations in both the P and the C strains were in close agreement with each other, and it was decided to take the mean values of the last five generations (where repeatability was the highest, *i.g.*, 57.3 percent) to detect the effectiveness of X-ray treatment. The mean deviation from Lot 1 in the last five generations of each lot is shown in Table 2. From the analysis of variance it was found that the variation between strains and between directions of selection was highly significant. Effects of X-ray treatment were also marked, the mean square being highly significant. Responses in male-treated lots were significantly larger than those in female-treated ones. Differences among irradiated lots as well as between double (both sexes treated) and single (single sex treated) doses were significant at the five percent level. The second order interaction is highly significant. This is partly due to the fact that Lot 3 showed larger response than Lot 5 in the P strain though the difference is not significant. The effectiveness of selection in different treatments of irradiation stands in the the following order:

Both sexes treated = *Male treated* > *Female treated* > *None treated*

From this relationship, it may be concluded that the effect of treatments of males was the main cause of the increased response to selection under irradiation.

ESTIMATION OF RATE OF INCREASE IN VARNIANCE DUE TO IDUCED MUTATION BY X-RAYS

The estimation of mutation rate in polygenic systems is more difficult than in major genes, and information on polygenic mutations is scanty. The mutation rate of such genes may be measured in terms of the average increment of genetic variance due to mutation per generation for spontaneous mutation, or by the variance increment per unit dose of radiation for induced mutation. Experimental results on spontaneous mutability of bristle number in *Drosophila* have been reported by Durrant and Mather (1954), Clayton and Robertson (1955), and Paxman (1957). Information on mutability of polygenes induced by irradiation in *Drosophila* is also rather limited. Clayton and Robertson (1955) obtained ten times the spontaneous mutation frequency by using X-rays

Table 3. Mutation rate in abdominal bristles per unit dose of X-rays, in the term of average increments of variance per generation, estimated from the selection response

Estimated from the response in	The P strain	The C strain	P & C combined	Doubling dose (R)
Lot 3	15.7×10^{-5}	24.9×10^{-5}	20.3×10^{-5}	24
Lot 4	10.1×10^{-5}	11.2×10^{-5}	10.7×10^{-5}	44
Lot 5	28.0×10^{-5}	28.2×10^{-5}	28.1×10^{-5}	17
Average (both sexes treated) = 29.6×10^{-5}				
Doubling dose = 16R				

with 1,800R. They studied the difference in the response to selection between control and irradiated inbred strains. On the other hand, Yamada and Kitagawa (1961) found 6.7×10^{-5} per unit dose for mutability of abdominal bristles in terms of increments of variance. They used the isogenisation method with dominant marked inversions and estimated mutation rate within irradiated and un-irradiated populations.

In the present experiment the average selection response in each generation is related to the increments of variance due to irradiation. Estimates of the amount of additive genetic variance within a generation can be obtained from the selection pressure applied (as reflected by the quantity $\bar{r}$), the genetic gain (ΔG), and the phenotypic standard deviation observed (σ_p). Thus,

$$\sigma_g^2 = \frac{\Delta G \cdot \sigma_p}{\bar{r}}$$

where ΔG is the regression coefficient of the increment of bristle number of generation, $\bar{r} = 1.353$ (as obtained from Fisher and Yates's table (1938) with a selection pressure of 20 percent), and σ_p is an average of the phenotypic standard deviation over all generations of Lots 2-5. From this formula increments of additive genetic variance due to irradiation in the three irradiated lots in each strain were calculated. The results are shown in Table 3. It is interesting to note the similarity between the C and the P strains in mutation rates, in spite of the difference in genetic variability in the base populations.

DISCUSSION

Selection experiments for bristle characters in *Drosophila* have been made by several investigators after the pioneer study by Mather and Harrison (1949). Radiation such as X-rays have been shown to increase polygenic variation that can be utilized for artificial selection. It may be expected that two factors, the induction of mutations and the increase in recombination under irradiation, might be involved in the production of new variability in polygenic characters. Concerning the effectiveness of artificial selection under irradiated conditions, Scossiroli (1953) has shown a very strong response to

selection for sternopleural bristle numbers in irradiated lines which had previously reached a plateau without irradiation. He suggested that the main source of the new variation utilized in further progress was induced mutations in polygenic systems. Scossiroli and Scossiroli (1959) have studied the relative importance of X-ray induced mutations and recombinations in regard to the degree of increase of genetic variability available for artificial selection. They concluded that X-ray-induced increase in recombination rates did not seem to be an important factor in the progress of selection.

However, the early work by Mavor and Svenson (1923, 1924a, b) indicated that irradiation can increase recombination in *Drosophila* when the female flies are irradiated. Muller (1925) reported regional effects of X-rays on recombination; that is, recombinations in the central regions of long autosomes were enhanced by X-rays. Whittinghill (1951) carried out an experiment with a Gamma-ray treatment of 4,000 R given to adult females. He concluded that increase in recombination in the third chromosomes is greatest near the middle in the spindle attachment region, and the effect becomes progressively less toward the terminal parts, and becomes negative near the two ends. From the present experiment it is obvious that no more than a few percent increment of recombination could have occurred near the spindle attachment region in treated females (Lots 4 and 5) in our experiment deducing from the results of Muller (1925) and Whittinghill (1951).

It is well known that crossing over does not take place in the male fly under normal conditions. However, a few percent crossing over in male zygotes has been confirmed, when larvae, pupae, or young adults are irradiated, and the amount of recombination in irradiated male zygotes has been found to be about equal to the increment of recombination value in irradiated female flies (Friesen, 1933; Patterson and Suche, 1934; Moriwaki, 1935, 1936; Whittinghill, 1955). In the present experiment, adult male flies, a few days old, were irradiated and immediately mated. Their offspring were collected from the second and third subculture (the third or sixth day after irradiation), so that the X-ray treatment presumable had little effect on male recombination. X-ray-induced increase in recombination rates in treated males in this experiment would appear practically negligible.

In the P strain of this experiment, the sexual difference in mutability can be obtained from the results of Lot 3 and Lot 4, whereas the role of induced recombinations can be estimated by a comparison between the P and the C strains of Lot 4. In the P strain, Lot 3 progressed more rapidly in response to selection and showed a higher mutation rate than Lot 4. From the difference between Lots 3 and 4 in the C strain, it can be concluded that the role of induced recombination could not be neglected as a source of the radiation-induced variability. However, both the response to selection and mutation rate in Lot 3 of the C strain were larger and higher than those in Lot 4, and the same tendency was observed in the P strain. The difference between progress of selection and mutation rate in irradiated lots of the C and the P strains was very small in the present experiments. In Lots 4 and 5, similar values were found for mutation rates, in

spite of the great difference in genetic variability observed in the base populations.

From the above observations, it appears that increase of genetic variability due to induced mutation was the principal source of materials for artificial selection, and the acceleration of recombination, if any, was only a secondary source. This conclusion agrees with Scossiroli's opinion.

A common basis for comparing induced mutation rates is provided by calculating the doubling dose. Taking the average increment in variance per genome, per generation due to spontaneous mutation as 0.00475, which is an average of the value for abdominal bristles reported by Clayton and Robertson (1955) and Paxman (1957), the doubling dose calculated from the results of the present experiment, when both sexes were irradiated, is 16R (Table 3). Yamada and Kitagawa (1961) estimated a doubling dose of approximately 60R by the isogenisation method. Both these figures fall within the range of the doubling doses estimated for major genes in various organisms (see UNSCEAR Report, 1958, Annex H, Table VIII). But doubling dose of 16R estimated here seems to be smaller (corresponding to a higher induced mutation rate) than those for some major genes. This may be due partly to the irradiation of both sexes in the present experiment. The 24R obtained from the male treated lots and the 44R obtained from the female treated lots are closer to the values for major genes. Another possible cause of the higher mutation rate obtained here compared with that of Yamada and Kitagawa could be that the selection experiments were conducted under conditions of some inbreeding. Recently two papers were published in which these authors estimated the increase in variance per roentgen (Clayton and Robertson, 1964; Tobari and Nei, 1965). Estimates in the former report were much lower than ours, but the latter reported results which were slightly higher than those obtained in this experiment.

Some recent experiments have been carried out to estimate the mutation rate and action of individual genes in polygenic systems controlling viability (Bateman, 1959; Thoday and Boam, 1961; Thoday, Gibson and Spickett, 1964; Mukai, 1964; Mukai, Chigusa and Yoshikawa, 1964). Some of these works, however, include new terminology of the polygene, therefore they are not comparable with the results of experiments concerning the bristle characters.

From Table 3 the mutation rate in males seems to be about twice that in females. For mutation rate in some genes having major effects in *Drosophila* it has been known that the induced mutation rate in mature spermatozoa is higher than that in eggs (see UNSCEAR Report, 1958, Annex H, Table IV). It is of interest that a similar tendency was observed in the present study on polygenes.

SUMMARY

1. The number of abdominal bristles of *D. melanogaster* was selected in both high and low directions. The response of hybrid strains (Oregon-R × Samarkand) was

generally higher than that of pure strains (Oregon-R), presumably because the former had higher genetic variability at the start of the experiment.

2. Genetic variability, probably originating from mutation and recombination in polygenic systems, was induced by the irradiation, and contributed to the effectiveness of artificial selection. From the variance analysis, the grade of response of each lot was ranked as follows: both sexes treated=only males treated>only females treated>both sexes untreated. The possible difference in effectiveness between induced mutation and induced recombination is discussed.

3. The mutation rates induced by X-rays, in terms of increments of variance, have been estimated from the selection responses. They are 28.1×10^{-5} (both sexes treated), 10.7×10^{-5} (only females treated) and 20.3×10^{-5} (only males treated) per unit dose, respectively.

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