29. The Persistence of Some Recessive Lethal Genes in Natural Populations of *Drosophila melanogaster*. III

Difference between Lethal and Semi-Lethal Genes^{*)}

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Introduction. The genetic variation in viability concealed in a natural population of *Drosophila* could be revealed in the distribution of homozygous effects of isolated chromosomes. The figure is usually bimodal as shown by several investigators. The first peak lies at the level of ten per cent less than the mean viability of heterozygotes (index=100) and the second peak lies at the level of complete lethality. The population size of *D. melanogaster*, as well as other species, changes seasonally. The accumulation of lethal genes in breeding season has been observed by Ives¹⁾ (1954), Hiraizumi and Crow²⁾ (1960) in American populations and also by Minamori (unpublished) in Japanese populations. According to Dubinin³⁾ (1946), the reduced population in Russia should be reflected in a decrease of lethal genes. However, Goldschmidt *et al.*⁴⁾ (1955) could not observe any so-called "Dubinin cycle" in an Israeli population by examining six samples collected at various seasons. As a matter of fact, it is almost impossible to estimate the relative frequency of lethal chromosomes in dormant season, and it is assumed that lethal heterozygotes are eliminated fairly severely in that season, but some heterotic ones would take more opportunities of intercrossing with each other especially in the last period of breeding season. In the present study, the complementary effect on viability of trans- or cis-heterozygous flies for two non-allelic lethal genes in the second chromosomes is examined. Such a knowledge is not only important for understanding genic interaction from the biochemical view-point, but also may help us to know how many lethal genes are maintained in natural populations. Furthermore, difference in the complementary effect between lethal and semi-lethal genes could be found.

The distribution of homozygous effects of isolated chromosomes:

About five hundred second chromosomes were isolated from the Suyama-Juriki populations in the breeding season of 1962 and they were individually duplicated by the multiple inversion method. The distribution of viabilities manifested by individual homozygous

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chromosomes was not different from that found in the previous year population, and both data have been put together in the figure.

The distribution figure is similar to those obtained by Dawood⁵⁾ (1961), Greenberg and Crow⁶⁾ (1960) and Goldschmidt *et al.*⁴⁾ (1955) in Egyptian, American and Israeli natural populations respectively, although the population sizes are probably dissimilar. The frequency of lethal chromosomes was usually about three times of that of semi-lethal chromosomes.

Viabilities of lethal and semi-lethal heterozygotes: As reported in my previous paper⁷⁾ (1962), the pre-adult viabilities of heterozygous flies for lethal and normal chromosomes were estimated by the *Cy-Pm* technique devised by Wallace⁸⁾ (1956). These lethal heterozygotes were on the average three per cent less viable than normal heterozygotes. However, the viability of trans-heterozygotes for two non-allelic lethal chromosomes was found to be rather better than that of single lethal heterozygotes. To confirm such a complementary effect on viability, the following experiments were carried out.

Experiment (1). Ten normal and ten lethal chromosomes isolated in 1961 from the Hiroshima and the Suyama-Juriki populations respectively were used. Both populations are about 700 kilometers apart, and assumed to be genetically unrelated. The results are given in Table I.

Experiment (2). Several chromosomes on which two lethal genes located had been isolated from the Hiroshima populations by Dr. Minamori (Hiroshima University) in early summer of 1961. These lethal genes were separated by recombination and found again in the fall lot of the same population. Sixteen normal, six single lethal

Table I. Relative viabilities of normal, single and double lethal trans-heterozygotes between the Hiroshima and the Suyama-Juriki populations, in comparison with those of normal heterozygotes within the populations

Chromosome combination	Pooled basis		Line basis	
	No. of counted flies	Relative viability	No. of lines	Relative viability
$+_h/+_h$	15,858	1.119 ± 0.0186	45	1.139 ± 0.0239
$+_{s-j}/+_{s-j}$	13,950		45	
$+_h/+_{s-j}$	34,713	1.086 ± 0.0166	100	1.105 ± 0.0202
$+_h/l_{s-j}$	70,388	1.083 ± 0.0115	200	1.100 ± 0.0139
$+_{s-j}/l_h$				
l_h/l_{s-j}	37,673	1.117 ± 0.0165	100	1.121 ± 0.0179

The viability of *Cy/Pm* fly=1.0000. The same for the other experiment.
 $+_h$, l_h : normal and lethal chromosomes isolated from the Hiroshima populations respectively. $+_{s-j}$, l_{s-j} : normal and lethal chromosomes isolated from the Suyama and Juriki populations, respectively. * significance at the 5% level.

Table II. Relative viabilities of double lethal cis-heterozygotes in comparison with those of normal and single lethal heterozygotes in the Hiroshima populations

Chromosome combination	Pooled basis		Line basis	
	No. of counted flies	Relative viability	No. of lines	Relative viability
$+ / +$	28,816	1.096 ± 0.0185	60	1.123 ± 0.0284
$+ / l$	25,970	1.072 ± 0.0201		1.093 ± 0.0293
$ll / ++$	23,071	1.148 ± 0.0217		1.171 ± 0.0304

** significance at the 1% level, * significance at the 5% level.

and three double lethal chromosomes were used. The results are tabulated in Table II.

The mean viability of single lethal heterozygotes was less than that of normal heterozygotes in the former experiment whether any coadaptation system existed or not. On the other hand, double lethal heterozygotes without regard to trans- or cis-form were superior in their mean viability to single lethal heterozygotes and even to normal heterozygotes in the latter experiment. Their complementary effects were recognized significantly at the 5% level as compared with single heterozygotes in the former experiment and normal heterozygotes in the latter experiment.

Experiment (3). Sixteen normal and fifteen semi-lethal chromosomes isolated from the Suyama-Juriki populations in 1961 were used in the repeated experiments. These results are given in Table III.

Table III. Relative viabilities of normal, single and double semi-lethal trans-heterozygotes within the Suyama-Juriki populations

Chromosome combination	Pooled basis		Line basis	
	No. of counted flies	Relative viability	No. of lines	Relative viability
+ / +	53,851	1.160±0.0144	120	1.177±0.0184
<i>sl</i> / +	102,336	1.166±0.0105	240	1.186±0.0137
<i>sl</i> / <i>sl</i>	41,069	1.128±0.0160	102	1.147±0.0214
+ / +	55,302	0.999±0.0121	110	1.006±0.0136
<i>sl</i> / +	60,991	0.983±0.0114	121	0.982±0.0134
<i>sl</i> / <i>sl</i>	48,625	0.934±0.0122	106	0.942±0.0124

sl: semi-lethal chromosome. * significance at the 5 % level, ** significance at the 1% level.

The results obtained in the above experiments were pooled together and the mean viability of semi-lethal heterozygotes was standardized by that of normal heterozygotes. The results are shown in Table IV.

Table IV. Relative viability of single semi-lethal heterozygotes

First exp.			Second exp.
No. of semi-lethal chr.		15	11
No. of normal chr.		16	11
Relative viability	+ / +	1.160±0.0144	0.999±0.0121
	<i>sl</i> / +	1.166±0.0105	0.983±0.0114
	+ / +	1±0.0124	1±0.0121
	<i>sl</i> / +	1.005±0.0091	0.984±0.0114
Pooled	+ / +	1±0.0088	
	<i>sl</i> / +	0.996±0.0071	

It could be recognized concerning the difference between lethal and semi-lethal chromosomes that the mean viability of single semi-lethal heterozygotes was not much inferior to that of normal heterozygotes and their detrimental effects were emphasized on the viability of two non-allelic semi-lethal trans-heterozygotes.

Discussion: Although few natural populations of *D. melanogaster* in the dormant season have been analyzed genetically or ecologically, their sizes are assumed to be reduced. Goldschmidt *et al.*⁴⁾ (1955) have found in even such a population in Israel that not only was the variation in viability maintained continuously, but also the relative frequency of lethal chromosomes was rather increased. During the last period of the breeding season, the population size

would be gradually reduced, but the decrease in relative frequency of lethals might not follow it. If so, there may be chances that survived lethal heterozygotes breed together and double lethal trans-heterozygotes are produced. Heterozygous flies for many lethal genes except heterotic ones would be eliminated, but these double lethal trans-heterozygotes of nearly normal viability would survive through the dormant season.

In the early period of the breeding season, double lethal cis-heterozygotes which might have been originated from the double lethal trans-heterozygotes by recombination, were actually found in natural populations in Hiroshima by Minamori and by Karlik and Sperlich⁹⁾ (1962) in a natural population on Lipari Island. Wallace⁸⁾ (1956) estimated the adaptive values of flies heterozygous for two drastic chromosomes extracted from laboratory strains by the *CyL-Pm* technique. He observed that they were less viable than heterozygous flies for two normal chromosomes and also those carrying one normal and one drastic chromosome. He could recognize no complementary effect on viability like that found in my experiment, although this might be owing to his method of calculation including both lethal and semi-lethal chromosomes.

Dorn and Burdick¹⁰⁾ (1962) studied the complementation on wing-length with various genetic combinations of nine mutant genes in the miniature-dusky region and suggested that these genes could be represented as a functional continuum. Glassman¹¹⁾ (1962) extracted enzymes having no activity of xanthine dehydrogenase from *ma-l* and *ry* mutant flies respectively; and he found that the mixture of both extracts produced the enzyme activity by incubation. He interpreted such a complementation between two loci in terms of either a "combining-subunits" or a "catalytic activator" hypothesis. His experiment was performed *in vitro*, but his idea might be applied for the heterozygous condition *in vivo*. The complementary effects on viability of double lethal heterozygotes might be understood as an interaction between two loci carrying lethal genes in the genetic background which has experienced natural selection.

As shown in the distribution curve, the frequency of semi-lethal chromosomes of 20~30 per cent viability was most scarce. Hadorn¹²⁾ (1961) tried to explain this fact by assuming a reaction in the developmental physiology of the mutant genotype fluctuating around a threshold value. Greenberg and Crow⁶⁾ (1960) suggested by the comparison of loads due to mildly detrimental mutants and lethals that (1) mutants with small effects occur with no greater frequency than lethals, or (2) they have more dominance than lethals and hence are eliminated relatively more rapidly as heterozygotes. The second as-

sumption does not seem possible, but the first one seems to be sustained by my experimental results. The semi-lethal chromosomes seem to have accumulated numerous mildly detrimental genes and the enhanced detrimental effects on viability of double trans-heterozygotes of such chromosomes may be due to duplication of some common mild mutant genes.

Summary: The distributions of viabilities manifested by individual homozygous second chromosomes isolated from the Suyama-Juriki populations of *D. melanogaster* was examined. The viability of heterozygous flies for single lethal and double lethal chromosomes was estimated and compared with that of normal heterozygotes. Complementary effect was recognized in viability of double lethal trans- or cis-heterozygotes either with coadapted genetic background or without it. This effect is assumed to be due to interaction between two loci carrying lethal genes. The mean viability of semi-lethal heterozygotes was estimated to be similar to that of the normal heterozygotes. The detrimental effect of two semi-lethal trans-heterozygotes is emphasized. The difference between lethal and semi-lethal genes is discussed.

References

- 1) P. T. Ives: Genetic changes in American populations of *D. melanogaster*, Proc. Nac. Acad. Sci., **40**, 87-92 (1954).
- 2) Y. Hiraizumi and J. F. Crow: Heterozygous effects on viability, fertility, rate of development, and longevity of *Drosophila* chromosomes that are lethal when homozygous, Genetics, **45**, 1071-1083 (1960).
- 3) N. P. Dubinin: On lethal mutations in natural populations, Genetics, **31**, 21-38 (1946).
- 4) E. Goldschmidt, J. Wahrman, A. Ledermann-Klein, and R. Weiss: A two year's survey of population dynamics in *Drosophila melanogaster*, Evolution, **9**, 353-366 (1955).
- 5) M. M. Dawood: The genetic load in the second chromosomes of some populations of *Drosophila melanogaster* in Egypt, Genetics, **46**, 239-246 (1961).
- 6) R. Greenberg and J. F. Crow: A comparison of the effect of lethal and detrimental chromosomes from *Drosophila* populations, Genetics, **45**, 1153-1168 (1960).
- 7) C. Oshima: The persistence of some recessive lethal genes in natural populations of *Drosophila melanogaster*, II, Proc. Jap. Acad., **38**, 278-283 (1962).
- 8) B. Wallace: Studies on irradiated populations of *Drosophila melanogaster*, Jour. of Genet., **54**, 280-293 (1956).
- 9) A. Karlik und D. Sperlich: Frequenz und alleliegrad autosomaler letalfaktoren einer Inselpopulation von *Drosophila melanogaster*, Zeitschrift für Vererbungslehre, **93**, 229-236 (1962).
- 10) G. L. Dorn and A. B. Burdick: On the recombinational structure and complementation relationships in the *m-dy* complex of *Drosophila melanogaster*, Genetics, **47**, 503-518 (1962).
- 11) E. Glassman: *In vitro* complementation between nonallelic *Drosophila* mutants deficient in xanthine dehydrogenase, Genetics, **48**, 1491-1497 (1962).
- 12) E. Hadorn: Developmental Genetics & Lethal Factors, Methuen, London, p. 355 (1961).