Genet. Res., Camb. (1971), **17**, *pp.* 103–111
With 4 text-figures
Printed in Great Britain

Influence of the population genetic background on the persistency of a recessive lethal in *Drosophila melanogaster*

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(*Received* 2 *February* 1970)

SUMMARY

In a population of *Drosophila melanogaster* started from an inbred wild-type strain the recessive second chromosome lethal studied had shown overdominance which after many generations was lost. In the present study the persistence of this lethal was tested in three series each of five populations. The genetic backgrounds of the different series of populations were obtained from (*a*) the inbred strain, (*b*) the above original population after the overdominance had been lost, and (*c*) a population started from the same inbred strain and where another lethal had shown overdominance which subsequently had been lost. The lethal was overdominant in the (*a*) background but detrimental to the heterozygous carriers on the other backgrounds. The detrimental effect of the lethal was stronger in the (*b*) background than in the (*c*) background. The varying behaviour of the lethal is possibly due to different adapted background genotypes and/or different degrees of heterozygosity of the gene pools.

1. INTRODUCTION

From studies on *Drosophila* populations it is known that recessive lethals may be favourable to their heterozygous carriers (e.g. Mukai & Burdick, 1959, 1960; Oshima & Kitagawa, 1961; Salceda, 1967; Ytterborn, 1968*a*; Dyer, 1969). The high fitness of such lethal heterozygotes may persist for many generations. However, the overdominance of the lethal sooner or later seems to be lost and the lethal is eliminated as fast as, or even faster than, is expected for a completely recessive lethal (Ytterborn, 1968*a*).

The present experiments were designed to obtain some information on the causes of the loss of overdominance of a second chromosome lethal. The persistency of the lethal was studied in populations of three genetic backgrounds which had different histories but were originally from an inbred wild-type strain which had contributed the background of the population where the lethal once had shown overdominance.

2. MATERIALS AND METHODS

(i) *The strains used and their relationship*

(1) *In* $(2L+2R)Cy$, $al^2Cylt^3L^4sp^2/In(2LR)Pm$, Pm. Throughout the rest of this paper this strain will be called CyL/Pm.

(2) Strain R, a wild-type strain, which was repeatedly isogenized in the second chromosome by the standard CyL technique (Wallace, 1956). A newly re-isogenized line replaced the old line every fourth to tenth generation. Since few animals are used in the isogenization process the strain was also inbred with regard to the other chromosomes. The line of the R strain to be used in the present experiments had been reproduced for eight generations after the isogenization.

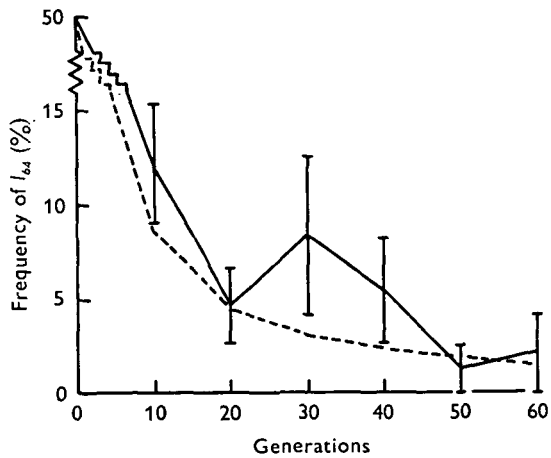

Fig. 1. Observed frequencies with 95 % confidence intervals of l_{64} in the original population 64. Dotted curve: elimination expected for a completely recessive lethal.

The strains below were extracted from the R strain after this strain had been isogenized several times. Therefore, all strains used may be considered to contain the X, III and IV chromosomes from the CyL/Pm strain. The Y and II chromosomes of strain R were originally from the Canton S strain.

(3) *In* $(2L+2R)Cy$, $al^2Cylt^3L^4sp^2/l_{64}$. This strain will be called CyL/l_{64} below. The lethal, l_{64}, was obtained in a test for second chromosome recessive lethals after X-irradiation of spermatogonia in young larvae from strain R (Ytterborn, 1967). In a recombination test l_{64} was localized at about 2-70 on the genetic map. In a salivary gland analysis no aberration was detected in the chromosome containing l_{64} (Ytterborn, 1968*b*). The persistency of the lethal was studied in a population called population 64, which was started with non-CyL flies obtained from the cross CyL/l_{64} ♀ × R ♂. Fig. 1 shows that the lethal was recovered for many generations at higher frequencies than expected for a completely recessive lethal. In later generations the results indicate that the overdominance had been lost and l_{64} was neutral or almost neutral for the heterozygotes (Ytterborn, 1968*a*).

(4) Strain +64 was set up from the animals of the 61st generation of the above

population 64. By this generation the overdominance of l_{64} had already been lost and the frequency of the lethal was low. Thus the strain, which was reproduced on a broad basis, probably still contained l_{64} at a low frequency.

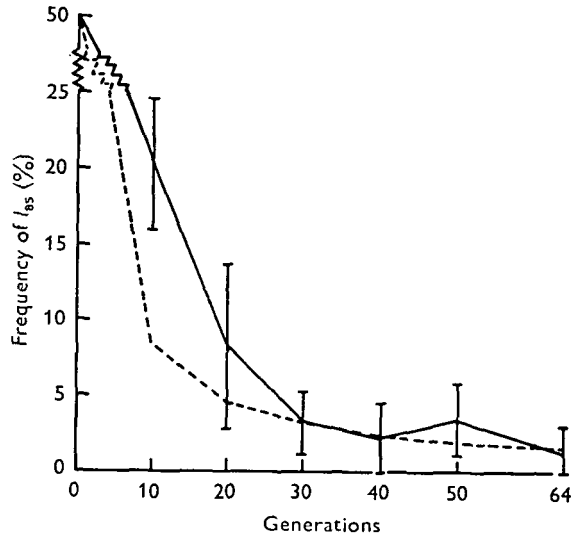

Fig. 2. Observed frequencies with 95 % confidence intervals of l_{85} in population 85. Dotted curve: elimination expected for a completely recessive lethal.

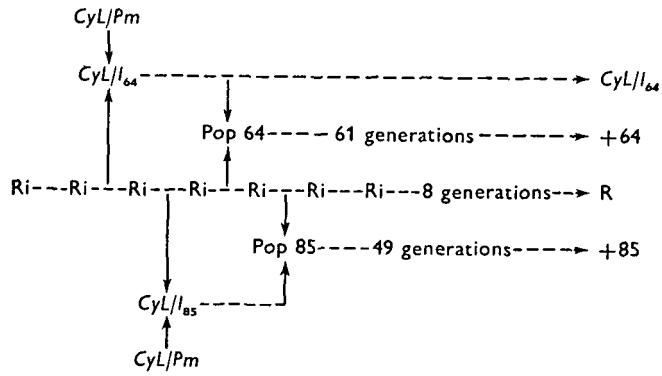

Fig. 3. Schematic representation of the relationship between the strains CyL/l_{64}, R, +64 and +85 used in the experiments. Ri = second chromosome re-isogenization of strain R by the *CyL* technique.

(5) Strain +85 was set up from the animals of the 49th generation of population 85. This population had been started with non-*CyL* flies from the cross CyL/l_{85} ♀ × R ♂. As can be seen in Fig. 2, l_{85} behaved in a similar way to l_{64} in the population 64. l_{85} had been obtained in the same experiment as l_{64} and was located close to the *Bl*-locus (2-54.8). l_{85} was not associated with any detectable chromosomal aberration. The +85 strain probably contained l_{85} at a low frequency as this was the

case in the population from which it was founded. This strain also was reproduced on a broad basis.

The relationship between the strains is schematically summarized in Fig. 3.

(ii) *The populations*

Three series of five populations have been studied in the present work. The matings necessary for the start of the new populations were performed on a broad basis with several hundred flies in order not to lose too much of the genetic variation present in the strains.

Each population of the first series was started with 500 females from the R strain and 500 non-*Cy L* males from the cross R♀ × *Cy L*/l_{64} ♂. These populations will be referred to below as 'R background' populations, though the *Y* chromosome and 25% of the autosomes were from the *Cy L*/l_{64} strain.

The populations of the two other series were started in the same way but the R strain was replaced by the + 64 and the + 85 strain respectively. These populations are consequently referred to as the '+ 64 background' and the '+ 85 background' populations.

At the start of the populations the frequency of l_{64} was 25 % in those with R and + 85 backgrounds. In the + 64 background populations the lethal frequency may have been slightly higher because of the probable presence of the lethal in the + 64 strain.

One or two populations were started on consecutive weeks. When two populations were started simultaneously they had as a rule different genetic backgrounds.

Each population was kept in three bottles ($\frac{1}{3}$ l.) on the usual corn-meal agar medium. The generations were discrete. The flies of each generation were allowed to stay in the bottles for two days and after that they were discarded. Two weeks after the egg-laying the flies of the new generation were transferred to an empty bottle. After mixing, the flies were divided into three equal groups and transferred to three bottles with fresh food. The population size was usually about 1500–2500 per generation and population.

The animals from which the populations were started are referred to as belonging to generation zero. Tests for the frequencies of l_{64} were performed in the fifth and the tenth generations. Between 150 and 500 males were collected in order to test for the frequency of the lethal. The varying number of males collected was due to technical limitations.

The males sampled for the lethal test were individually mated to two or three *Cy L*/*Pm* females. From each culture one male *Cy L*/? was collected and mated to two or three females *Cy L*/l_{64}. If at least 30 *Cy L* flies, including the maximum four parents, and no others were found, the tested chromosome was considered to contain l_{64}.

All populations and test cultures were kept in an incubator at 25 ± 1 °C. For further information on the handling of the populations see Ytterborn (1968*a*).

3. RESULTS

It is not known which fitness component or components are affected by the lethal. Therefore, no selective values have been computed. Instead, when judging the effect of the lethal on the fitness of the heterozygotes the observed lethal frequencies are compared with the frequencies theoretically expected for a completely recessive lethal.

Table 1. *The occurrence of* l_{64} *in the populations of different backgrounds*

(n = number of tested chromosomes, a = number of chromosomes with l_{64}, p = relative frequency of chromosomes with l_{64}.)

	Generation 5			Generation 10		
Pop. no.	n	a	p	n	a	p
			R background			
503	398	59	0·148	273	30	0·110
505	342	58	0·170	325	41	0·126
510	256	57	0·223	292	16	0·055
511	265	51	0·192	186	25	0·134
513	260	72	0·277	273	34	0·125
			+64 background			
506	454	30	0·066	337	10	0·030
508	307	17	0·055	444	3	0·007
512	338	13	0·038	273	10	0·037
514	156	11	0·071	132	7	0·053
515	262	19	0·073	328	8	0·024
			+85 background			
501	471	56	0·119	455	23	0·051
502	375	43	0·115	322	18	0·056
504	375	46	0·123	476	19	0·040
507	326	24	0·074	332	22	0·066
509	236	17	0·072	325	9	0·028

The results of the population tests are presented in Table 1 and in Fig. 4. The expected frequencies in Fig. 4 have been calculated on the assumption that generation zero consisted of wild-type females and lethal heterozygous males. The calculations were performed according to the formula

$$p_n = \frac{p_0}{1+(n-1)p_0},$$

where p_n is the frequency expected in generation number n and $p_0 = 0{\cdot}25$ is the frequency of the lethal in generation zero.

In Table 2 the results are summarized in average lethal frequencies and their standard errors. These values have been calculated according to the formulae

$$\bar{p} = \frac{\Sigma a_i}{\Sigma n_i} \quad \text{and} \quad \text{S.E.} = \frac{1}{\bar{n}}\sqrt{\left[\frac{(\Sigma a_i^2 - 2\bar{p}\Sigma a_i n_i + \bar{p}^2\Sigma n_i^2)}{C(C-1)}\right]}$$

https://doi.org/10.1017/S001667230001209X Published online by Cambridge University Press

(Snedecor and Cochran (1967), p. 241), where a_i stands for the number of lethals and n_i for the number of tested chromosomes of the ith population. Furthermore C is the number of populations, i goes from 1 to C and $\bar{n} = \Sigma n_i/C$. The above formula for the standard error was used since χ^2 tests showed that there was a significant heterogeneity among the replicates in some of the series and generations.

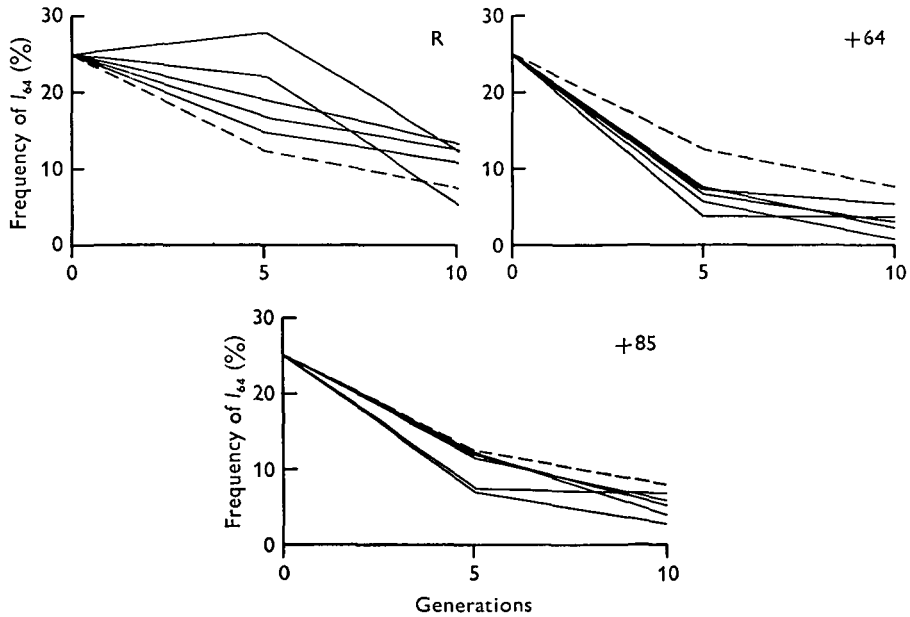

Fig. 4. Observed frequencies of l_{64} in the populations with R, +64 and +85 backgrounds. Dotted curve: elimination expected for a completely recessive lethal.

The average lethal frequencies were higher than expected for a completely recessive lethal in the fifth and the tenth generations on the R background but lower than expected on the other backgrounds. The results of comparisons by t tests between the observed average frequencies and the expected frequencies in Table 2 show that the deviation from expected was statistically significant in one of the tested generations in the R and the +85 background respectively, and in both tested generations in the +64 background.

The comparisons between the tenth-generation average frequencies and the expected frequency based upon the lethal frequency in generation zero do not tell anything about the effects of the lethal on the heterozygotes from the fifth to the tenth generation. However, the observed average frequencies of the tenth generation can be compared with the frequencies expected for a completely recessive lethal calculated on the basis of the fifth generation average frequencies using $p_n = p_0/1+np_0$, where p_0 is the initial frequency and p_n the expected frequency after n generations. In this comparison the average lethal frequency was higher than expected in the R background and lower than expected in the other backgrounds.

The above comparisons very obviously show that the lethal was overdominant in the R background but detrimental to the heterozygous carriers in the +64 and the +85 background.

In Table 2 are also presented the results of pairwise comparisons by t tests between average lethal frequencies observed in different backgrounds and generations. As can be seen there are not only statistically significant differences between the lethal frequencies in the R background and the other backgrounds but also between the +64 and +85 backgrounds. Apparently the lethal was more detrimental for the heterozygous carriers in the +64 background than in the +85 background.

Table 2. *Average lethal frequencies and their standard errors in different backgrounds*

(Also given are t values for comparisons between the observed frequencies and those expected for a completely recessive lethal (p exp) and between observed frequencies in different backgrounds.)

Background	Generation 5			Generation 10		
	$\bar{p} \pm$ S.E.	p exp	t	$\bar{p} \pm$ S.E.	p exp	t
R	0·195 ± 0·022	0·125	3·18*	0·108 ± 0·015	0·077	2·07
+64	0·059 ± 0·006	0·125	11·00***	0·025 ± 0·007	0·077	7·43**
+85	0·104 ± 0·010	0·125	2·10	0·048 ± 0·006	0·077	4·83**
Comparisons between backgrounds						
R to +64			5·91***			4·88**
R to +85			3·79**			3·75**
+64 to +85			3·75**			2·56*

* $P < 0{\cdot}05$; ** $P < 0{\cdot}01$; *** $P < 0{\cdot}001$.

In generation zero of the +64 background populations there may have been lethal heterozygous females at a low frequency because of the probable presence of l_{64} in the +64 strain. The average frequencies of the lethal in this background were lower than in the other backgrounds and also lower than expected for a completely recessive lethal based on the assumption that only the males of generation zero were lethal heterozygotes. This means that the detrimental effects of l_{64} in the +64 background have been somewhat underestimated.

4. DISCUSSION

In some studies on the persistence of recessive lethals it has been shown that the fitness of the lethal heterozygotes is dependent on linkage, or linkage and interaction between the lethal and a specific gene or gene complex (Frydenberg, 1963, 1964; Chung, 1967; Ramel, 1966). In the present experiments the situation must have been more complicated. If the lethal studied had been associatively overdominant due to a linked gene or gene complex, the results should have been

similar in the R background and the +85 background populations. The chromosome containing the lethal had not earlier been introduced into the genetic background of the strains contributing the main part of the gene pools of these populations.

It seems possible that the effects on the lethal of the different backgrounds are connected with the population fitness. Since the R strain by the isogenization process was inbred and thus relatively homogeneous the fitness of the populations started from this strain was probably low. Under these conditions the lethal could show overdominance.

The fitness of the original populations 64 and 85 was also probably low in early generations. By natural selection there was in these populations an accumulation of polygenic mutations and/or complexes of polygenes increasing the population fitness, and simultaneously leading to the loss of the overdominance of the lethals. Thus, already at the start of the new populations with +64 and +85 backgrounds there were available relatively well adapted genotypes which were superior to the heterozygotes for l_{64}.

The lethal heterozygotes in the +64 background had a relatively lower fitness than those in the +85 background. This may be explained by there having developed in populations 64 and 85 different genetic systems affecting the population fitness and affecting the fitness of the lethal heterozygotes in different ways.

An alternative explanation to the varying behaviour of the lethal might be differences of the degree of the background heterozygosity *per se*. As was shown in Fig. 3 the strains contributing the main parts of the backgrounds had been extracted from the repeatedly isogenized R strain at different times. By accumulation of mutations during different numbers of generations the degree of heterozygosity might have been lowest in the R background, higher in the +85 background and highest in the +64 background.

The experimental results do not favour one proposed explanation rather than the other. The varying behaviour of the lethal might even be due to both different degrees of heterozygosity and different fitness-affecting polygenic systems in the three backgrounds. Nevertheless, the results quite clearly show the importance of the genetic background for the fitness of the lethal heterozygotes.

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