locality being treated separately and the sums of squares then combined. Since this analysis of variance showed significant differences between different combinations of chromosomes, for further work the average of the frequencies of wild-type flies for the different cultures of a single combination of chromosomes was considered as the basic variable. Then Star/Lethal $\times$ Normal/Normal at Emboaba, for example, might have a smaller frequency of wild type than Star/Normal $\times$ Normal/Normal at Emboaba simply because the chromosome combinations of the first type chosen by chance happened to give a smaller frequency of wild-type. We can say the difference is due to the presence of the lethal chromosome only if it is significantly larger than the variability between chromosome combinations. This can be tested by an ordinary two sample t test as in table 2. Because of small numbers in many of the fourteen groups an estimate of the error variance based on all the data was used. Then t is approximately normally distributed with unit variance, and the t values can be combined by adding them (taking account of signs) and dividing by the square root of the number of t 's added. This combined value will again be approximately normal with unit variance. Returning to the example of Emboaba, Star/lethal $\times$ Normal/Normal is based on twenty chromosome combinations and has adequate accuracy. Unfortunately, Star/Normal $\times$ Normal/Normal is based on only two combinations and this is the limiting factor in the sensitivity of the comparison. Most of the labor in obtaining the twenty combinations is wasted; in fact, three combinations of each type would have given a more accurate comparison. A more delicate and complicated test, based on the analysis of variance, gave substantially the same results. Mr. Birnbaum and the author of this footnote hope to discuss the statistical aspects more fully elsewhere.

SELECTION AGAINST HETEROZYGOTES FOR AUTOSOMAL LETHALS IN NATURAL POPULATIONS OF *DROSOPHILA* *WILLISTONI*

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In an accompanying article, Cordeiro shows that the second chromosomes of *Drosophila willistoni* which are lethal when homozygous, produce a significant lowering of the viability of heterozygous flies as well. The method used in the experiments of Cordeiro is comparison of the ratios of flies heterozygous for lethals and of flies which are free of such lethals. Cordeiro estimates that, under the environmental conditions of his experiments, the average lowering of the viability produced by heterozygosis for a second chromosome lethal is approximately 7% (his coefficient of inviability). The present note reports an attempt to compare the average adaptive values of individuals heterozygous for second chromosome lethals and of individuals free of such lethals in natural populations of *D. willistoni*.

The genetic structure of natural populations of *D. willistoni* has been

studied by Pavan, *et al.*,¹ who have published data on the frequencies of second chromosomes which are lethal or semilethal to homozygotes. Dobzhansky, Spassky and Spassky² have obtained estimates of the mutation rates which produce these lethals and semilethals. Ives³ and Wallace⁴ have computed the probable number of loci which mutate to lethals and semilethals in the second chromosome of *D. melanogaster*. The second chromosomes of *D. willistoni* and *D. melanogaster* are homologous and probably contain the same loci.⁵ Professor C. Pavan⁶ has kindly communicated to us his unpublished data on the frequency of allelism of second chromosome lethals isolated from various Brazilian populations of *D. willistoni*.

The method used for the estimation of the adaptive value of heterozygotes for lethals in natural populations involves the comparison of the rates of the origin of such lethals by mutation and of their elimination in homozygotes. These rates should be equal if all lethals in natural populations were completely recessive. Wright^{7, 8} has given the necessary equations which describe the relationship just stated (Wright's notation will be followed throughout). For the case of complete recessivity the balance of gains and losses at equilibrium is as follows:

$$V(1 - Q) = \frac{PQ^2(1 - Q)}{1 - PQ^2} \quad (1)$$

$$V \simeq PQ^2 \quad (1)'$$

where:

Q = the equilibrium frequency of lethal chromosomes,

V = the mutation rate producing lethal chromosomes,

P = frequency of allelism of lethal chromosomes, i.e., the proportion of zygotes bearing two allelic lethal chromosomes among the zygotes which carry two lethal chromosomes.

The left side of equation (1) represents the rate of gain by mutation and the right side the rate of loss through homozygosis. Q , V and P may be estimated experimentally. It should be noted, however, that the experimentally determined value of P will be an underestimate if an appreciable amount of inbreeding occurs normally in the population. If the mutation rate (V) is higher than the rate of elimination (PQ^2), as is the case in all *Drosophila* populations studied so far, then the amount of selection against lethal heterozygotes required to account for this difference should be as follows:

$$S = \frac{V - PQ^2(1 + V)}{Q(1 + 2V) - 2PQ^2(1 + V)} \quad (2)$$

where:

S = the mean selection coefficient of heterozygotes for lethal chromosomes.

Equation (2) still assumes random breeding. Wright^{7,8} has considered the more general case where some elimination of lethals will be due to inbreeding as well as to semidominant deleterious effects of the lethals. There is evidence, however, that the populations of *D. willistoni* are panmictic,⁶ and that their genetically effective size may be taken as infinite (unpublished data of Prof. C. Pavan).

In such populations the frequency of the allelism is approximately equal to the frequency of allelism of independently arising lethal chromosomes (P_{∞} according to Wright's notation). For the second chromosome of *D. melanogaster*,^{3,4} this value is $P_{\infty} = 0.0026 (\pm 0.00057)$. Assuming the second chromosomes of *D. melanogaster* and *D. willistoni* carry the same

TABLE 1
FREQUENCIES OF LETHAL CHROMOSOMES (Q) AND SELECTION COEFFICIENTS OF HETEROZYGOES FOR LETHALS (S) IN VARIOUS POPULATIONS OF *Drosophila willistoni*

POPULATION	Q	S
Belem, Pará	0.339	0.025
Rio Branco and Rio Negro	0.541.	0.015
Arce	0.463	0.017
Goyaz	0.417	0.020
Catuní, Bahãa	0.443	0.018
Pirassununga, São Paulo	0.423	0.019
Mogi, São Paulo	0.386	0.021
Vila Atlantica, São Paulo	0.392	0.021
Iguassú, Paraná	0.375	0.022
Mean	0.412	0.020

loci subject to lethal mutation⁵ this figure ($P = 0.0026$) can be used in equation (2), together with the estimate of the mutation rate, $V = 0.0088$, obtained by Dobzhansky, Spassky and Spassky.²

In table 1 there are presented the values of S obtained for nine natural populations of *D. willistoni* in which Pavan, *et al.*¹ determined the frequencies of lethal and semilethal chromosomes (semilethals are assumed to be effectively lethal under natural conditions). Different values of P were tried out by substitution in equation (2) in order to determine how great are the differences in the estimates of S which depend on experimental errors in the determination of P . If values of P twice as high or half as high as 0.0026 are used, the resulting estimates of S are not appreciably changed.

Considering the sources of error contributing to these estimates of S , a discussion of the variations of S between populations would be meaning-

less. All the examined populations of *D. willistoni* may be roughly characterized by the value obtained using the mean Q , namely $S = 0.020$. This value is of the same order of magnitude as the estimates made for natural populations of *D. pseudoscura*,^{7,8} 0.014, 0.02, 0.007 and of *D. melanogaster*,^{3,9} 0.054, 0.028, 0.016, 0.011. It therefore seems justified to state that lethals in natural populations of *Drosophila* are on the average slightly deleterious in the heterozygous condition.

The above estimates for natural populations vary from 0.007 to 0.05 for different species and different populations. The experiments of Cordeiro reported in the preceding article show, however, that under laboratory conditions the viability of heterozygotes for lethals in *D. willistoni* is lowered in some localities by as much as 14% (his coefficient of inviability), although in other localities it is only lowered by 0.8%. These estimates are not exactly comparable to the estimates of S calculated in this paper. In the first place, the experiment of Cordeiro measures the relative viabilities of different genotypes between the egg stage and the hatching of the adults from pupae under conditions of severe crowding in laboratory bottles. These estimates of S measure the adaptive values under natural conditions where larval competition for food may not always be a limiting factor. On the other hand, the relative fecundities, longevities, sexual activities, etc., of the carriers of different genotypes influence the value of S , while they do not affect the viability estimates, such as those offered by Cordeiro. Finally it should be noted that the estimates of S , as well as of the coefficient of inviability, describe merely the average situations. In reality, some lethals may be more deleterious in heterozygotes than others, as actually demonstrated by the data of Cordeiro.

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³ Ives, P. T., *Ibid.*, **30**, 167–196 (1945).

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⁶ Pavan, C., personal communications (1952).

⁷ Dobzhansky, Th., and Wright, S., *Genetics*, **26**, 23–51 (1941).

⁸ Wright, S., Dobzhansky, Th., and Hovanitz, W., *Ibid.*, **27**, 363–394 (1942).

⁹ Dubinin, N. P., *Ibid.*, **31**, 21–38 (1946).