The Viability of Individuals Heterozygous for Recessive Lethals[1]

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The significance of recessive lethals for the dynamics of populations is often considered solely in relation to their effect in homozygous or hemizygous state. The assumption is thus made that individuals heterozygous for these lethals are equivalent to homozygotes free from the lethal alleles. This assumption has been tested for 33 sex-linked lethals in *Drosophila melanogaster* and found to be incorrect for the majority of them.

TABLE 1

RESULTS OF TESTS FOR VIABILITY OF HETEROZYGOTES FOR 33 SEX-LINKED LETHALS

No. and source of lethals	Females heterozygous for		
	lethal	normal	doubtful
26, from irradiated sperm ..	4,860	5,210	236
7, from control sperm	1,366	1,551	75

The sex-linked lethals tested consisted of 7 spontaneous lethals and 27 lethals discovered in low-dosage X-ray or gamma-ray irradiation experiments. A considerable number of these "experimental" lethals must be spontaneous ones which have arisen independently of the irradiation. All lethals occurred in an X-chromosome derived from the highly homogeneous Canton-S stock of *Drosophila*.

The test for equivalence or lack of equivalence of flies heterozygous for a lethal with flies homozygous for the nonlethal allele was carried out as follows: Females carrying a so-called Muller-5 X-chromosome ($sc^{81}B$ In-S $w^a sc^8$) and a lethal-carrying chromosome were mated to Canton-S males. The F_1 females heterozygous for the lethal were mated to Muller-5 males and individually placed in culture bottles. Theoretically, their female offspring (F_2) should consist equally of Muller-5/+ and Muller-5/lethal genotypes. Individual progeny tests of these F_2 females were performed in order to determine which of these two constitutions was present in any specific individual. For each lethal an average of 472 F_2 females were thus tested. Any test culture which yielded one or more wild type males was classified as signifying the maternal genotype Muller-5/+; and any test culture with no wild type males and at least 6 Muller-5 males was regarded as signifying the maternal genotype Muller-5/lethal. Those cultures which yielded no wild type males but less than 6 Muller-5 males were considered as doubtful and listed separately. Finally, a fourth category was constituted of females which gave no offspring due to death, often by accident, or sterility of these females or their mates.

A summary of the data is presented in Table 1. If one excludes "doubtful" and sterile tests, one may calculate for each lethal a percentage of lethal-bearing among all adequately tested females. The amount of this percentage is, of course, subject to a statistical error. Taking the observed values without consideration of their individual errors, one would expect approximately equal numbers to fall above 50% and below 50%, provided the viability of the genotype heterozygous for any one lethal were like that of a lethal-free genotype. In addition, the spread of values above and below 50% should be identical within statistical limits.

Actually, a plot of the viability values for the 33 lethals shows a twofold asymmetry (Table 2). There were 5 lethals within the class 49.6–50.5. Above this class only 5 values occurred; below it, 23. The values above 50.5% ranged within 4 classes; those below extended over 8, the lowest value being as low as 42.1%. Even within equal range of 4 classes above and below the 49.6–50.5 class, the inequality of numbers of lethals is striking, being 5 and 16, respectively. These facts indicate that most sex-linked lethals tested have a considerable effect in decreasing the viability of females heterozygous for them.

In reaching this conclusion it has been assumed that the often large numbers of sterile or "doubtful" females were a random sample of the tested populations. This assumption is probably close to truth, since much of the sterility or low fertility may have been due to accidental causes in handling the cultures. Possibly, some of these sterile or low-yielding cultures owe their characteristic to the heterozygous lethal genotype. If this were the case, a partial explanation would be provided for the deviations of lethal-bearing heterozygotes from the theoretical value of 50%. These deviations would to some extent be due to a higher number of sterile females or of those of low fecundity among lethal heterozygotes than among females free from a lethal.

From the point of view of a population even a slight decrease in the viability of individuals heterozygous for a lethal would be of greater significance for its well-being

TABLE 2

DISTRIBUTION OF VIABILITY VALUES FOR HETEROZYGOTES OF 33 SEX-LINKED LETHALS IN PER CENT OF FEMALES ADEQUATELY TESTED*

41.6 – 42.5	42.6 – 43.5	43.6 – 44.5	44.6 – 45.5	45.6 – 46.5	46.6 – 47.5	47.6 – 48.5	48.6 – 49.5	49.6 – 50.5	50.6 – 51.5	51.6 – 52.5	52.6 – 53.5	53.6 – 54.5
1	..	2	4	2	5	6	3	5	3	1	..	1

* "Doubtful" cases were excluded.

[1] This paper is based on work performed for the U. S. Atomic Energy Commission at the Atomic Energy Project, University of Rochester.

than the loss of lethal homozygotes. In any given generation the frequency of homozygotes is defined by p^2—the square of the frequency, p, of the gene in the population—whereas that of the heterozygous carriers is $2p(1-p)$. For a rare gene (p being small and $1-p$ close to 1) the number of carriers may become hundreds of times as large as that of the homozygotes, so that a decrease in vigor of the carriers by, for instance, 5% will have a far greater effect than the complete elimination of the much rarer homozygotes.

The data presented here are of a preliminary nature. Retests of lethals may result in some changes in the specific figures given but will hardly lead to fundamental alterations in the conclusion.

In Vivo Iodination of Tissue Protein Following Injection of Elemental Iodine[1]

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The work of Dvoskin (*2*) indicated that subcutaneous injection of elemental iodine into rats resulted in the synthesis of thyroxin-like material. This conclusion was reached from a study of the effects of the injected iodine on the histological appearance of thyroids of thiouracil-treated animals as well as on the growth curves of thyroidectomized young rats. It seemed reasonable to expect that this treatment would result in the formation of protein-bound iodine (PI) very probably due to the direct iodination of protein, similar to the purely *in vitro* production of iodinated protein.

TABLE 1

Effect of Subcutaneous Injection of Elemental Iodine in Propylene Glycol Solution on Plasma Protein-bound Iodine of Rats

Treatment	Plasma PI
	γ/100 cc
Unoperated + propylene glycol for 30 days	4.6
" + 4 mg of I_2/kg/day for 1 day	34.8
" + 4 mg of I_2/kg/day for 30 days	86.3
" + 16 mg of I_2/kg/day for 30 days	260.7
Thiouracil + propylene glycol for 30 days	1.3
" + 4 mg of I_2/kg/day for 30 days	60.0
" + 16 mg of I_2/kg/day for 30 days	338.0
Thyroidectomized + propylene glycol for 30 days	1.1
" + 16 mg of I_2/kg/day for 30 days	251.0

In order to test this hypothesis, albino rats of the Sprague-Dawley strain were injected subcutaneously with either 4 or 16 mg of elemental iodine (I_2)/kg of body weight, dissolved in propylene glycol (PG); the solvent alone was injected into controls. The use of propylene glycol eliminated the complications arising from the NaI required to dissolve I_2 in water or alcohol. The procedure for determination of PI was that recently described from this laboratory (*1*), with the modification that 0.5 ml of 1.5% As_2O_3 solution in 1N NaOH is used in the trap of the iodine-distilling apparatus instead of the Na_2SO_3 originally described. This alteration eliminates the aeration step, since there is no SO_2 present. It should be unnecessary to emphasize that every precaution must be taken to avoid contamination of the PI fraction being studied with elemental or inorganic iodine.

Table 1 shows the considerable increase in plasma PI after several different periods of injection. Even a single injection at the 4-mg level produced a considerable elevation in plasma PI by 24 hrs, and the values reached remarkable heights when 16 mg/kg was injected each day for 30 days.

TABLE 2

Tissue Protein-bound Iodine in Rats 24 Hrs After Single Injection of Propylene Glycol or Elemental Iodine in PG

Tissue analyzed		Protein-bound iodine after	
		propylene glycol (PG)	16 mg of I_2/kg in PG
Plasma	(γ/100 cc)	2,75	96.0
Thyroid	(γ/gland)	8.2	8.3
Kidney	(γ/100 gm)	11.7	86.8
Liver	(γ/100 gm)	17.9	46.7
Heart	(γ/100 gm)	10.4	25.6
Skeletal muscle	(γ/100 gm)	8.9	19.8
Injection site	(γ/100 gm)	0.0	36,230

Parallel determinations of oxygen consumption were performed on the animals shown in Table 1. These results indicate that the thiouracil-treated and thyroidectomized groups given the 16-mg/kg/day dose were the only ones to show increased metabolic rates. This finding suggests that a large proportion of the iodine combined with the plasma proteins must have been in a form other than thyroxin.

The possible role of the various organs of the animal body in the elaboration of the PI was investigated by comparing the tissue PI levels for kidney, liver, muscle, heart, and thyroid with that found at the site of injection. As can be seen from the results of one such experiment (Table 2), there can be little doubt that iodination of the tissue protein occurred primarily directly where the I_2 injection was made, since this PI value was so extremely high. Indeed, it would seem quite unlikely that free elemental iodine could exist in sufficient quantities in the blood plasma or in the lymph to be carried as such to liver or kidney for synthesis purposes. It is apparent from the thyroid results that this gland is not a major factor in the formation, and probably not in the breakdown, of the PI. On the other hand, the elevated kidney PI most likely denotes some excretory or "detoxifying" function of this organ.

[1] This investigation was supported by a research grant from the Division of Research Grants and Fellowships, National Institutes of Health, U. S. Public Health Service.

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