[7] It would be interesting to know whether corals and calcareous algae deposit as much $CaCO_3$ in the dark as in the light. Corals from deep water are smaller, more fragile, and deposit less $CaCO_3$ than those of shallow water, but the same is true of animals without symbiotic algae. The deposition is, however, related to the pH, since Palitzsch has shown that the pH decreases with depth.

[8] *Amer. J. Sci., New Haven*, **41**, 1916, (473).

AN OENOTHERA-LIKE CASE IN DROSOPHILA

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Although the large bulk of the Drosophila work has been remarkably self-consistent, and amenable to orderly and definite rules of factor transmission, yet from the outset the ideal scheme has been confronted with two unconformable cases. These are the cases of beaded wings and of truncate wings, both of which seemed to belie the idea of clear cut segregating gens. In the case of beaded wings, which will be briefly reported here,[1] many generations of selection were carried out by Morgan with the purpose of obtaining a pure breeding stock, yet for several years it was impossible to attain this object. The character showed all the peculiarities which would be expected as a result of factor fluctuation and miscibility. It was increased in intensity as a result of selection yet its essential variability remained, and the latter was proved by crosses to be genetic, for Morgan found that reversed selection produced a marked and immediate retrogression in the proportion of beadeds thrown. Finally, however, he did obtain a race which threw no normals, but the reason for this change in behavior seemed now just as difficult to discover as the cause of the previous variability. On crossing, various apparently irregular results and aberrant ratios followed.

The work of Dexter, which showed that environmental conditions and factors in both the second and third chromosomes are all concerned in the development of this character, provided valuable information for the present investigation. Starting from Dexter's finding that there was a chief factor for beaded in chromosome III[2] an attempt was made by the writer to find the precise location of this gen. It proved to lie at the extreme right hand end of the known factors in the third chromosome, being two and a half units beyond the factor for rough eyes, which is otherwise the furthest factor to the right. It was found also that the apparently pure beaded stock is not homozygous for beaded, but in reality contains two very different kinds of third chromosomes. It was by investigating this phenomenon, with the aid of the data secured in

the linkage study, and by dissecting, by means of crossing over, each of these two kinds of chromosomes separately, that a complete explanation of the beaded case was finally obtained.   It would be impossible here to give even an outline of the detailed steps of analysis, but the following are the concrete results and theoretical conclusions which have been arrived at.

1. The difficulty which was experienced in getting pure stock was due to the fact that the chief factor for beaded—B_d'—is lethal, killing all flies homozygous for it.   Heterozygous beadeds are not killed but usually show the beaded character.   Thus B_d', like yellow in mice, is dominant for its visible effect and recessive for a lethal effect.   The dominance of B_d' is variable, however.

2. The reason that a race which bred true to beaded was finally secured is not because a condition of homozygosis was at last established, but, on the contrary, because of the establishment of a state of enforced heterozygosis, wherein not only the homozygous beadeds but also the homozygous normal winged flies were prevented from hatching. This was due to the appearance, by mutation, of another lethal factor, $l_{III\,1}$, in that third chromosome of the impure stock which contained the normal allelomorph of B_d'.   This lethal, like B_d', kills all flies which are homozygous for it, although, unlike B_d', it has no visible effect when it is heterozygous.   Since, in the flies of this heterozygous race, it arose in the chromosome containing the factor for normal wings, no homozygous normals will be able to appear except those in which $l_{III\,1}$ has been separated by crossing over from the normal allelomorph of B_d'.   The usual amount of crossing over between these loci of $l_{III\,1}$ and of B_d' is 10%, as $l_{III\,1}$ was found to be 10 units to the left of B_d'.   On this basis it is to be expected that the selected beaded stock would throw 90% beaded flies and 10% normal winged crossovers.

3. In this selected stock, however, not even 10% of the flies have normal wings, because of the existence of another mutant factor, C', which almost entirely prevents crossing over in the region of the chromosome in which $l_{III\,1}$ and B_d' lie. $l_{III\,1}$. on this account, always remains with the normal allelomorph of B_d' and all the homozygous normal winged, as well as the homozygous beaded flies are thus prevented from appearing.   It should be noted that the factor C', too, always remains heterozygous, for it is contained only in the chromosome having $l_{III\,1}$ and the normal allelomorph of B_d', not in the chromosome with B_d' itself. This state of heterozygosis for C' is also a necessary condition for the mechanism whereby only beaded flies are produced, since C' produces its inhibition of crossing over only when it itself is heterozygous.   Aside

from its influence on crossing over, no other effect of this factor has been discoverable. The locus of C′·is within 10 units of that of sooty body color, being to the left of the locus of $l_{III\,1}$, and to the right of the locus of kidney eyes. C′ probably existed in the chromosome of beaded stock now containing it before $l_{III\,1}$ arose in that chromosome by mutation.

4. This remarkable genetic situation, wherein both types of homozygotes are prevented from appearing by the action of lethal factors lying in opposite chromosomes, may be termed a condition of 'balanced lethal factors.' Surprising as it may seem, it appears that such a condition is no mere 'freak of nature,' and that it is apt to arise wherever dominant mutant factors exist which either have some natural survival value, or have, like beaded, been artificially selected for. This conclusion is based upon the following experimental results and theoretical considerations.

(a) In an attack upon this question, an investigation was undertaken by the writer to determine how generally dominant mutant factors of Drosophila are lethal when homozygous. There were nine dominant mutants known (excluding the intensifiers of beaded and truncate), and they were distributed equally among the three large chromosomes. The viability of the three sex-linked dominants was, of course, already known; the remaining six dominants were tested. In all, it was found that three of the nine are not lethal, one (in chromosome III) is semilethal, and five (one in chromosome I, two in II and two in III) are completely lethal when homozygous. Thus it is a phenomenon of common occurrence in Drosophila for dominant mutant factors to be lethal when homozygous.

(b) It would be very far fetched to assume that the natures of the characters produced by dominant factors differ as a class from those produced by recessives. We must therefore believe that lethals are very frequent among recessive factors also. It should be noted, however, that in the case of recessive factors a lethal action prevents or greatly hinders their discovery, whereas with factors dominant in respect to some visible character, a lethal effect, when homozygous, does not interfere with their being detected; for this reason it is quite in accord with expectation that a much smaller proportion of lethals has actually been found among the recessives than among the dominant mutants. The evidence for the frequency of origin of recessive lethals is not entirely by analogy, however, for in the case of sex-linked factors the discovery of lethals is easier, owing to their effect upon the sex ratio, and here a considerable number of lethals has in fact been found, by

various observers. Following up, now, our original inference regarding the high frequency of lethals among recessive mutants, it should further be pointed out that since recessive mutants as a class are much more numerous than dominant mutants, recessive lethals also should arise much oftener than dominant ones.

(c) It now remains to join these two results together in one conclusion. Suppose that a race already contains a dominant mutant factor which is favored by selection. Firstly, as shown in (a), this is likely to be lethal when homozygous. Then, as shown in (b), it is likely that a recessive lethal will some time, in some line of individuals, arise by mutation in the opposite chromosome. Since the first factor is being selected for, and the presence of this second lethal will cause the production of a smaller proportion of individuals not showing the desired dominant character, the line containing the second lethal in addition will tend to be selected. Thus a condition of balanced lethal factors will automatically become established, just as it did in the case of beaded wings. Factors which prevent crossing over, or balancing lethals which cross over less frequently with the desired dominant, will of course also be favored by selection, provided they occur, for the less crossing over there exists between the two balanced factors, the more perfect is the balance and the greater is the proportion of individuals showing the advantageous character. The frequency of factors like C' is however unknown, although they have been discovered in nearly a dozen stocks of Drosophila. In the case of the beaded stock, the presence of C' seems to be just a happy coincidence, as it probably existed there before $l_{III\,1}$ arose. But, however that may be, it is evident that the present case is but a special instance of a general class of cases of balanced lethal factors that will probably confront the geneticist in increasing numbers.[3]

5. What will be the distinguishing characteristics of races in this condition? (a) In the first place, crosses of these varieties to other races will result in the production of hybrids of two types, according to which of the chromosomes of the balanced pair they receive. Thus, flies of beaded stock crossed to normal give 50% beaded and 50% normal in F_1. In cases where one of the lethal containing chromosomes is not dominant to the chromosomes of the foreign race in any 'visible' factor, one of these hybrids (in our case the normal) will appear to breed true, while the other will show segregation in subsequent generations. By introducing other mutant factors besides into the balanced chromosomes of beaded stock, these results were made more striking and made to apply to a number of different characters at once.

(b) Still more unusual results can be and were obtained by crossing a

balanced race with another which also contained lethal factors (either the same or different in nature and grouping). In such cases not only twin but also multiple hybrids may be produced, that may or may not be constant. The results, however, always came out according to the prediction based on knowledge of the factorial composition of the flies. One such result which was especially noteworthy was a prearranged cross in which a dominant character present in one of the parent flies was caused to disappear completely, being absent from all the progeny of the cross and all subsequent generations.

(c) A lowered productivity is of course noticeable in balanced races, owing to the action of the lethal factors.

(d) In stocks in which other recessive mutant factors had been introduced into one or other of the chromosomes containing the lethals, these factors, of course, usually failed to manifest themselves, owing to the enforced heterozygosis. Occasionally, however, one or more crossed over from the lethal factor with which it was bound, and so was enabled to become homozygous. As crossing over occurs with predictable frequencies, these individuals showing characters abnormal to the stock were thrown continually in a definite, very small per cent of cases. This caused the stock to appear 'eversporting.' Crossing over between the lethal factors themselves also occurred very rarely, giving rise to individuals no longer exhibiting the unusual genetic behavior due to balanced lethals.

6. The striking parallel between the above behavior and that exhibited in Oenothera make it practically certain that this, too, is a complicated case of balanced lethal factors, and that some (if not most) of the so-called mutations in O. lamarckiana are but the emergence into a state of homozygosis, through crossing over, of recessive factors constantly present in the heterozygous stock. Proof of the spuriousness of some of the mutations in Oenothera is, however, not an argument against the validity of the modern mutation theory; the fact of real mutation has been amply demonstrated in Drosophila as well as elsewhere, and it should be emphasized that these mutations can here be distinguished with certainty from the superficially similar phenomena that are observable in the beaded stock, because the genetic constitution of the flies can be analyzed in detail.

In Oenothera a form of the balanced lethal explanation was suggested by de Vries only to account for his double reciprocal crosses, but it is evident from the analogy of the beaded case that it probably lies at the root of nearly all the unusual genetic phenomena of the genus. The two cases differ in detail, however, in that one or more of the lethals in

Oenothera produce their effect upon the gametes, rather than upon the zygotes.

Double throwing stocks (Matthiola) present another case of balanced factors. This too differs in detail from the beaded case, for one of the factors acts very early, producing its lethal effect directly upon the gametes (pollen), as in Oenothera, whereas the other, although it affects the zygotes, does not act as a lethal to their soma, but merely causes their sterility. It is this factor which causes the double flower.

7. The condition of balanced lethal factors must slowly lead to a par-. tial degeneration of the chromosomes containing these lethals. For any new lethal recessive factors that arise in these chromosomes will never have the opportunity of becoming homozygous and producing their harmful effect, and so there will be no cause for natural selection to eliminate them. Lethal recessive mutant factors of all sorts (including 'deficiencies') will therefore gradually accumulate in the chromosomes of the affected pair. Moreover, although $l_{III\ 1}$ is the first lethal recessive which has been found in an autosome of Drosophila, theoretical considerations and the experiments above reported lead to the conclusion that in the course of time the number of such mutations will have been not inconsiderable, as they probably form a large proportion of all the mutations that occur. For similar reasons, chromosomes of stocks which are continually outcrossed, and the Y-chromosome in all species containing it, should undergo degeneration, because these chromosomes, too, are always protected, by heterozygosis, from the action of natural selection.

8. Not only are mutants of an undesirable nature not eliminated from balanced chromosomes by natural selection, but recessive mutant factors of a desirable type also are prevented from becoming homozygous and producing their effects, and so they cannot be selected for. On account of this latter circumstance, evolution is hindered in these varieties. As each chromosome of the balanced pair degenerates, however, it must gradually lose the dominant normal factors that prevented recessive mutant allelomorphs in the opposite chromosome from manifesting themselves. The balanced races might, moreover, eventually return completely to a condition of normal genetic behavior, owing to the occurrence of doubling or non-disjunction, which might make two normal pairs of chromosomes out of one balanced pair.

9. The inheritance of beaded is complicated not only by balanced lethal factors, but also by a modifiability of the character under the influence of environmental conditions, and by multiple factors. A number of the well known mutant factors for totally different characters

than beaded have been found to intensify or inhibit the development of the latter, and there is besides, as Dexter has shown, a factor in the second chromosome of the selected beaded stock itself which has no visible effect other than to increase the degree of beading. This must have arisen by mutation and have been perpetuated in the process of selection. Crosses made in the course of the present work have shown that this intensifier, I_{Bd}', is partially dominant, but is not a lethal, and, in contrast to the other factors involved in beaded stock, that it exists here in homozygous condition. At least one mutant factor has also been found, by the writer, which can produce a character similar to beaded even when the factor B_d' itself is not present; this mutant is not ordinarily present in beaded stock, however. All the facts of the present section may be summed up in the single generalization that beaded is a character depending upon a developmental reaction that is readily modifiable.

The complete formula of the selected beaded race, representing all the pairs of factors wherein it differs from the wild type, may now be given:

$$\frac{I_{Bd}' \quad c'l_{III\,1}\,B_d'}{I_{Bd}' \quad C'l_{III\,1}\,b_d'}$$

10. The beaded case illustrates to great advantage the danger of confusing characters with gens and of drawing radical conclusions concerning the behavior of gens on the basis of uncritical experiments. The work of the first four years upon the inheritance of beaded wings gave evidence which would to many have appeared most elaborate and convincing, that the hereditary material in this case was fluctuating and miscible, consisting of vague and plastic "tendencies," rather than definite physical particles. Precise analysis, of a sort comparable to that of chemistry, has, however, been possible here, and it has demonstrated that a very different set of processes from those that might have been imagined is responsible for the peculiar results—processes which in their essence conform strictly to the genotype conception.

It will accordingly be necessary in other cases also not to accept evidence apparently in favor of factor inconstancy until factorial analyses of a similarly rigorous character have proved such an interpretation to be correct. A similar criticism applies to the acceptance of results that seem to be non-Mendelian; and also to the incautious estimation of apparent mutations at their face value. 'Non-Mendelian' results of all kinds and also 'mutations' may be prearranged and brought about at will with the beaded flies, but here analysis has made the

Mendelian machinery at work evident. Unwelcome as these conclusions may sound to obscurantists and to those in general who have an antipathy for exact modes of procedure, the necessity for such refined methods here should be obvious. In particular, it will be desirable to examine more intensively those cases which show the characteristics described in Section 5 for balanced lethal factors.

[1] The full account of this case will appear subsequently, and also an account, by Altenburg and Muller, of the truncate case.

[2] Sturtevant also had performed certain linkage experiments in which beaded was present; these showed that it was well on the other side of sooty from pink.

[3] Since the above has gone to press, a case in *Campanula* which may be due to balanced lethals has been reported by Miss Pellew in the *Journal of Genetics.*

IS DEATH FROM HIGH TEMPERATURE DUE TO THE ACCUMULATION OF ACID IN THE TISSUES?

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I find that there is a converse relation between the rate of oxygen consumption in reef corals and their ability to resist high temperature, those corals which are most readily killed by heat having the highest metabolism (rate of oxygen consumption).

NAME OF CORAL	CONSTANT TEMPERATURE EXPOSURE TO WHICH CAUSES DEATH IN ONE HOUR	RELATIVE RATE OF OXYGEN CONSUMPTION PER GRAM OF LIVING SUBSTANCE IN EACH CORAL
	°C.	
Acropora muricata....................	34.7	18.7
Orbicella annularis....................	35.60	6.1
Maeandra areolata....................	36.80	5.5
Favia fragum........................	37.05	3.8
Siderastrea radians....................	38.20	1.0*

* At 28.5°C. 1 gram of living substance of *Siderastrea radians* consumes 0.0256 cc. of oxygen per hour. The oxygen being measured at 0°C. and 760 mm. pressure.

Also, if sea water be super-saturated with carbon dioxide gas, the toxic effect is in the same sequence as that of high temperature. That is to say, those corals which are readily killed by heat are also correspondingly easily killed by H_2CO_3.

This toxic effect of carbon dioxide is not due to its replacing some of the oxygen of the sea water, for I find that corals are remarkably insensitive to a reduction in the oxygen supply, all species except *Acropora* living more than eleven hours in sea water under an air pump which reduced the oxygen to less than 5% of that of normal sea water; and even *Acropora* can withstand six hours of this treatment.