On the Change that Takes Place in the Chromosome in Mutating Stocks.

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Two new eye mutations, tinged and blood have appeared in my cultures of the fruit fly that throw light upon the question as to the nature of the change that takes place in the chromosome when a new character appears. Both mutations show typical sex-linked inheritance, consequently they are expressions of changes in the X chromosome. Both mutants give the same linkage values when measured with other sex-linked characters. When measured with yellow body color a linkage of 1.2 results; with miniature wings 33; with bar eyes 44. Morgan has described three sex-linked eye mutants, white, eosin and cherry, which give the same linkage values. Consequently, we now have five sex-linked eye mutants, namely, white, tinged, eosin, cherry and blood, which give an increasing color series from white to the bright red of the wild fly. A study of their linkage relations shows that they either lie very closely together on the X chromosome or that they are but different modifications of the same gene. The two possibilities involve the question of the origin of mutations as well as the fundamental make-up of an hereditary factor.

Mendel evidently thought of something in the germ cell that stood for round (R) and something that stood for wrinkled (W) and that these two things could not coexist in the same gamete. That is, (W) is allelomorphic to (R).

The origin of mutation in the light of the above assumption would seem to depend upon the splitting up of more complex hybrids—the bringing to the surface of units already created. Evolution in the light of such a conception would seem to depend upon the shifting together of desirable units.

Bateson viewed the matter in a different light. He knew of the origin of new forms by mutation. He postulated a definite something in the germ cell that stands for the character, as for example (T) which stands for the tallness in peas, which when lacking makes the pea a dwarf (t). In other words, instead of two separate factors he regards the tallness and dwarfishness merely as an expression of the two possible states of the same factor,—

its presence and its absence. Hence his well-known Presence and Absence theory. In this case (T) is allelomorphic to its absence (t). The inheritance of combs in chickens is a beautiful application of such a conception. Mutations according to this theory appear as the result of losses.

Bateson pushed this idea to its logical conclusion in his Melbourne address where he speculates on the possibility that evolution has come about by the loss of something. These somethings he assumes to be inhibitors. (Science, August 28, 1914).

" . . . As I have said already, this is no time for devising theories of evolution, and I propound none. But as we have got to recognize that there has been an evolution, that somehow or other the forms of life have arisen from fewer forms, we may as well see whether we are limited to the old view that evolutionary progress is from the simple to the complex, and whether after all it is conceivable that the process was the other way about.

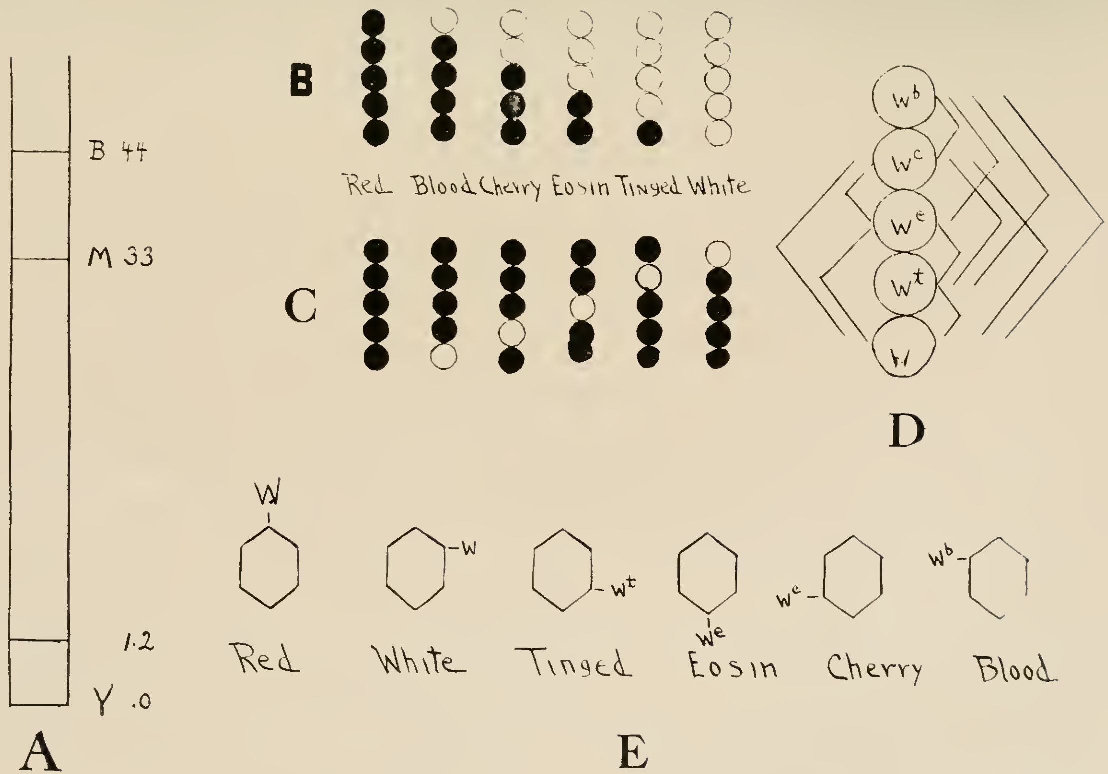
" . . . At first it may seem rank absurdity to suppose that the primordial form or forms of protoplasm could have contained complexity enough to produce the divers types of life.

" . . . Let us consider how far we can get by the process of removal of what we call "epistatic" factors, in other words those that control, mask, or suppress underlying powers and faculties.

" . . . I have confidence that the artistic gifts of mankind will prove to be due not to something added to the make-up of an ordinary man, but to the absence of factors which in the normal person inhibit the development of these gifts. They are almost beyond doubt to be looked upon as *releases* of powers normally suppressed. The instrument is there, but it is "stopped down." The scents of flowers or fruits, the finely repeated divisions that give its quality to the wool of the merino, or in an analogous case the multiplicity of quills to the tail of the fantail pigeon, are in all probability other examples of such releases.

" . . . In spite of seeming perversity, therefore, we have to admit that there is no evolutionary change which in the present state of our knowledge we can positively declare to be not due to loss. When this has been conceded it is natural to ask whether the removal of inhibiting factors may not be invoked in alleviation of the necessity which has driven students of the domestic breeds to refer their diversities to multiple origins."

Another idea as to the way these factors may find expression in the germ cells has been advanced by Morgan under the heading of Multiple Allelo-



Figures A, B, C, and E.—Explanation given in Text.

morphs. According to this conception there is a definite something (W) located at point 1.2 on the X chromosome which stands for the red eye of the wild fly. (Fig. A.) This gene underwent some kind of change and gave rise to white eyes (w). In another stock the same particle mutated and gave rise to eosin (w^e). In still another stock the same particle changed and gave rise to cherry (w^c). (W) is allelomorphic to (w), to (w^e) and to (w^c). each of these in turn is allelomorphic to each other; hence they form a system of Multiple Allelomorphs. This view is supported by a large amount of experimental data by Morgan and his co-workers, but strange as it may seem the numerical results can be interpreted in terms of the Presence and Absence theory provided the mutants are the result of losses of several factors that stand for red in a completely linked chain of loci.

The assumption that these three mutants are the result of changes in loci lying very closely together on the chromosome as demanded by the Presence and Absence theory has been tested by Morgan and others by means of their linkage relations in three possible combinations as given in Fig. D. (Shown by the broken lines on the left.) The discovery of the two new mutants has made it possible to carry out the test in eight additional ways. The evidence which involves data from something like a half-million animals weighs heavily against the Presence and Absence theory and is entirely in accord with the assumption that something analogous to isomerism may change an hereditary factor resulting in the production of a new form. I have attempted to visualize this in Fig. E. If this is the correct interpretation the possibilities locked in a small amount of chromatin may be almost infinite, for a great many different arrangements are possible from a few things.

There are some points worthy of consideration as tending to give weight to the Multiple Allelomorph theory.

1. On the Presence and Absence theory, it is necessary to assume that in the region of 1.2 on the X chromosome there is a chain of five completely linked loci (very close together) upon which the color of the red eye of the wild fly depends. Multiple Allelomorphs accounts for all of the facts while postulating but one locus.

2. Gratuitous to the Presence and Absence theory let us assume that the loci are in jutaposition. If we assume that blood, cherry, eosin, tinged and white have appeared as a result of successive losses as shown in Fig. C, we encounter a difficulty. When any two of these mutants are crossed the

two chromosomes are brought together in the female, each restores the missing part to the other and a red-eyed female should result in the F_1 generation. As a matter of fact no red-eyed female appears. She is invariably a compound, that is, in each case she is intermediate between the eye colors of the two stocks used as parents.

Again the evidence is fairly conclusive that when the two X chromosomes are brought together in the female they break and reunite at apparently all levels on the chromosome. Accordingly, it would seem that a break and reunion would occasionally take place between the members of this chain of loci. If such a phenomena should occur a complete chain of loci would result like the chain in Fig. C (on the extreme left), which would express itself in the F_2 generation in the production of a red-eyed male. But in all the possible attempts to break up such a line, as shown in Fig. D, no such a red-eyed male has been found. To be sure the loci may be so close together that crossing over would take place infrequently, but the evidence from such large counts as have been made in which the red-eyed male has been specifically looked for would weigh heavily against its ever taking place.

3. The mutations may be due to losses according to the scheme represented in Fig. B., one loss produced blood, two losses produced cherry, and so on. Such an assumption would seem to accord with the fact that when any two of these stocks are crossed no red females are produced in the F_1 generation. On the other hand it should be expected that the chromosome in which the least number of losses had occurred would act as a dominant. For example, when blood and tinged are crossed, the females should be like blood. But no such result is obtained. The female is intermediate in color.

Again we should expect from the phenomena of crossing-over that, in a cross for example between blood and white occasionally a cherry, or an eosin, or a tinged male would appear in the F_2 generation, but none has been observed.

4. The history of the appearance of the members of this multiple allelomorph system shows that they are rare phenomena. Careful observation by Morgan, Sturtevant, Muller, Bridges, myself and others show these mutants to have appeared but a few times. It would be safe to say, I think, that only one has occurred in five million times. I have represented blood by one loss from the chromosome. Tinged is the result of four losses in this completely linked chain of loci. The possibility of such mutants appearing involves so many simultaneous losses that there would be one chance

in millions. It seems almost impossible to believe that we should have ever found such a mutant.

5. The experimental evidence shows there are many factors arranged in a linear series on the X chromosome. Some affect wings, some body colors, others the shape of the eye, and so forth. Sturtevant has pointed out the significance of the fact in light of the above statement that the characters which behave as members of a multiple allelomorph system are closely related physiologically.

6. If the mutants are the result of changes as shown in Fig. D it would seem as if a mutated stock would more readily give rise to subsequent mutations, since fewer simultaneous losses are necessary. As a matter of fact four of the members mutated directly from red while eosin came from white.

7. Morgan has emphasized the idea that it is difficult to account for reverse mutations on the assumption of losses from a completely linked chain of loci, as the Presence and Absence theory postulates. On the other hand it is conceivable how such a reaction could come about if the mutant is the result of an expression of something analogous to an isometric change.

8. Is chromatin such simple material that the only change conceivable is a loss?

Literature Cited.

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