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*THE MUTATION THEORY OF ORGANIC EVOLUTION.**

The Mutation Theory of Organic Evolution, from the Standpoint of Animal Breeding: W. E. CASTLE, Assistant Professor of Zoology, Harvard University.

The mutation theory, as I understand it, is not designed to replace Darwin's theory of natural selection, nor is it capable of replacing that theory. Natural selection must still be invoked to choose between different organic forms, preserving the more efficient, destroying the less efficient. The question raised by this new theory is, What sort of forms are subjected to the action of natural selection? Is there a complete gradation of forms between two extreme conditions and is natural selection called upon to choose from this whole series the one which is organically most efficient, or is the task simpler and is the choice made merely between two widely separated conditions of the ideal series? Thus, we find within a species two varieties, one larger than the other. Have they diverged by gradual cumulation of minute differences in size, or by a single step? These alternative views are known, respectively, as the selection theory and the mutation theory. Both views were recognized by Darwin as possibilities, though he seems to have attached more importance to the process of gradual modification. Most of his followers have given attention exclusively to this process, but a few, like Bateson and de Vries, have regarded modification by

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steps as the more important process, if not the only one efficient in the formation of new species. Bateson ('94) has called modifications of this sort discontinuous variations, but de Vries (:01–:03) calls them mutations, and the latter designation seems likely to be generally adopted.

Darwin rightly attached great importance to the variations of domesticated animals and plants as throwing light on the origin of species. He recognized that there is no essential difference between breeds and species, and that if we can ascertain how breeds originate we can infer much as to the origin of species. He made an extensive study of breeds of animals as well as of plants, but no one has followed this up or even recognized its great importance until within very recent years. What we need to know is how, precisely, are new breeds formed. We know that they are forming under our very eyes all the time and that this has been going on since the earliest historic times and no doubt a great deal longer, yet the method eludes us.

The successful practical breeder, the man who originates breeds, is a keen observer, a man of unusual intelligence and skill and of infinite patience. Yet if we ask him how, in general, he does his work, or how a particular result was obtained, we rarely get a satisfactory answer. This is sometimes because, for commercial reasons, it is well to leave a cloud of obscurity surrounding the origin of a successful breed, lest its production be duplicated. More often, however, it is because the breeder himself does not know how the result was attained. He may be able to tell us that such and such animals were mated, such and such of their offspring selected, and after a certain length of time the breed was established and put on the market. But this, after all, gives us little information as to the real nature of the material used and the processes involved in the formation of the new breed. The aims of the biologist are so different from those of the practical breeder that to solve the theoretical problems involved in the formation of breeds the biologist must himself turn breeder, and see new organic forms arise out of material with which he is thoroughly familiar, and under conditions which he can control. So little work of this kind has yet been done that its fruits are scarcely ready to be gathered. Generalizations can as yet be made only tentatively, based on cases dangerously few, or on the rather uncertain and often contradictory testimony of practical breeders and the half-truths told by stock registers.

So far, however, as these various sorts of evidence go, they indicate that the material used by breeders for the formation of new breeds consists almost exclusively of mutations. The breeder does not set to work with some purely imaginary form in mind, toward which he seeks by selection gradually to mold his material. He commonly either *discovers* the new breed already created and represented by one or more exceptional individuals among his flock, or else he seeks by cross-breeding to combine in a single race characters which he finds already existing separately in different races. In both cases he deals with mutations, *i. e.*, with characters unconnected by a series of transition stages with the normal form. An illustration from my own experience may help to make this clear. A little more than four years ago I obtained a number of ordinary smooth-coated guinea-pigs and began breeding them with a particular experiment in mind. Among nine young produced by a certain pair, there was one which had a supernumerary fourth digit on one of its hind feet. Neither of the parents had such a digit, nor had I ever heard of the existence of such a character before, either in any of the wild Caviidæ, or among domesticated cavies or guinea-pigs. Further, I have been able to find no reference to such a thing in the literature of the group, though I have several times since found this same mutation in other herds of guinea-pigs. The mother of my four-toed pig never produced another similar individual, though she was the mother in all of thirty young. The father, however, who sired in all 139 young, had five other young with extra toes, but these were all by females descended from himself, so that it seems certain that the mutation had its origin in this particular male. By breeding together the four-toed young and selecting only the best of their offspring I was able within three generations to establish a race with a well developed fourth toe on either hind foot. This race was not *created* by selection, though it was *improved* by that means. Like the poet, in the proverb, it was *born,* not made. Any amount of selection practised on other families of my guinea-pigs would probably never produce a four-toed race, for though carefully watched through as many as seven generations no four-toed pig has appeared among them.

In a second family of my guinea-pigs, which, like the other, was for the purpose of a particular experiment inbred, a different mutation made its appearance. A few individuals were found to have hair about twice as long as that of their parents and grandparents. Intermediate conditions did not occur. Long-haired individuals mated together were found to produce only long-haired young, so that a new breed was already fully established without the exercise of any selection. It was found, in short, that the long-haired character is a Mendelian recessive in relation to the normal short coat, so that matings between long-haired and short-haired animals produce only short-haired young. But these young bred *inter se* produce a definite proportion (about one fourth) of long-haired young, and if no selection is practised among their offspring, but all are allowed to breed freely, the race will continue to contain this proportion of long-haired individuals.

If such a mutation as this occurred in a state of nature, and such a possibility we can scarcely question, a dimorphic species would be the immediate result, containing two varieties alike in every respect except length of hair, in which they would be sharply separated. The two varieties would coexist in the same habitat and might continue to interbreed freely without the destruction or necessary modification of either. Natural selection would now come into operation to choose between the two that one which was more advantageous and the other condition would be gradually eliminated from the race. Or if the two conditions were each the better in a different habitat, then by the gradual destruction of the other in that habitat the two varieties would become geographically separated, though they might continue to coexist in an intermediate zone.

The second method which I mentioned for the artificial production of new breeds is to combine in one race characters already found in different races. This is accomplished through cross-breeding and is made possible by the facts (1) that mutations are alternative in heredity to the normal condition, and (2) that one mutation is entirely independent of another in heredity. If, for example, we cross long-haired with short-haired guinea-pigs, we get, among the second-generation offspring, a mixture of long-haired and of short-haired animals, but, as a rule, no intermediates. Further, if in the original cross one parent was four-toed and the other three-toed, then in the second generation offspring we get all possible combinations of the characters involved in the cross, viz., long-haired four-toed animals, long-haired three-toed, short-haired four-toed and short-haired three-toed. From this array of forms the breeder may now select the particular combination of characters which suits his purpose.

Can we doubt that in nature a similar choice is offered between every mutation and its opposite, combined or uncombined with every other mutation then present in the race?

It is true that cross-breeding may affect to a greater or less extent the nature of the characters involved in a cross, but this sometimes facilitates the creation of desirable breeds, for it serves to induce new mutation, which in some cases is progressive, in others regressive. For example, in guinea-pigs, a cross between a coal-black animal and an albino may restore in the young the ancestral, or 'agouti,' coat consisting of black hairs ticked with reddish yellow, or in other cases may result in the production of a black-white spotted animal. By selection either of these conditions may be perpetuated in a distinct breed. The one is a regressive or reversionary change, the other progressive in that it leads to the production of a new type of pigmented coat.

On the whole, it appears that the formation of new breeds begins with the discovery of an exceptional individual, or with the production of such an individual by means of cross-breeding. Such exceptional individuals are mutations.

An examination of stock registers points in the same direction. The beginnings of new breeds are small. Pedigrees lead back to a few remarkable individuals or to a single one, as in the Ancon sheep. But given the exceptional individual, and a new breed is as good as formed. The few generations which the breeder usually employs in 'fixing' or establishing the breed and during which he practises close breeding serve principally to free the stock from undesirable alternative characters, not to modify the characters retained.

Modification of characters by selection, when sharply alternative conditions (*i. e.*, mutations) are *not* present in the stock, is an exceedingly difficult and slow process, and its results of questionable permanency. Even in so-called 'improved' breeds, which are supposed to have been produced by this process, it is more probable that the result obtained represents the summation of a series of mutations rather than of a series of ordinary fluctuating variations. For mutations are permanent; variations transitory. A moment's reflection will indicate the probable reason. Variations which are distributed symmetrically about a modal condition, so as to produce when graphically expressed a frequency of error curve, represent the result of a number of causes acting independently of each other. These causes are principally external, consisting in varying conditions of food-supply, temperature, density, moisture, light, etc. These conditions alter from generation to generation, and so do effects dependent upon them. Mutations, on the other hand, have an internal origin, in the hereditary substance itself. They are relatively independent of the environment, being affected only by such causes as affect the nature of the hereditary substance itself, one of which apparently is cross-breeding.

There are, however, frequently found in breeds of domesticated animals conditions which are *not* sharply alternative in heredity to the corresponding characters of other breeds. It is an open question whether such conditions could be maintained if cross-breeding were freely allowed with animals of a different character. If not, they could scarcely become racial characters, under the action of natural selection. The race would then become, not sharply dimorphic or polymorphic, as is the case where inheritance is sharply alternative, but subject to extremely great fluctuating variations. It is open to question whether blending characters of this sort found in many breeds may not have been created by selection from masses of fluctuating variations. It will be important to know further whether or not these extreme fluctuating series have had their origin in mutations. Not improbably, as de Vries has in part suggested, one-sided variation curves indicate the occurrence of mutations of this sort.

The Mutation Theory From the Standpoint of Cytology: EDWIN G. CONKLIN, professor of zoology, University of Pennsylvania.

I. The mutation theory is founded upon the idea that mutations are primarily germinal, that they arise in one or both of the sex cells and only later appear in the adult organism. In contradistinction to certain theories of evolution which are concerned chiefly with the modifications of adult structures, the mutation theory is primarily concerned with modifications of the germ, and here it comes into direct relation with the science of cytology.

De Vries tells us that the foundations of the mutation theory were laid in his doctrine of intracellular pangenesis. Like Darwin, Galton, Weismann and many others, he recognized the fact that the method of evolution is at bottom a problem of inheritance and that, in the words of Osborn, 'When we have reached a heredity theory that will explain the phenomena of inheritance, the method of evolution will itself be a thing of the past.'

It seems like a mere truism to affirm that the evolution of animals and plants must be accompanied by an evolution of their germ cells, and that the principal problem of evolution is not how modifications are produced in adults, but how they arise in the germ. And yet with few exceptions previous theories of evolution have concerned themselves only with the transmutations of adult forms and have paid no attention to the modifications of the egg or sperm or embryo. The mutation theory is a theory of the evolution of organisms through the evolution of their germ cells and it is, therefore, founded primarily upon cytological phenomena.

An antecedent objection to any such theory is the very general opinion that the germ cells are composed of 'simple, undifferentiated protoplasm' and that they do not contain specific morphological elements upon which evolutionary forces might act. However, such a view is supported neither by observation nor by the latest and most careful experiments. We know that the cell is vastly more complex than was assumed a few years ago, and there is no good reason for supposing that all of its visible structures are now known. The fact that fragments of eggs may in some instances give rise to entire embryos does not necessarily imply, as is usually assumed, that the egg is undifferentiated. In eggs, as in adult forms, the degree of differentiation may be largely independent of the power of regeneration or regulation, and certainly such experiments do not nullify the most positive and direct evidence, drawn from many sources, as to the complexity of the germ.

Extensive studies which have been made upon the structure of the nucleus have brought to light a degree of organization in this part of the cell which was wholly unexpected. It has long been known that in any given species the number of chromatic threads or chromosomes in the nucleus is constantly the same in all kinds of cells, except in the last stages of the formation of the sex cells, where the number is one half the normal; in the union of the egg and sperm nuclei in the fertiliza-