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Some results of an experiment on dominance in poultry, with special reference to polydactyly. By Prof. R. A. FISHER, F.R.S. (Visitor).

WHAT I have to say concerns mutations, but mutations viewed from an aspect so different from that of the exponents of the mutation theory that I must begin by emphasizing the contrast. Exponents of the mutation theory, such as T. H. Morgan (I), regard it as an alternative theory to Darwin's theory of selection. The course of evolutionary change is thought to be *explained* by mutations. If so, then necessarily mutations are the true agencies of the creation of living things. The mutant animal, or plant, as it appears in our cultures, should be regarded on this view as a step in evolutionary progress, new-minted, as it were, from the hand of the Creator. If theistically inclined, we should perhaps regard it with some awe—God's new idea for *Drosophila melanogaster.* At all events, they are regarded as the actual causes of evolutionary change—but are they? That is the question I want to discuss, and to answering which I hope such facts as I have to give may contribute.

The question deserves our most careful consideration, so careful that I must ask my audience to assist me in a very difficult undertaking. It is not that I mean to put forward any complicated argument—on the contrary, all I shall do is to describe a simple, though prolonged experiment, and to exhibit some of the results. The really difficult thing that I ask is to avoid *assuming,* at least during our discussion, either that mutations do, or that they do not, govern evolutionary change—to maintain an open mind on this point while the evidence is being considered, and so to give the evidence a fair chance of carrying whatever conviction it may be entitled to.

This caution is made necessary by the fact that the assumption is a very old one in biological thought. Whatever novel elements mutationists may associate with their evolutionary views, their basic assumption was taken for granted by the pre-Darwinian evolutionary writers. That stalwart Lamarckian, Samuel Butler, put it thus :—'To me it seems that the "Origin of Variations", whatever it may be, is the only true "Origin of Species".' Indeed, the assumption is implicit in Lamarckism. To the earliest writers the problem of evolution appeared merely to be one of explaining mutations, that is to say of explaining heritable innovations. Effort and striving, use and disuse, hormones, and orthogenetic urges are all attempts to set up such an explanation. All the time it was assumed that if the explanation *worked,* if the mutations were duly produced, then evolutionary change would follow. That the evolutionary effect should fail, even though the mutations were duly produced, was a possibility that never seemed to require consideration. So far from being a novelty, therefore, the mutation theory is rather a bare residuum of the older alternatives to natural selection, when each is stripped of its more distinctive features.

The very name 'Mutation-theory' must have a certain attraction for the leading workers with *Drosophila,* who have discovered so many mutations. Yet it does not follow that their discoveries support the theory. A survey of the mutations found in this fly reveals three outstanding facts, which, I believe, are not disputed :—

(i.) The mutations are found, some certainly, and the remainder probably, to be recurrent; many have appeared repeatedly in ordinary cultures, and others are found to be inducible at a measurable rate by X-rays. We should probably think of the whole group as occurring spontaneously at the rate of about one in a million in each generation. A few have higher rates, but of those with rates much lower it is probable that few have occurred, and been discovered, in experimental cultures. Mutations with much lower rates may therefore exist, but at present we can know nothing about them. The relatively frequent mutations which are available for study, have spontaneous mutation rates sufficient to ensure that many thousands, or more probably millions of mutations of these kinds occur in the species in every generation.

(ii.) They are, as a whole, markedly deleterious in their effects on the fly, often the effect is sublethal, while the largest class of those readily detectable is absolutely lethal in its effect.

(iii.) In their inheritance, the mutations are nearly all recessive. In a summary of 221 non-lethal mutations in *Drosophila melanogaster* I found 208 described as recessive,

while in the remaining 13, though they are conventionally called dominants, this only means that the heterozygote is distinguishable from the wild type, and not that it is indistinguishable from the homozygous mutant, from which, I understand, it differs in every case. In these cases, therefore, dominance is absent or incomplete. I understand that in other species of *Drosophila* there are a few cases in which dominance may be regarded as complete, but such rare instances, even if they are well substantiated, do not affect the general tendency for the recessives enormously to outnumber the dominants.

It is interesting to recall that East and Jones (3), discussing similar facts in maize, perceived that this immense preponderance of recessives required an evolutionary explanation. They suggested that, owing to the prevalently deleterious effect of the mutations, it might be accounted for by the selection of genotypes in which the mutation-rate of dominants was extremely low, while such adverse selection would be much less in recessives. I do not think that the selection of mutation-rates can itself be effective at the very low levels which these rates ordinarily possess, though it would be at higher levels. As I was led later (2) to suggest an evolutionary explanation of the prevalence of recessiveness among mutations by a somewhat different process, I should like here to acknowledge the priority of the interesting suggestion which East and Jones put forward.

My own suggestion was based on a very large number of observations, made since East and Jones wrote, showing that the effects of Mendelian factors, or, more concretely of gene-substitutions, can be largely modified by other heritable factors. One way of putting this is, that what we call the effect of a mutation should be regarded as the reaction of the organism as a whole to that particular gene-substitution, a reaction which naturally depends as much on the nature of the organism as on that of the substitution concerned. Another way of putting it is that the effects of a gene depend on the internal environment which the organism provides, and in which it exerts its developmental effects. In any case, it is abundantly proved that the same gene-substitution produces very different effects in different organisms, and that the effect of a Mendelian factor has frequently been much modified by intentional or unintentional selection.

My theory of the modification of dominance is merely the application of this general fact to that particular feature of a Mendelian factor which we call dominance—that is, to the extent to which the heterozygote resembles one of the two corresponding homozygotes more nearly than the other. The theory was put forward only after a deliberate examination

of the magnitude of the changes to be expected from the selection of factors affecting dominance, and after finding that, though these were very minute, they were yet of an order of magnitude which, unless some unknown cause opposed them, would certainly produce nearly complete or complete recessiveness in mutations which had persisted in occurring at the current rates for anything like a million generations.

The fact that different species show mutations which may be shown to be homologous seems to prove that many mutations must be extremely ancient; further, if we take the view that a mutation such as albinism is the same in different orders of mammals, or even in more distant verte-brates, we must think of this mutation as having continued to occur over an enormous period.
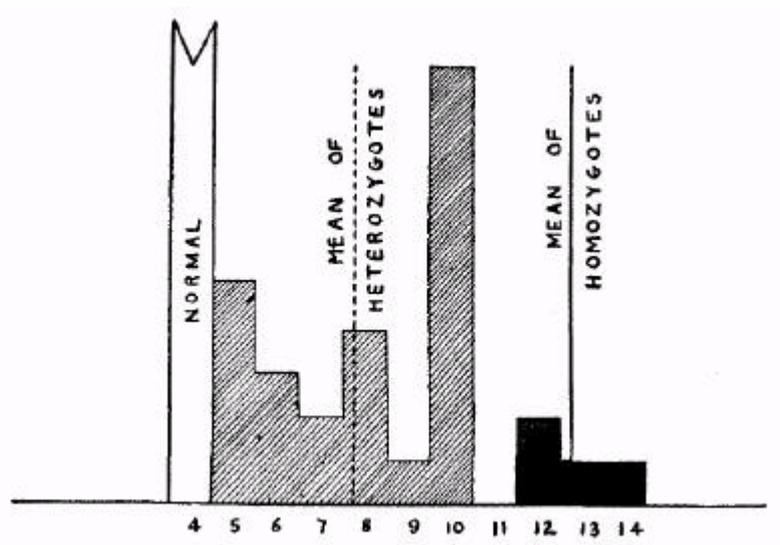
I need not now go into the further evidence which, since I originally put forward the suggestion, has extended the application of the theory of dominance modification to a range of phenomena, especially in the polymorphic species, much wider than that on which I originally put it forward. Let me turn at once to the case of domestic poultry, with which, since it was supposed to exhibit facts contrary to those on which my theory was based, I was led to commence experi-mentation about five years ago.

A large number of the factors in which domestic breeds differed from the wild jungle-fowl had been described by poultry geneticists as dominants. From the literature, one would judge that in many of these cases dominance was complete. In a number of cases it is now known that this impression is misleading, and factors like those for Frizzled plumage, for Spangle, or for Pea-comb can at once be set aside as showing no more complete dominance than do the *Drosophila* mutations. Nevertheless, it is clear that domestic poultry seem to differ from all other species equally thoroughly investigated, both in the large number of apparent dominants in the domesticated breeds and in the comparative completeness of the dominance when it was observed.

In puzzling over this exceptional state of affairs, it occurred to me that possibly human selection during the process of domestication had been responsible for both these features, and in particular that, if we suppose the jungle-fowl to have been brought into domestication, at first gradually, by jungle tribes, they could not, and would scarcely have attempted to, prevent their flocks from being freely covered by wild cocks. In these circumstances, the novelties, by which man is always attracted, could only be perpetuated if they were at least partially dominant; so that an excessive proportion of partial dominants might, for this reason alone, be expected

in our domesticated breeds. Further, if, as seems probable, selection was exercised among the offspring in favour of a more marked development of each characteristic, such selection applied to heterozygotes would constantly favour those modifiers which tended to make the factor more dominant or less recessive.

It was to test this possibility that human selection was responsible for the apparently exceptional genetic phenomena exhibited by poultry that I commenced, in 1929, to cross domesticated breeds, known to contain some of the best known dominants, back into the wild jungle-fowl. For, by introducing each of these supposedly dominant factors separately by repeated crossing into a wild strain, it seemed

that we should be able to ascertain what the genetic behaviour of the factor had been before any human selection had been exercised. The experiment was made possible by the kind co-operation of the Zoological Society and by funds generously supplied by Mr. J. Spedan Lewis and by the Royal Society.

In all I used seven supposedly dominant factors, of which three affected pigment, namely Pile or 'dominant' White, the sex linked mutant Barred, and the Black mesodermal pigment. Four affected structural characteristics, namely, Crest, Rose-comb, Polydactyly, and Feathered feet. For three of the seven factors tested, the results are so clear as to be already substantially complete, and these I have reported in a preliminary account now in the hands of the Royal Society. For the remainder, though I do not think

the results will show any substantial difference, it would be premature, at present, to report definite conclusions until test matings can be completed during the next two years. To avoid confusion, I will speak to-day principally of a single factor—polydactyly. I gave a full account of the results for Crest, which, incidentally, turned out to be the same as the recessive Hernia, at the Genetical Society last December.

Polydactyly was obtained from Japanese 'silky' pullets, which were crossed, in 1929, with a wild jungle cock from the Zoo. During the four next years, polydactyl offspring from the previous year were continually mated with a wild strain presented by Mr. Spedan Lewis. In the sixth year, 1934, polydactyl young were interbred for the first time, thus making possible the production of homozygous polydactyls. My experience in the previous years had been confined to heterozygous birds, and I had no idea what further modifications, if any, to expect. If polydactyly had been properly described as a dominant, the homozygotes should, of course, have been indistinguishable from heterozygotes, and I should merely have obtained a frequency ratio of three polydactyls to one normal.

The results of the crossings of the first five years were as follows:—

	Normal.	Polydactyl.	Total.
1929	17	17	34
1930	63	81	144
1931	—	—	—
1932	14	11	25
1933	6	4	10
	100	113	213

In 1934 four broods out of five showed feet of a new type, readily distinguishable from the heterozygotes. Of the chicks hatched there were six of these homozygotes out of twenty-five, or, including embryos which died in the shell, six out of thirty-one. Either proportion is as near as we should usually get to the 25 per cent. expected. Of the homozygotes, two pullets survive, and can be tested next year. Of the remaining four, which have died at various ages, I have preparations among the exhibits.

To appreciate the differences between the two types, it is necessary to examine the feet of birds known to be heterozygous in some detail:—

(A) Among these there are a few with normal feet. A small proportion, perhaps 10 per cent., but probably less, have both feet normal, and cannot be enumerated in the mixed broods. When one foot is normal and the other polydactyl, of which I have seven cases out of a sample of twenty-five,

the normal foot is always on the right side, in accordance with the rule stated by Bond in 1920 (7).

(B) Rarer in my material, even than normal feet, is a foot with four toes, but with an extra joint in the hallux, making two phalanges in addition to the metatarsal and the claw. In my sample of fifty feet this appeared only once ; but I have other cases, and the frequency may be a little more than 2 per cent.

(C) A second type with three bones may be described as having a normal hallux, with an additional bone carrying a claw floating freely beside the phalanx or fused with the phalanx to form a Y. In this type, as in the last, one can count only three bones on the foot, apart from the claws. In my sample there were 28 per cent. of this type.

(D) The fullest development of the polydactyl foot in my heterozygotes has two halluces carried on different metatarsals, which may or may not be fused, and of these the outer or extra-hallux has always two phalanges, while the inner hallux is normal. There are, therefore, five bones to be seen in this type, which is the commonest, being found in twenty-eight feet out of fifty—or 56 per cent.

Apart from other variations, if we take the number of bones in this region, counting both feet together, as a quantitative variate, so that a normal bird has four bones, the numbers in my sample of twenty-five range from five to ten, with an average just under eight, so that the average, including a few birds normal in both feet, may be about seven and a half.

The birds presumed to be homozygotes in the 1934 broods are all characterized by having three phalanges in the extra hallux. In one case this is shown in only one foot, the corresponding terminal joints of the other foot being fused at a visible junction to form an abnormally long second phalanx. Neither foot would be mistaken for that of a heterozygote, for, in addition to the extra toe being long and stiffly articulated, the metatarsals of all the homozygous birds are abnormally large. Instead of resting against the cannon-bone, they project across or along it on the outside, so that they can be felt and seen on the outside of the foot. I have never seen this development in a heterozygote. The numbers of bones in the four available specimens are eleven*, twelve, thirteen, and fourteen respectively, the average being twelve and a half, to be compared with an average of seven and a half to eight for the heterozygotes and of four for the normals.

* These are the four homozygotes shown in the figure, p. 75; it is now clear that the bird to which the number eleven refers had these distinct phalanges in both extra halluces. The number should, therefore, be twelve, as shown in the figure.

The case is, therefore, a typical one of absence of dominance. The heterozygote is intermediate, and usually distinguishable from both homozygotes, though occasionally it resembles the normal. Such slight departure from complete inter-mediacy as exists is in the direction of recessiveness.

In its dominance, therefore, this factor bears out entirely the anticipations with which the experiment was planned, as do also the factors for Crest and Hernia and for Barred, The case of Crest is particularly interesting, in exhibiting a phenomenon the importance of which was first pointed out by Ford, in that, like several other mutations having more than one effect, it is completely recessive in the cerebral hernia, but shows lack of dominance in its relatively harmless manifestation—that is, in the crest itself.

The barred factor inclines, as the exhibits show, to reces-siveness, though here again the heterozygote is clearly intermediate and distinguishable from both homozygotes. In this factor it is interesting that, since the barred female resembles the *heterozygous* male, the factor when introduced into wild stock produces a sexual differentiation, apparently the same as that which Punnett and Pease have utilized in the development of their new breed, the Cambar.

In the light of the reaction of the wild jungle-fowl to poly-dactyly, we may consider the three views which have been formed on the behaviour of this factor in crosses between domesticated breeds.

First, Bateson did not consider that dominance was imperfect in this case, but that its incidence was variable and irregular. He drew the distinction with some emphasis in 1909 (4, p. 53).

'Imperfection of dominance does not even obscure the application of Mendelian analysis. The cases in which difficulty does arise are those in which dominance is irregular and the recessive class cannot be distinguished with certainty In the fowl, for instance, the extra toe is usually a dominant, but in some strains there is irregularity, and birds without the extra toe may nevertheless transmit it.'

With respect to the cause of the irregularities he adds :—

'It is not impossible that they may be ascribed to inter-ference caused by the presence of other factors in various combinations, and sometimes, no doubt, to disturbance by external conditions.'

The next view I need quote is that put forward by Punnett and Pease, who assembled the results of a large number of matings involving this factor. Their conclusions are as follows (5):—

'It is evident also that this factor can be carried by an apparently normal 4-toed bird. This is probably due to the

existence of a factor (or possibly factors) inhibiting the action of the factor for polydactyly, and this factor (or factors) may be carried by normal recessive 4-toed birds. Further, since the evidence points to polydactylous birds being also capable of carrying the inhibitor, we must suppose that we are also concerned with some other factor, or factors, rendering possible the manifestation of the polydactylous effect in spite of the presence of the inhibitor. But although we have devised various schemes along these lines we have not found one which we consider satisfactory. Our failure, however, has been due more to lack of necessary data than to antagonistic facts.'

These authors, therefore, seek to explain the apparent irregularity of dominance by postulating, *first,* an inhibitor capable of reducing genetically polydactylous birds to the four-toed condition, and, *second,* a super-inhibitor capable of permitting the expression of the five-toed factor, even when the inhibitor is present. I need only mention one consequence of this theory, namely that, if it were true, it must be possible to make up two strains, both uniformly four-toed, which on crossing will throw a proportion of five-toed young in the second generation. This has never been done. It must be possible further, by the use of the super-inhibitor, to make up two more strains, both uniformly five-toed, which on crossing will yield a proportion of four-toed young in the second generation. This also has never been done. Until at least one of these feats has been accomplished, it seems highly conjectural to postulate the existence of either of these inhibitors.

Immediately following the paper by Punnett and Pease, J. B. Hutchinson(6) put forward the view that the whole of the data could be simply explained without the aid of inhibitors, on the view that dominance in polydactyly varied in different breeds from almost complete dominance at one extreme to almost complete recessiveness at the other, these differences being due to modifying factors capable of influencing the degree of dominance of polydactyly. This proposal of Hutchinson's is in entire accord with the imperfect dominance found in the wild fowl and with the small proportion of heterozygotes with normal feet. It requires that in some breed-crosses this proportion is larger than I have found, and suggests that in other crosses the heterozygotes may overlap or even be indistinguishable from the homozygous polydactyls.

Let us now consider the mutant for polydactyly, in the light of the mutation theory, as a potential agency of evolutionary change. If the mutation, or something having like effect, did not occur in other birds and at other periods of the earth's history, it would be an odd coincidence that it should have

occurred in the particular bird of which we have the best evidence and in the human period. We should be straining at probabilities if we did not suppose that it occurred, perhaps with varying mutation-rates, in the other ten thousand species of birds, and had occurred throughout the fifty or hundred million years of their evolutionary history. I am told, in fact, that it has been found in ducks, and in pigeons, but I can say nothing of its inheritance in these species. If we admit this view as probable, we may ask, ' What has been the evolutionary effect of all this mutational activity?' and, as far as wild species are concerned, the answer is certainly that it has had absolutely no effect in increasing the number of toes. Something like a dozen species, say one per thousand, have *lost* a toe in the course of descent, and the ostrich is, I believe, unique in having lost two toes, but the extra-hallux has not established itself in even a single species. Of course, a *selectionist* would say 'Why should it?' but it is to mutationists that I put this case, as a fair sample of the efficacy of mutation as a means of controlling evolutionary change.

Selectionists naturally are not inclined to deny the importance of mutations in general as a condition of evolutionary progress in the future. This function is quite a different one from that ascribed to them by mutationists. However, ineffectual mutations may be as direct causes of evolutionary change, they serve, after the more definitely deleterious have been sorted out, to replenish the fund of heritable variation carried by every species, and to prevent that fund from ever becoming exhausted. This fund is the raw material from which further adaptive improvements can be fashioned. If, as is practically inconceivable, it could be exhausted, further selective improvement would cease. To acknowledge this is very far from admitting that the argument can be short-circuited to the conclusion that mutations are the effective cause of evolutionary change ; for this would be to eliminate the whole chain of complex processes, by which differential rates of death and reproduction are brought about, and in turn modify the heritable composition of the species. It would be roughly equivalent, logically, to saying that the weekly toll of deaths on our roads is caused by the fact that wheels will turn on axles!

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COMMENT

The original paper is followed by a discussion which includes a reply by Fisher.