A SUGGESTION CONCERNING THE POSSIBLE ROLE OF PLASMAGENES IN THE INHERITANCE OF ACQUIRED ADAPTATIONS

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(With One Text-figure)

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1. INTRODUCTION

The idea that acquired characters can be inherited recurs with a persistence which can largely be attributed to two factors. There are many circumstances in which an ability to inherit acquired adaptations would appear to be advantageous; and to anyone understanding little of the nuclear organization of the principal genetic determinants, the idea is a natural one which presents no special difficulties.

But whenever this idea has been put forward, it has been rejected by most geneticists. The reason has been partly the lack of critical evidence, and the fact that such inheritance was quite contrary to common experience; and partly the difficulty of imagining any mechanism by which the hereditary determinants could be altered by environmental influences in an adaptive manner. During the past decade or so we have come to know very much more about the properties of these determinants, and it is worth while re-examining, in the light of our greater knowledge, the possibilities for the existence of a material basis for the inheritance of acquired adaptations.

2. CONSERVATISM AND FLEXIBILITY

It seems reasonable to suppose that the regular inheritance of all adaptations would be disadvantageous. Genetic systems are a compromise between two opposing principles, conservatism and flexibility (for a fuller discussion, see Thoday, 1953). If the average genotype of a population of one species is that best fitted to the environment, and if the latter does not change through many generations, it is obvious that maximum efficiency of inheritance requires the maintenance of the same average genotype through many successive generations. It is less obvious, but equally true, that the same thing holds when the environment fluctuates from generation to generation, without there being any progressive change in it; with such fluctuations, it may be quite impossible from the environmental conditions of one generation to predict those of the succeeding one, and any adaptations acquired by the former generation may be quite irrelevant for the latter; their inheritance might then be worse than useless.

Nevertheless, environmental fluctuations have to be met by the species. To a certain extent this is achieved by selection altering the average genotype of the population. But this is inefficient; not only does it involve excessive wastage of zygotes, but

essentially the same argument applies here as was used in the previous paragraph. Much more efficient is phenotypic plasticity, where any one genotype may have a range of phenotypic expression, arising from environmental influences and sometimes related in an adaptive way to them, but not being capable of transmission in a hereditary manner. The ideal system would be one in which environmental fluctuations are met by phenotypic variability while continuity is maintained by a conservative hereditary mechanism; such a mechanism is well provided by nuclear genes, relatively unchanging except for rare, irrelevant mutation.

3. Adaptation to a new environment

But notwithstanding the preceding discussion, a good case can be made for the view that there are certain circumstances in which the ability for adaptations to be inherited would be of advantage. Such a circumstance would arise in the quite different situation where there is sudden progressive, more or less permanent, change in environment, whether this arises from an alteration in the characteristics of the particular environment or from migration into a different geographical area. In this case, the adaptive modifications of a generation in an unusual environment will be relevant for its succeeding generation, for this will now find itself in conditions tending to resemble those of its parent generation rather than those normal to the species.

Even if this situation could be met by an extension of the range of phenotypic plasticity, it is unlikely that this would be efficient enough to be a permanent solution. In experiments with *Drosophila melanogaster*, Waddington (1952, 1953) produced a phenocopy of crossveinless. At first, this was a typical acquired character, not heritable, and an expression of the phenotypic plasticity of the flies used. But after fourteen generations of artificial selection for this character, it was found that its appearance had become partly subject to genetic control; the environmental stimulus became less important for its production than the appropriate genotype. The implication of this is that while high phenotypic plasticity may serve for a few generations, it is inefficient when compared with genetic control of adaptively desirable modifications; in these experiments there was selection pressure favouring genetic control rather than phenotypic plasticity. This question has also recently been discussed by Simpson (1953).

If the conclusions of the preceding paragraph are correct, and if acquired characters can never be directly inherited, then it would appear that the most efficient way in which a species can adapt itself to a new environment is by high phenotypic plasticity (comparatively inefficient) holding the situation while natural selection modifies the genotype in the appropriate direction; modification by natural selection is far too slow for natural selection to be the only agent in such adaptation. There still remains the disadvantage that each generation would have to start from practically the same point as did the preceding one.

From these considerations it seems to the author that it can reasonably be argued that, in the circumstances we are considering, it would be of advantage to the second generation in a new environment if it could inherit to some degree at least the adaptive modifications of the first, and so start life already adapted in some measure to the still abnormal environmental circumstances (i.e. abnormal for the species). If one could imagine a genetically controlled mechanism whereby this inheritance of acquired adaptation could be brought about, one could go further and suggest that if such a mechanism is possible,

then because of its advantage it could be expected to have come into existence through the ordinary processes of natural selection.

There is clearly a difficulty in supposing the simultaneous advantages of conservatism and flexibility in heredity, and the difficulty would be even greater if one tried to suggest that the same genetic mechanism was responsible for both. There is no justification at all for departing from the long-established belief that nuclear genes cannot be agents of the inheritance of acquired characters. Nor is there any need to do so.

The main reason for the rejection of Lamarckian ideas, both old and new, has been the implication in them that qualitative genetic change is involved; that is, that the nature of genetic determinants may not only be altered by environmental influence, but altered in such a way that their new activity leads to greater adaptation of the organism. There is no evidence acceptable to the author of any environmentally induced change in gene structure, apart from the purely random effects of mutagenic agents; while the possibility that any induced change should be adaptively related to the causal agency seems to be so very slight that the idea of such a remarkable coincidence has quite properly been discarded. There is no point at present in looking for any induced adaptive gene change of a qualitative character.

4. QUANTITATIVE GENETIC CHANGE

The situation with regard to quantitative change is very different, and two possibilities suggest themselves.

First, consider ordinary Mendelian inheritance. One of the most important properties of the chromosomes is that in actively growing undifferentiated tissues, they reproduce themselves as a general rule at the same rate as the cells containing them. Further, the different members of a chromosome set reproduce at the same rate as one another. This leads naturally to the assumption that the genes reproduce at the same rate as the cells containing them, and at the same rate as one another. There is no intention here of departing from this assumption, but it must be emphasized that it is only an assumption, and one for which we have no direct evidence; it arises from the belief that the gene always reproduces at the same rate as the chromosome. The contrary assumption, of different rates of multiplication of different genes within one genome, would not only raise problems of dominance; there is also against it the consideration that one of the most important properties of the chromosome system may be that it is a way in which gene reproduction can be tied to cell reproduction; any serious discrepancy could lead not only to genetic unbalance, but to loss of a gene altogether. It is probable that in the early evolution of a structured genome, it was precisely this tying together of cell and gene reproduction that gave a selective advantage to the formation of chromosomes and led to the evolution of mitosis (Crosby, 1955).

We therefore need not consider the quantitative relationships of nuclear genes any further. On the other hand, it is well established that there are genetic determinants whose reproductive activity is not firmly tied to that of the cell; these are the cytoplasmic determinants, of which only plasmagenes will be considered as specific examples.

There seems to be no particular reason why plasmagenes should reproduce in step with the cell. In fact, we know that they do not always do so. For example, working with killer strains of *Paramecium*, Preer (1946) showed in one strain that under conditions favourable for rapid growth of this unicellular organism, the kappa particles failed to keep

up the same reproductive rate as the organism; thus they declined in concentration per cell, and, what is particularly relevant to this discussion, the killer activity was lost before their concentration reached zero. This is clearly a genetic change brought about by a quantitative plasmagene change, and there is no doubt that it is heritable. It is also reversible.

Darlington & Mather (1949) discuss this question of reproductive rate of plasmagenes. They point out that change in concentration of plasmagenes may occur in another way—by shortage of their specific precursors or food materials, which impairs their reproduction. The stress they lay on this aspect leads Darlington & Mather to the conclusion that any change in the normal plasmagene-cell balance must be in the direction of slower plasmagene reproduction and consequent decrease in concentration, and they say: 'The plasmagene can adapt itself directly to change outside the unprotected simple cell. But it can do so only by suicide. The effect is Lamarckian, but it is an effect of disuse only and not of use.'

Not only is this negative attitude towards plasmagene reproduction rejected in the present paper, but the contrary suggestion is made that the plasmagenes may in fact constitute a mechanism by which phenotypic adaptation may be inherited.

The idea can perhaps best be put forward by means of an entirely imaginary example.

Consider a plant A which is adapted to the relatively mild conditions usual for its species, but whose resistance to low temperature may be aided by plasmagenes which can be called R. We will suppose that under usual conditions the equilibrium concentration of R per cell is quite low. Now imagine that some seeds of A find themselves in a colder climatic area. The concentration of R in the seeds, inherited from their parent A, will now be too low; it may be so low as to afford no assistance to the germinating seeds. The resultant seedlings, B, will find growth difficult at the lower temperature, and many may die; those that live will grow slowly, that is, they will have a relatively low rate of cell reproduction. Now if we make the fundamental assumption that reproduction rate of R does not fall to the same extent, then its concentration per cell will steadily increase. By the initial proposition, a young plant B will consequently become more able to withstand the colder conditions; although its growth rate will then increase, the reproduction rate of R will remain for a time greater than that of the cells, and R will continue to increase in concentration, although more slowly with time. Eventually, a new equilibrium concentration of R may be reached, and it will be higher than that of the parent plant A which was growing in the milder conditions.

The logical consequence of this is that the seeds and young embryos produced by the plants B will have a considerably higher cell concentration of R than had the seeds and embryos produced by A (which are the seeds and embryos from which B developed), since these were formed in the milder conditions in which A was growing.

Now, unless we have very wide dispersal, the majority of seeds produced by B will come to germinate in temperature conditions similar to those in which they were formed, that is, cold ones. But these seeds and their embryos already have a high R concentration, and the seedlings C developing from them are therefore from their germination much better adapted to withstand the cold. Thus the plants of this next generation C begin life having inherited the adaptation to cold achieved by their parent generation B. This would clearly be of great advantage to them, since they can get away with a much better

start than the seedlings B, and correspondingly with a better start than they would have had if they had not been able to inherit this adaptation to cold from B.

The situation would not of course be so simple as this. Not all the cells of a plant divide at the same rate. Some cease division and become non-meristematic or dormant; the question is, what then becomes of the plasmagenes? If their division also slows down, equilibrium concentration may not be reached in differentiated cells, and the meristematic tissues would in the end be expected to have the highest concentration of R; on the other

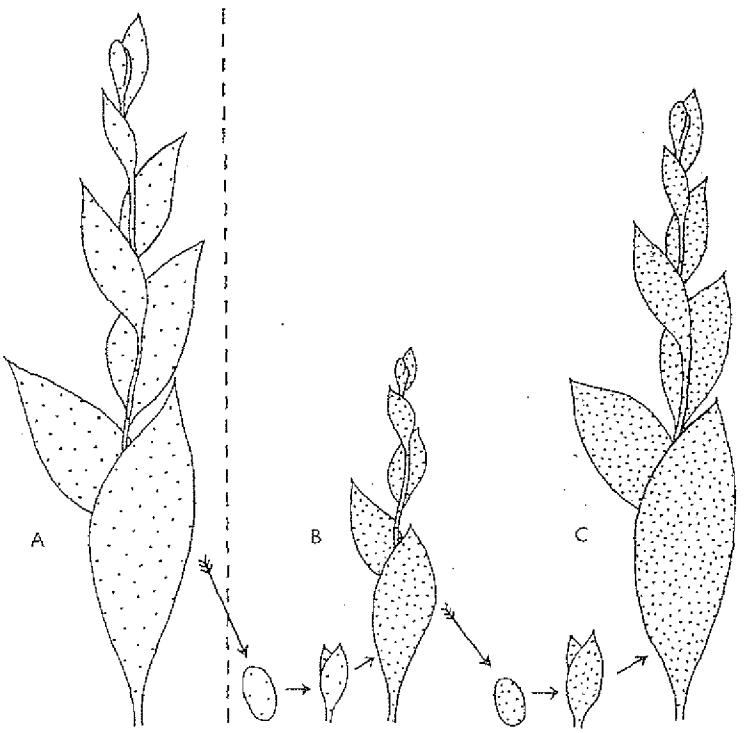

Fig. 1. Diagram illustrating the argument in the text. It shows mature plants of A, B and C, seeds of A and B, and seedlings of B and C developed respectively from these. The density of the dots represents the concentration of the plasmagenes R. The colder conditions in which B is growing are imagined to have decreased the rate of cell reproduction of B, but not of its plasmagenes. B therefore has fewer cells than A and is smaller, but has roughly the same number of plasmagenes. The higher plasmagene concentration appears consequently in the seeds of B, and in the resultant seedlings. The plant C is thus better adapted from the beginning to the cold, and has a higher growth rate than B; this also means that if there is any increase in concentration of R during the growth of C, it is much less than that during the growth of B.

hand, if plasmagene reproduction proceeds unabated in cells which have become non-dividing, then the non-meristematic tissues would come to have the highest concentration. But this consideration does not seriously affect the main argument; it is not unreasonable to suppose that the distribution of R among the different tissues of the mature plants is relatively the same for A, B and C. The author is not concerned with showing that a particular phenomenon exists, but only with showing that it must be considered as a reasonable possibility.

The relatively simple example which has been put forward suggests that a mechanism for Lamarckian inheritance might have an advantage for some organisms at least, and if

this mechanism could be under nuclear control there does not seem to be any reason why it should not come into existence by the selection of nuclear genes controlling plasmagene properties and reproduction. That nuclear genes controlling plasmagene reproduction exist can reasonably be inferred from the demonstration by Preer (1946) that in one of his killer strains of *Paramecium*, however he altered the rate of fission, the kappa concentration remained steady; that is, rate of kappa reproduction was tied to rate of cell reproduction. This indicates a genetic difference between the strains in regard to plasmagene reproduction.

If this is a general phenomenon, then it should be possible for a situation such as that exemplified here to evolve by the ordinary process of natural selection. Indeed, considering the advantage that may derive from the inheritance of adaptations, it would be surprising if it has never done so.

The simple way suggested here in which a plasmagene concentration may change is not the only possible one. If there is competition between plasmagenes within an organism, due for example to competition for substances necessary for reproduction, then the balance between the different plasmagenes would be quite likely to be upset by environmental changes, and this would result in changes in their concentrations. It would be as though there were a process of natural selection of plasmagenes within one organism in a single generation; environmental changes would alter the plasmagene concentration by first altering the selection pressures. Change of plasmagene concentration from this cause would work perfectly well in a system of inheritance of acquired adaptation, though perhaps such a change would be less frequently of adaptive value than one in the simpler circumstances imagined earlier; on the other hand, it might perhaps be more specific.

5. Controlled plasmagene systems

There is another way of looking at this question. The existence of chromosome organization suggests the high selective value of co-ordination of gene and cell reproduction. The fact that there exist genes independent of the chromosomes suggests that they too have a special part of their own in the machinery of heredity; it may well be supposed that this part is connected with their special property of not being tied in reproduction to mitosis, and that the resultant advantage to the organism possessing them has been the determining factor in the establishment and survival of plasmagene systems.

There are a number of ways in which such systems could play an important part. The view that plasmagenes are significant in differentiation is held by a number of workers. Senescence may well be due in some degree at least to changing plasmagene concentration (possibly resulting from loss of control by the nuclear genotype). But the kinds and properties of the cytoplasmic determinants may be many and various, and the demonstration of particular functions for some of them would not exclude the existence of different functions for others.

It must not be thought that the reproduction of a plasmagene, merely because it is not tied to nuclear reproduction, is therefore autonomous. Such a plasmagene system as is suggested in this paper would remain in being only if it were under nuclear control, just as it could only have evolved by a process of selection of the nuclear genes controlling it. This leads to a parenthetical but important conclusion; one fundamental difference between viruses and plasmagenes is that the reproduction of the former is largely out of

the control of the nucleus. If viruses ever do become plasmagenes, one condition must be that their reproduction has come under nuclear control; conversely, if a plasmagene of one organism becomes a virus in another, it must be because the genotype of the second organism lacks the necessary control; the King Edward potato comes to mind here (Salaman & Le Pelley, 1930).

6. WHERE EVIDENCE SHOULD BE SOUGHT

To the conclusion that one would expect Lamarckian methods of inheritance to have evolved through an orthodox process of natural selection of nuclear genes, the obvious objection arises that many workers have devised experiments to find Lamarckian effects, and have failed. This objection is not a serious one. The only kinds of adaptations likely to be inherited in the way suggested in this paper are those of a very general nature, bound up with conditions of growth and vigour. The activity of the plasmagenes involved is likely to be more general even than that of simple 'polygenes'. At the moment, it is only suggested that such a scheme would work where retarded or enhanced cellular reproduction would lead to change in plasmagene concentration, this change itself tending to restore the former rate of growth.

It is evident that many of the 'acquired characters' that have been used in Lamarckian studies fall well outside the requirements of this scheme. For example, such a thing as the inheritance of a learned ability in rats could not possibly arise on this basis; positive results are not to be expected from such experiments, because the investigators have been looking at the wrong kind of acquired characters. If the arguments presented in this paper are unconvincing, it is hoped that at least they may lead some of those concerned with trying to demonstrate the inheritance of acquired adaptation to look at the right kind of characters.

If the inheritance of acquired adaptation occurs at all, it is best looked for in general characters of growth and vigour, in response to environmental conditions affecting them. It may be more profitable to look for it in plants than in animals; in the latter, especially warm-blooded ones, the sex cells are developed at an early age, and are well protected from direct action of the environment. In many flowering plants, the flowers are developed late in life from meristematic tissue almost fully exposed to the effect of the environment. The plant embryo would seem to have more time and possibility than the animal embryo to acquire the ultimate adaptive plasmagene concentration of its parent. Besides, many animals have the ability not only to choose their own environments, but to choose the places where their young will develop, and the ability to inherit acquired adaptations may not have a very high selective importance in animals.

7. ADAPTATION IN BACTERIA

Some reference must now be made to bacteria. Here, the situation is very different from that we have been considering. A bacterial cell has a very high probability of being in the same environment as the cell from which it was derived—the environment remains constant for many generations; while if the environment does alter, there is little possibility that after one generation it will change back again. The question of environmental fluctuation does not arise. If a bacterial colony begins to grow in a strange environment, subsequent generations of bacteria within the colony will still be in the same strange

environment. The ability to inherit an adaptation is therefore of greater importance i bacteria than it is in higher organisms where environmental fluctuation without progres sive change is the rule. Moreover, the adaptations required by bacteria are often specifi adaptations to certain nutrients or other substances, and the purely general mechanism suggested in this paper could not suffice. A picture of the adaptation situation in bacteri has been given by Hinshelwood (1953).

It may be very significant that in one group where an efficient and more specific systen for the hereditary fixation of adaptation is required, it does seem to have in fact evolved It may not be unreasonable to suppose that in higher organisms, where the requirement: are simpler and more general, a system of Lamarckian inheritance may also have evolvec through natural selection acting on the system of nuclear genes, which have the supreme control of all other kinds of genetic determinants within the organism.

8. Summary

The view is put forward that acquired adaptation of a very general nature could be inherited by a system in which, when the growth rate of an organism is retarded by environmental conditions, the rate of reproduction of plasmagenes affecting that growth rate is retarded to a lesser degree or not at all. The consequent increased concentration of these plasmagenes is supposed to tend to restore the original growth rate (the organism thus becomes adapted to the new conditions). This leads to a new, higher, equilibrium concentration of the plasmagenes, and it is further supposed that this is passed on in reproduction to the next generation, which in this way inherits the adaptation.

It is further argued that rate of plasmagene reproduction is subject to control by nuclear genes, and that systems such as that suggested could have come into being by the ordinary processes of natural selection of nuclear genes.

Inheritance of acquired adaptations must be looked for in general characters of growth and vigour, and not in specific characters such as those of morphology or behaviour.

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