

CANALIZATION OF DEVELOPMENT AND THE INHERITANCE OF ACQUIRED CHARACTERS

By DR. C. H. WADDINGTON

Zoological and Strangeways Laboratories, Cambridge

THE battle, which raged for so long between the theories of evolution supported by geneticists on one hand and by naturalists on the other, has in recent years gone strongly in favour of the former. Few biologists now doubt that genetical investigation has revealed at any rate the most important categories of hereditary variation; and the classical 'naturalist' theory—the inheritance of acquired characters—has been very generally relegated to the background because, in the forms in which it has been put forward, it has required a type of hereditary variation for the existence of which there was no adequate evidence. The long popularity of the theory was based, not on any positive evidence for it, but on its usefulness in accounting for some of the most striking of the results of evolution. Naturalists cannot fail to be continually and deeply impressed by the adaptation of an organism to its surroundings and of the parts of the organism to each other. These adaptive characters are inherited and some explanation of this must be provided. If we are deprived of the hypothesis of the inheritance of the effects of use and disuse, we seem thrown back on an exclusive reliance on the natural selection of merely chance mutations. It is doubtful, however, whether even the most statistically minded geneticists are entirely satisfied that nothing more is involved than the sorting out of random mutations by the natural selective filter. It is the purpose of this short communication to suggest that recent views on the nature of the developmental process make it easier to understand how the genotypes of evolving organisms can respond to the environment in a more co-ordinated fashion.

It will be convenient to have in mind an actual example of the kind of difficulties in evolutionary theory with which we wish to deal. We may quote from Robson and Richards¹: "A single case will make the difficulty clear. Duerden² has shown that the sternal, alar, etc., callosities of the ostrich, which are undoubtedly related to the crouching position of the bird, appear in the embryo. The case is analogous to the thickening of the soles of the feet of the human embryo attributed by Darwin³ 'to the inherited effects of pressure'. As Detlefsen⁴ points out, this would have to be explained on selectionist grounds by the assumption that it was of advantage to have the callosities, as it were, preformed at the place at which they are required in the adult. But it is a large assumption that variations would arise at this place and nowhere else."

In this case we have an adaptive character (the callosities) of a kind which it is known can be provoked by an environmental stimulus during a single lifetime (since skin very generally becomes calloused by continued friction) but which is in this case certainly inherited. The standard hypotheses which come in question are the two considered by Robson and Richards: the Lamarckian explanation in terms of the inheritance of the effects of use, which they cannot bring themselves to support at all strongly, and the 'selectionist' explanation, which, in the form in

which they understand it, leaves entirely out of account the fact that callosities may be produced by an environmental stimulus and postulates the occurrence of a gene with the required developmental effect. A third possible type of explanation is to suppose that in earlier members of the evolutionary chain, the callosities were formed as responses to external friction, but that during the course of evolution the environmental stimulus has been superseded by an internal genetical factor. It is an explanation of this kind which will be advanced here.

The first step in the argument is one which will scarcely be denied but is perhaps often overlooked. The capacity to respond to an external stimulus by some developmental reaction, such as the formation of a callosity, must itself be under genetic control. There is little doubt, though no positive evidence in this particular case so far as I know, that individual ostriches differ genetically in the responsiveness of their skin to friction and pressure. If we suppose, then, that in the early ostrich ancestors callosities were formed by direct response to external pressure, there would be a natural selection among the birds for a genotype which gave an optimum response.

The next point to be put forward is the one which is, perhaps, new in such discussions, and which therefore requires the most careful scrutiny. It is best considered as one general thesis and one particular application of it.

The main thesis is that developmental reactions, *as they occur in organisms submitted to natural selection*, are in general canalized. That is to say, they are adjusted so as to bring about one definite end-result regardless of minor variations in conditions during the course of the reaction.

The evidence for this comes from two sides, the embryological and the genetical. In embryology we have abundant evidence of canalization on two scales. On the small scale of single tissues, one may direct attention to the obvious but not unimportant fact that animals are built up of sharply defined different tissues and not of masses of material which shade off gradually into one another. Similarly, from the experimental point of view, it is usual to find that, while it may be possible to steer a mass of developing tissue into one of a number of possible paths, it is difficult to persuade it to differentiate into something intermediate between two of the normal possibilities. Passing from the scale of tissues to that of organs, it is not too much to claim it as a general rule that there is some stage in every life-history (though it may be an extremely early and short stage) when minor variations in morphology become 'regulated' or regenerated; and that is, again, a tendency to produce the standard end-product. Of course neither of these types of canalization is absolute. Morphological regulation may fail if the abnormalities are too great or occur too late in development; and intermediate types of tissue can occasionally be found, particularly in pathological conditions.

The limitations on canalization which are important for our present purposes can better be seen when the problem is viewed from the other, genetical, side. The canalization, or perhaps it would be better to call it the buffering, of the genotype is evidenced most clearly by constancy of the wild type. It is a very general observation to which little attention has been directed (but see Huxley⁵, Plunkett⁶, Ford⁷) that the wild type of an organism, that is to say, the form which occurs in Nature under the influence of natural selection, is much less variable in appearance than

the majority of the mutant races. In *Drosophila* the phenomenon is extremely obvious; there is scarcely a mutant which is comparable in constancy with the wild type, and there are very large numbers whose variability, either in the frequency with which the gene becomes expressed at all or in the grade of expression, is so great that it presents a considerable technical difficulty. Yet the wild type is equally amazingly constant. If wild animals of almost any species are collected, they will usually be found 'as like as peas in a pod'. Variation there is, of course, but of an altogether lesser order than that between the different individuals of a mutant type.

The constancy of the wild type must be taken as evidence of the buffering of the genotype against minor variations not only in the environment in which the animals developed but also in its genetic make-up. That is to say, the genotype can, as it were, absorb a certain amount of its own variation without exhibiting any alteration in development. Considerable stress has been laid in recent years on certain aspects of this buffering. Fisher⁸ and many authors following him have discussed 'the evolution of dominance', by which the genotype comes to be able to produce the standard developmental effects even when certain genes have been replaced by others of less efficiency. Again, Stern⁹ and Muller¹⁰ directed attention to the phenomenon of 'dosage compensation', by which it comes about that a single dose of a sex-linked gene in the heterogametic sex has the same developmental effect as a double dose in the homogametic. These two processes are part of the larger phenomenon which we have called the canalization of development. This also includes other, at first sight unrelated, features of the genotypic control of development. For example, attention has been directed (Waddington¹¹) to genes which cause certain regions of developing tissue to take an abnormal choice out of a range of alternative possible paths; Mather and de Winton¹² have recently spoken of such genes as 'switch genes'. Finally, Goldschmidt has shown that environmental stimuli may, by switching development into a path which is usually only followed under the influence of some particular gene, produce what he has called a 'phenocopy' of a previously known mutant type.

There seems, then, to be a considerable amount of evidence from a number of sides that development is canalized in the naturally selected animal. At the same time, it is clear that this canalization is not a necessary characteristic of all organic development, since it breaks down in mutants, which may be extremely variable, and in pathological conditions, when abnormal types of tissue may be produced. It seems, then, that the canalization is a feature of the system which is built up by natural selection; and it is not difficult to see its advantages, since it ensures the production of the normal, that is, optimal, type in the face of the unavoidable hazards of existence.

The particular application of this general thesis which we require in connexion with 'the inheritance of acquired characters' is that a similar canalization will occur when natural selection favours some characteristic in the development of which the environment plays an important part. It is first necessary to point out the ways in which the environment can influence the developmental system. If we conceptually rigidify such a system into a definite formal scheme, we can think of it as a set of alternative canalized paths; and the environment can

act either as a switch, or as a factor involved in the system of mutually interacting processes to which the buffering of the paths is due. This is, of course, too dead and formal a scheme to be a true picture of development as it actually occurs. In so far as it is always to some extent, but not entirely, a matter of convenience what we decide to call a complete organ, so far will it be a matter of convenience what we consider to be different alternative paths; and the question of whether a given influence is thought of as a switch mechanism or a modification of a path will depend on how we choose our alternatives. There are some cases, however, in which the alternatives are very clearly defined. Thus it is commonly assumed that the evolution of sexuality passed through a stage in which, as in *Bonellia*, the environment acted as a switch between two well-defined alternatives; later, genetic factors arose which superseded the environmental determination by an internal one.

More commonly, however, the original environmental effect will be to produce a modification of an already existent developmental path. Thus in the case of the ostrich ancestors, the formation of callosities following environmental stimulation is a response by a developmental system which is normally present in vertebrates. This system must, in all species, be subject to natural selection; outside certain limits, too great or too low a reactivity of the skin would be manifestly disadvantageous. If we suppose that the callosities, when they were first evolved, were dependent on the environmental stimulus, then the evolution appears as a readjustment of the reactivity of the skin to such a degree that a just sufficient thickening is produced with the normally occurring stimulus.

There would appear to be two possible ways in which such a development might be organized. It might on one hand remain uncanalized, the formation of the thickening in each individual depending on the reception of the adequate stimulus, to which the response remained strictly proportional. If this possibility was realized, the well-known difficulty of accounting for the hereditary fixation of the character remains unimpaired. The alternative is that the development does become canalized, to a greater or lesser extent. In that case, the magnitude of the response would not be proportional to that of the stimulus; there would be a threshold of stimulus, above which the optimum (that is, naturally selected) response would be formed. In so far as the response became canalized, the environment would be acting as a switch.

Systems of either type can be built up by natural selection, and one can point to examples of them in animals at the present day. The reaction of the patterns on Lepidopteran wings (for example, in *Ephestia*, Kühn¹³) to temperature during the sensitive period scarcely seems to involve thresholds, while the metamorphosis of the axolotl, for example, clearly does. In general, it seems likely that the optimum response to the environment will involve both some degree of proportionality and some restriction of this by canalization. The most favourable mixture of the two tendencies will presumably differ for different characters. It is easy to see why a much sharper distinction between alternatives is generally evolved in connexion with sex differences than with the degree of muscular development, for example; but even the former is to some extent modifiable by extreme and specialized environmental disturbances

(heavy and early hormone treatment), and even the latter has some degree of genetic determination.

The canalization of an environmentally induced character is accounted for if it is an advantage for the adult animal to have some optimum degree of development of the character irrespective of the exact extent of stimulus which it has met in its early life; if, for example, it is an advantage to the young ostrich going out into the hard world to have adequate callosities even if it were reared in a particularly soft and cosy nest. Now in so far as the development of the character becomes canalized, the action of the external stimulus is reduced to that of a switch mechanism, simply in order that the optimum response shall be regularly produced. But switch mechanisms may notoriously be set off by any of a number of factors. The choice between the alternative developmental pathways open to gastrula ectoderm, for example, may be made by the normal evocator or by a number of other things (the mode of action of which may be through the release of the normal evocator (cf. Waddington¹⁴), but which remain different to the normal evocator nevertheless). Again, we know many instances in which several different genes, by switching development into the same path, produce similar effects; and attention has already been directed to the 'phenocopying' of a gene by a suitable environmental stimulus. Thus once a developmental response to an environmental stimulus has become canalized, it should not be too difficult to switch development into that track by mechanisms other than the original external stimulus, for example, by the internal mechanism of a genetic factor; and, as the canalization will only have been built up by natural selection if there is an advantage in the regular production of the optimum response, there will be a selective value in such a supersession of the environment by the even more regularly acting gene. Such a gene must always act before the normal time at which the environmental stimulus was applied, otherwise its work would already be done for it, and it could have no appreciable selective advantage.

Summarizing, then, we may say that the occurrence of an adaptive response to an environmental stimulus depends on the selection of a suitable genetically controlled reactivity in the organism. If it is an advantage, as it usually seems to be for developmental mechanisms, that the response should attain an optimum value more or less independently of the intensity of stimulus received by a particular animal, then the reactivity will become canalized, again under the influence of natural selection. Once the developmental path has been canalized, it is to be expected that many different agents, including a number of mutations available in the germplasm of the species, will be able to switch development into it; and the same considerations which render the canalization advantageous will favour the supersession of the environmental stimulus by a genetic one. By such a series of steps, then, it is possible that an adaptive response can be fixed without waiting for the occurrence of a mutation which, in the original genetic background, mimics the response well enough to enjoy a selective advantage.

¹ Robson, G. C., and Richards, O. W., "The Variation of Animals in Nature" (London, 1936).

² Duerden, J. E., "The Inheritance of the Callosities in the Ostrich", *Amer. Nat.*, 54, 239 (1920).

³ Darwin, C., "The Descent of Man and Selection in Relation to Sex" (London, 1901).

⁴ Detlefsen, J. A., "The Inheritance of Acquired Characters", *Physiol. Rev.*, 5, 244 (1925).

⁵ Huxley, J. S., "Evolution: The Modern Synthesis", p. 74 (London, 1942).

⁶ Plunkett, C. C., "Temperature as a Tool in Research in Phenogenetics", *Proc. 6th Int. Congr. Gen.*, 2, 153 (1932).

⁷ Ford, E. B., "Genetic Research in the Lepidoptera", *Ann. Eugen.*, 10, 227 (1940).

⁸ Fisher, R. A., "The Possible Modification of the Response of the Wild Type to Recurrent Mutations", *Amer. Nat.*, 62, 115 (1928).

⁹ Stern, C., "Über die additive Wirkung multipler Allele", *Biol. Zbl.*, 49, 231 (1929).

¹⁰ Muller, H. J., "Further Studies on the Nature and Causes of Gene Mutations", *Proc. 6th Int. Congr. Gen.*, 1, 213 (1932).

¹¹ Waddington, *Growth Suppl.*, 37 (1940).

¹² Mather, K., and de Winton, D., "Adaptation and Counter-adaptation of the Breeding System in Primula", *Ann. Bot.*, 5, 297 (1941).

¹³ Kühn, A., "Versuche über die Wirkungsweise der Erbanlagen", *Naturwiss.*, 24, 1 (1936).

¹⁴ Waddington, C. H., "Organisers and Genes" (Cambridge, 1940); "Genes as Evocators in Development" (1940).

WORLD MINERAL RESOURCES: A SUGGESTED SURVEY*

By PROF. P. G. H. BOSWELL, F.R.S.

IN order that the Fourth Article of the Atlantic Charter ("... endeavour with due respect for their existing obligations, to further enjoyment by all States . . . of access on equal terms to the trade and to the raw materials of the world which are necessary for their economic prosperity") may be implemented, what preparatory work can usefully be undertaken? The terms of the clause are none too explicit, perhaps inevitably so. It is trite to say that the problems that arise in the international politico-economic field bristle with difficulties. But there are certain geological questions which, if the discussion of mineral resources is not to be entirely academic, should be borne in mind if we are to be prepared in any way for action when the time comes.

First, in the matter of assessing the world's resources of essential minerals. All will agree that knowledge of location and quantities is a pre-requisite of action. Our information dates from pre-war days. The very character of the present world war, however, has necessitated the exploitation of mineral deposits on a huge scale and may well prove to have permanently changed the relative importance of certain resources and the location of industries; and under post-war reconstruction the process will be continued. Re-assessment is thus necessary, but it can only be effectively undertaken after the War, when conditions once more allow of access and exploration.

Nevertheless, available knowledge forms a foundation on which we can build. Our sources of information include (a) publications of the Imperial Institute, Mineral Resources Bureau (mainly statistical and relating to production, imports and exports of various countries), (b) world conspectuses of individual minerals (such as gold, iron, copper, coal), prepared by the International Geological Congress, (c) publications of various official Geological Surveys, such as the mineral reviews of the U.S.A., and the quinquennial reports of the Geological Survey of India, and (d) various reference books and papers published by scientific and technical societies. Many of these contain compilations from returns issued by various countries. Considerations of strategy

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