278

THE DISCONTINUOUS INHERITANCE

By Sir Ronald Fisher

When considering the influence of Darwin on human thought during the last 100 years it is worth while to distinguish sharply between evolution as a historical fact on the one side, and the development of an operating theory of modification in descent on the other. It was the first of these that caught the popular imagination and staggered the Victorian age by its implications for religion and philosophy, and in all parts of the world has dealt a mortal blow to the traditional and superstitious mythologies with which men of all races have decorated their ideas about human origins.

Darwin, however, would never have brought about this revolution in human thought without developing his ideas on *how* modification in the course of descent was able to come about, and indeed how it must inevitably have come about in every branch of the living world. For the mere speculative notion of descent with modification was not new with Charles Darwin. It was an old fancy which had been revived by the *philosophes* of the eighteenth century, including Darwin's grandfather, Erasmus. It had, however, fallen into scientific discredit owing largely to the uncritical speculations of Lamarck, and, although suggestive and persuasive evidence in its favour had been accumulating on a large scale with the widening of biological enquiry, yet the biological world of the mid-nineteenth century was inclined, one might think rightly inclined, to ignore inconclusive evidence, unless and until the whole process could be rationalised. By persuading a group of critical minds such as Huxley, Hooker, and Lyell of the rational cogency of his theory of Natural Selection, Darwin was able to mobilise and make effectual an avalanche of suggestive evidence. Man's understanding of the world in which he finds himself took a leap forward. A leap, however, has the logical drawback of detaching people from the grounds of their reasoning.

How little popular understanding there was 100 years ago of the theory of Darwin and Wallace appears from the curious fact that in the public controversies that followed, the objections raised against this theory were frequently simply *rechauffés* of the objections developed against Lamarck's theory sixty years earlier. The distinctive character of the new views was, for controversial purposes, ignored, and indeed for the rest of the century the idea lingered even among biologists that Darwin's theory was just a bright idea, ready to be superseded by some other bright idea as the whim of fashion might dictate.

It has been the work of the last generation, in the mid-twentieth century, to consolidate Darwin's theory by restating it in genetic terms consonant with the great advances in our understanding of the process of inheritance which have been accomplished since 1900.

Darwin's theory, developed before the understanding initiated by Gregor Mendel, of the process of hereditary transmission, was imperfect and even contradictory. At least, it left grave difficulties which Darwin discussed with candour in the *Origin* but did not always resolve. It is interesting historically that Mendel, publishing only seven years later, in 1866, pointed out that some at least of these difficulties would be removed by the system of inheritance he had discovered in the garden pea (*Pisum*): however, this penetrating observation, like all Mendel's paper, was ignored, and even when in 1900 his work was discovered, it was so far taken for granted that his findings were opposed to Darwinian views that his remarks on the theory of evolution passed unnoticed. Thus, for the first two decades of the century the Mendelian discovery was not interpreted, as it was later seen to be, as revealing a mechanism consolidating Darwin's theory at its base, and radically incompatible with any alternative theory, but for a whole was felt as an embarrassment by selectionists, and as a weapon in the hands of their opponents.

Lamarck had argued that although the organisms traditionally familiar to European zoologists and botanists could with confidence be named and classified, yet that with the accretion in our collections of vastly more numerous forms from the continents recently discovered or explored, discontinuous classification had become impossible, for everything merges by insensible gradations into something else; and Nature has 'for the most part left us nothing at our disposal for establishing distinctions, save trifling and in some respects puerile particularities'.

Lamarck, therefore, was arguing to support the general theory of the gradual transformation of species in time from the *supposed* fact that the traditional discontinuous classification of Linnaeus had been shown, once the whole planet came under survey, to be impossible. The argument was never one of Darwin's and is not needed for his theory. In fact the taxonomists of the nineteenth century were not unequal to their task and demonstrated not the impossibility but the feasibility of both zoological and botanical classification in all countries. Darwin could point to the ramification of an established classification in groups subordinate to groups as evidence of the actual lines of descent.

Controversialists, however, will confuse every issue; and even into the twentieth century writers can be found who speak of Darwin's *failure* to disprove the distinctness of species. In the last quarter of the nineteenth century evidently many writers felt that the observable distinctness of living forms was a reason for rejecting the gradual evolution which Natural Selection could accomplish, and that an abrupt transition from species to species was required in the evolutionary process.

Bateson's major work of 1894, *Materials for the Study of Variations, treated with special regard to discontinuity in the origin of species*, and De Vries' *De Mutationstheorie* (1901) are products of this line of thought. It is historically curious that in Bateson's case his enthusiasm to prove discontinuous evolution led him to be in this country the champion and father of Mendelian studies, which, as population genetics became clearer, have decisively excluded just such a discontinuous theory as he favoured. It is inheritance that is discontinuous, not evolution.

The importance of discontinuous or particulate inheritance in population genetics lies in the conservation of the variability. Viewing the matter quantitatively we can recognise mathematically well-defined components of what is called the variance, such as the genetic variance, or that part which is available to give an immediate response to selection, or the genotypic variance which contains in addition reserves which can perhaps only be released gradually by recombination, or by other changes. With a particulate system these components are relatively permanent. Differences between brothers in our school population are due to exactly the same genes as were similar differences at the time of King Solomon, a hundred generations earlier. Little can be due to new mutations since that wise king's time; whereas with continuous inheritance nearly all human variability would be only a few generations old.

Theories of evolutionary change other than Natural Selection have always relied on supposed means of new variation or, in other words, on mutation, to bring about the evolutionary effect. Bateson quotes with approval an aphorism of Samuel Butler—'To me it seems that the "Origin of Variation", whatever it is, is the only true "Origin of Species"'. This states succinctly just what it is now impossible to believe.

At the fiftieth anniversary of the publication of the *Origin*, Professor A. C. Seward at Cambridge gathered in book form a number of able essays under the title of *Darwin and Modern Science* (1909). The contributors were eminent and representative, yet only two, the veteran August Weismann and E. B. Poulton of Oxford, devoted themselves primarily to Selection Theory, and they may have given the impression of an Old Guard facing a pack of confident critics. Both presented in beautiful detail instances of adaptation, for example in mimicry and protective coloration, which only a sensitive selective mechanism could explain. Neither recognised in the new genetic knowledge a powerful ally of their views. Nor, again, at that date could either point to examples of species in process of selective modification, or with polymorphisms maintained by a balance of selective tendencies.

Strong Selective Influences in Nature

The recognition, particularly by E. B. Ford and his colleagues at Oxford, of the central importance of selectively balanced polymorphisms for the elucidation of the evolutionary situation of wild species, in their actual habitats, has at the present time supplied a whole series of cases in which direct field observations, using quantitative methods and genetic analysis, have revealed strong selective influences in Nature.

Very striking is Kettlewell's demonstration of the selection by birds of non-melanic moths in regions blackened by atmospheric pollution, and the selection exercised by thrushes as shown by Cain and Sheppard on the shell colour of the snail *Cepea nemoralis*. These will, I hope, become classroom examples for the simplicity of the situations revealed. The more complex cases presented by the scarlet tiger-moth *Panaxia dominula* and the meadow brown *Maniola jurtina,* though equally clearly manifesting selection, have needed exhaustive studies, and give an indication of the complexity of the ecological situations likely to be encountered and the amount of detail that can be brought out. Among the most penetrating is an example in Man provided by the recognition, due pre-eminently to A. C. Allison, that variants of the blood-pigment haemoglobin found in malarial regions have been favoured by the infantile and child death-rates due to malarial infection, and constitute a relic of a polymorphism formerly balanced by the ravages of this disease.

In Darwin's time the evolution of the human species was obscure, largely through lack of fossil forms. The few that were discovered in the nineteenth century offered difficult problems in comparative anatomy and evidently covered only a small part of the story. During the twentieth century a great wealth of new material has been brought to light and the evolutionary history is more sharply defined. Several distinct species have been found, and the main evolutionary sequence of some of them is apparent.

The group of rather small mammals found in South Africa by Broom and Dart, the morphological affinities of which have been particularly examined by Le Gros Clark, lived perhaps three quarters of a million years ago. They were certainly man-like, or hominid, rather than ape-like. Their hip-joint shows a free running gait quite unlike the living species of ape; their arms and hands were free from locomotive duties. The head was *poised* in human fashion on the backbone. Nevertheless the face was pre-human, with an enormous jaw and prognathous muzzle, though the dentition and form of jaw clearly foreshadows the human feature. Perhaps the tongue was too big and awkward for articulate speech. The brain also was very small by human standards. It is doubted if they had fire or made tools, but certainly they used natural clubs like Samson's 'jaw-bone of an ass'. Perhaps it was never a common or widespread species, yet the remains are abundant and much may be expected from their further study. Many names have been given, but at present perhaps they may be grouped together as *Australopithecus*.

Javan Man

In the nineteenth century already Du Bois had discovered the 'Javan man', *Pithecanthropus erectus*. Since then in Java and in China many examples of probably the same species have been unearthed. With some variation, they fall as a group nicely intermediately between *Australopithecus* and our own species. The mouth, though still prognathous and heavy jawed, has much receded. The brain case, though still small, has increased notably. A continuous progression is indicated covering more than 500,000 years.

The earliest well-authenticated example of our own species was found in the Thames valley at Swanscombe. The skull fragment was buried deep in the 100-foot gravel terrace believed to be of middle interglacial age, though the sequence of glacial changes in this country and their minor fluctuations still offer difficulty. The French skulls at Fontechevade have fully confirmed the early occurrence of *Homo sapiens* in western Europe, which may indeed be the Garden of Eden of our own world-wide species. Neanderthal Man occupied much of Europe for part of the intervening period and presents something of a problem. The skeleton is different from ours in many ways, but the brain was as large as our own. He is classified as a distinct species, which has died out or perhaps in part been merged in the modern population.

The fossil record has thus already gone far enough to confirm Darwin's supposition that the human species has been derived in geologically recent time from pre-human but definitely hominid forms, and these from an ancestor common to ourselves and the tailless apes. The fossil record is not, however, the only source from which the evolutionary situation of mankind has been illuminated. The population genetics of our species has in this century, and especially since the last war, been revolutionised by the discoveries of the several systems of blood-groups.

Blood Transfusion

The transfusion of blood from animals to man, and from man to man, had been demonstrated experimentally at least as early as the time of the diarist Samuel Pepys. Until the beginning of the twentieth century it was, however, recognised to be too dangerous a procedure to be of service in medical practice. In 1900 Landsteiner published the experimental demonstration of the existence of four types of blood, now familiar through the activities of the blood-transfusion service as AB, containing both of two antigens on the red cells, A and B, containing one but not the other, and O, containing neither, all directly recognisable by the use of two testing fluids, anti-A and anti-B, which as Landsteiner showed could readily be prepared from human serum of the appropriate type.

This discovery was the first step towards making blood-transfusion a safe procedure, and its availability is now an essential part of medical care. By 1908 it was clear that the antigens were inherited as simple Mendelian characteristics;

probably they were the first normal characters in Man for which this was known. It was not until 1924 that Bernstein, using the statistical methods characteristic of population genetics, put forward the genetic theory that is now generally accepted. From this time, it was clear that the human race was polymorphic in this factor, though it required the more general theory of polymorphism, due principally to Ford, for its evolutionary significance to be appreciated.

The system of OAB proved to be the first of a series of systems discovered by similar methods, or by such refinements of them as the Coombs test. In 1927 Landsteiner and Levine reported two more systems obtained by making immune sera in rabbits and guinea-pigs. One of these, known as MNS, is the most powerful tool we possess in human genetics for such purposes as the identification of individual blood, the identification of the parentage of infants possibly misplaced in hospital, the recognition of paternity, and the diagnosis of identical twins. The other, the blood-group P, has not developed the same importance, though it also has been found to have further associations.

In 1939 Levine, followed quickly by Landsteiner and Weiner, found a fourth system, which has been named the Rhesus factor, from the circumstance that the blood of the Rhesus monkey was at one stage found useful in producing the first of the associated anti-bodies. The great medical importance of this factor arises from the fact that the majority of cases of haemolytic disease in the new-born, formerly an important cause of infant death, was due to the incompatibility of the parents in just this factor, the recognition of which has therefore been the means of saving many thousands of lives.

The Rhesus system has been of service not only in making the medical profession to some extent genotype-conscious but in demonstrating the genetic complexity of the regions of the germ-plasm responsible for the blood-group polymorphisms. In the case of the Rhesus factor there are at least three and probably four or more polymorphic loci closely linked on the same chromosome. The efforts to force a notation on the system which does not recognise its genetic character, has been, and perhaps still is, a source of controversy. Polymorphisms in other animals and the other blood-groups in Man, are, however, more and more exhibiting the same situation.

I have mentioned four blood-group systems; but if we include such similar factors as that responsible for the secretion of antigens into the saliva, and that responsible for the human polymorphism in capacity to taste the bitter substance phenylthiocarbamide, there are about a dozen kinds identifiably distinct, with other possibilities always in the offing. Most of these are new since the last war, so that little need be said of them individually. The work of Race and Sanger at the Lister Institute is the focal point, and not only for this country.

It is certain, however, that all the blood-group systems will in the comparatively near future yield new knowledge in two important fields. First, a number of associations with disease have been reported, chiefly owing to the energy and initiative of

J. Fraser Roberts, Harrison, Clark, and Sheppard. Secondly, all blood group factors will contribute to the exploration of racial differences in mankind, for the frequencies of the different genes vary notably from one race to another; the different races of Man, as populations, have become more distinct and better defined, than was possible by the older ethnographic methods. The reconstruction of racial history, though a distant aim, is not an unreasonable one. A. Mourant's book on the *Distribution of the Human Blood Groups* summarises as well as possible the state of our rapidly developing knowledge.

Thus, for our own age, selection is not a remote hypothesis, but an aspect of the natural world within reach of active study, equally in other animals and in Man. The age of the debaters and essayists like Samuel Butler has closed.—*Third Programme*