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ANY HEREDITARY CHARACTER AND THE KINDS OF THINGS WE NEED TO KNOW ABOUT IT

DR. OSCAR RIDDLE

CARNEGIE STATION FOR EXPERIMENTAL EVOLUTION

No one seems ever to have written the results of a serious inquiry as to which are the distinctly different kinds of knowledge that will be required for the adequate comprehension of a (any) hereditary character. It is possible that studies in heredity have lost and now lose something of perspective and of balance by the absence of some sort of gauge against which actual accomplishment in this subject can be measured against the total necessary accomplishment. The older and more inclusive science of biology has made far more definite and helpful classifications of its constituent aspects — as applied to organisms and to groups of organisms — than has heredity. These divisions or aspects of biological science — comparative anatomy, systematics, biochemistry, paleontology, behavior, embryology, evolution, pathology, ecology, microanatomy, physiology and distribution — are at once frank recognitions of the kinds of knowledge necessary to a comprehension of the organism, and of the limited scope and value of any single type of information. Heredity, or evolution, like biology as a whole, possesses an integrity which upon examination immediately dissolves into diversity. It is a crystal of many facies. The first purpose here is to attempt the identification of the radically diverse aspects presented by any single hereditary character. This attempt is the more opportune because some recent developments in sex studies now make it fairly clear that one or two new or hitherto imperfectly conceived aspects of a hereditary character can be identified as distinct and utilizable aspects of any hereditary character.

In addition to matters of theory, investigations current in heredity are confronted by a condition. The onrush of data and facts now proceeding from the world's laboratories of genetics would seem to bring assurance that the province of heredity and evolution will soon be covered with a body of precise and definitive knowledge — quite sufficient perhaps to satisfy the accumulated curiosity of two generations for broad and positive knowledge in this field. May a worker within this group, which conceives its work to be the study of "heredity and evolution," without

seeming too ungracious, raise a question as to whether our wealth of published contributions — and the investigations we are pursuing, directing or encouraging — really covers the required and now accessible range of information on heredity and evolution? Are we, as individual builders of a house of science, assured that our work is upon all its walls and foundations? Is it possible that it is rather a slender tower than a symmetrical home that engages our very effective efforts? Is this possibility at all worth considering? Does the sweeping cloud of data, great in volume but limited in kind, at all affect our vision of other important but missing kinds of facts? Do our enormous local successes mean a general advance all along the line? In connection with a principal purpose stated above it has seemed obligatory seriously to examine, however briefly, the point involved in these questions.

No one will momentarily doubt the great value or the gratifying volume of knowledge now being obtained in that part of the field of heredity known as genetics (breeding and cytology). This is all entirely obvious; and, in a statement condensed to the point of running other risks of misunderstanding, the writer trusts he may omit any review of actual accomplishment in this field without subjecting himself to the charge of either overlooking or of being unaware of its invaluable contributions. In general, this discussion is to emphasize limitations rather than accomplishment. Examination of our first point involves an estimate as to how far the data of genetics include a real or a complete knowledge of heredity and evolution. Besides dealing with the limitations inherent in the types of information now rapidly accumulating, it will be necessary to characterize and to consider specifically each of the additional kinds of information necessary to an adequate understanding of any hereditary character.

The conception presented here also involves the proposition that our knowledge of heredity and evolution will become essentially complete when we shall have learned all the necessary kinds of facts about one, any one, hereditary character; but that an infinite number of facts of the few (practically only two) kinds now being actively and most successfully gathered, can never give us more than an unfinished fragment of the knowledge necessary to a comprehension either of evolution or of any hereditary character.

The following diagram lists these wholly distinct, and now identifiable, aspects of any hereditary character:

Any Hereditary Character

a	b	c	d	e	f
Origin	Complete ontogeny	Foundation and localization in gametes and zygotes	Mechanism of distribution in gametes and zygotes	Intimate nature	Control or transformability in ontogeny (and phylogeny)

It may be well to state clearly and at once that some facts drawn from many or all branches of biological science, as well as from other sciences, will have to be utilized in obtaining the requisite knowledge concerning any one of these six aspects of any one hereditary character. For example, physics, chemistry and most or all of the groups of biological science mentioned in an initial paragraph may be involved in what is required for a complete knowledge of the origin or the *complete ontogeny* of a character. But the entire body of knowledge of any one of those science groups would probably not be involved in supplying the required information on the origin of all hereditary characteristics, and this requirement would be enormously reduced if applied to the case of any one such character. Certain parts of various branches of science may thus later become a part of the subject of heredity in precisely the same way as a part of cytology has already become a part of genetics.

It should also be made clear that we neither mean to state nor to imply that only *c* and *d* of the above classification are now receiving any attention by geneticists. The point raised here is that these aspects only are receiving anything approaching the share of active work which other aspects of heredity should now receive. Most geneticists were biologists before they became geneticists; many workers have realized the need of one or more additional kinds of information concerning the characters with which they work, and to one or another extent they have sought to supply some parts of this information for their own material. In large measure it is in consequence of those efforts that it now seems desirable and practicable to inquire specifically into which are the distinct kinds of knowledge really required for the comprehension of a character. This gathering of scattered and unrelated bits of such information among many characters has rendered a further service in that it now enables us more clearly to see the great importance of having all the necessary information gathered for some one — any one — character.

ORIGIN

Our classification or diagram gives first place to the *origin* of hereditary characters and factors. Under origin is of course ultimately implied: *Demonstration of occurrence*, with data capable of distinguishing the pathological or abnormal from that of constructive and evolutionary value. Changes of pathologic or abnormal origin can certainly be inherited, but they have a quite doubtful status in creative evolution. Such changes, though hereditary, may very little resemble the actual "origin" of characters. *Cause*, with the few or several sequences involved. *Method*, with the types of functional and structural changes concerned in the rearrangements of matter and energy. *Place*, with reference to other hereditary units and to the organism. It does not yet seem entirely beyond question that all characters ultimately of evolutionary value arise *first* in germinal tissue. *Time*, specific for individual case (or, much less important, historic appearance). It is clear that the attainment of complete knowledge here will be a difficult matter.

All will grant the great theoretic importance and need of this kind of information concerning any specific character. It seems to be true, however, that our definite knowledge dealing with what is certainly the origin of characters of evolutionary value is still essentially limited to evidence for the relative time and order of the appearance of a number of these in evolutional history — a minor contribution to this problem by paleontology and comparative anatomy. In addition, it is possible, but by no means certain, that we already have from current investigation in genetics some — though only a part — of the highly important facts that should sometime be found for the origin of characters as they arise in evolution. Some investigators in genetics have urged that certain types of mutation, and still other cases involving observed chromosomal rearrangement, have a right to be considered as actual origins of such new characters. But many or most biologists, including some geneticists, are quite unwilling to concede that proposition. There are weighty objections to considering either hereditary losses or gains following losses within a species as origins of things really involved in evolution. For present purposes it can be said that even if these cases be granted the status of such origins the amount of knowledge they bring concerning their origin, though of very great importance, is notably incomplete. We may perhaps well doubt that any line of investigation now in use will give us the information we most seek concerning the origin of any specific character. It is quite possible that the required information — if attainable at all — awaits the development of essentially new avenues of

approaching the problem of heredity; or probably of these combined with present methods of genetic study. The very special theoretic and practical importance of this deficiency in our knowledge may well give us composure while viewing contemporary triumphs in other related aspects of the study of heredity.

COMPLETE ONTOGENY

A second type of information (*b*) we have characterized as the *complete ontogeny* of a character. The requisite data here involve knowledge of each step of the action of the hereditary factor toward the differentiation of the corresponding hereditary character. Concerning this immensity, stretching from and preceding the quiescent gamete through embryonic stages to the finished — if ever finished — adult character, we now have only scattered traces of information. More regrettable still, nowhere may one find a considered program for bringing into existence this type of information for any hereditary character. Many items of such information have indeed been obtained, in a few cases as a real part of a genetic study, but largely as by–products of studies in embryology, biochemistry and chemical pathology. Most of even these few items can not be said actually to have been incorporated into the science of heredity.

It is perhaps well to cite a specific case in order to make clear our meaning and to attest the present practicability of such studies. In. the complete ontogeny of a character its form — expression in the embryonic series is perhaps incidental or quite negligible in the case of most hereditary characters; in a few of them it is probably of real importance. The most necessary data in work of this type will usually involve chemical aspects of ontogeny. In illustration one may cite a promising bit of information obtained in studies on the liver of the human foetus. Some of the steps by which one of the adult functions of the liver is attained have been disclosed through the observation that the purin bodies (protein constituents) are there broken down in successive stages by enzymes which first appear in an orderly time sequence. This order of enzyme production being — guanase, adenase, xantho–oxidase. That these represent orderly and successive steps in the ontogenetic development of a definitive function of the adult liver is made clear in these studies. Also, in this particular case, the far–reaching hereditary significance of this sequence is made further evident by the fact that the order of ontogenetic sequence of these enzymes is probably the order found in animal phylogenesis.

If another illustration were required it could be shown that the differentiation of the sex character also offers a quite favorable opportunity for studies of this nature. We shall here note only that "metabolic rate" is a thing susceptible of measurement in all stages in one or another organism; that the various form — expressions of sex in the embryonic series are perhaps as well known as for any character; and that in vertebrates much work has already been done on the nature and developmental effects of the substances elaborated by or in association with the gonads. These facts, gathered hitherto by workers in different fields and with most varied aims, supply a good beginning for a study of the complete ontogeny of this character.

There can be no doubt that this fairly obvious and almost entirely neglected field — now scarcely recognized as within the province of research in heredity — is a wholly essential part of the required knowledge of any hereditary character. It would, therefore, seem to be important that present workers in heredity recognize the need of adequately and permanently establishing this type of work as an essential aid to the problem of development — with heredity as the point of interest and as the aim of such study. At present we must rely upon chance information — the by–products of studies in pathology, embryology, biochemistry or medicine. Further, along with this recognition it would seem necessary to begin the training of investigators who, with new methods of study and independent outlook but well reinforced by interest and training in heredity, must in large measure be responsible for developing our knowledge of this aspect of heredity. In the task of securing and training these recruits it seems clear that geneticists, botanists and zoologists will first need to look to the breadth of training given within these subjects; and that they shall then have to secure the aid of their colleagues in chemical aspects of biology. A wide and thoroughgoing cooperative effort is here clearly required in order that we may hope later to attain this necessary information for any hereditary character. The circumstance that numerous fragments of data are known for different parts of the ontogeny of various characters does not even partially supply this need.

LOCALIZATION AND DISTRIBUTION

The *germinal foundations* of hereditary characters (*c*) have been so successfully examined during two decades of revolutionizing study and form so conspicuous a part of the contribution of modern genetics that, as already noted, this subject does not call for consideration here. This is

one of the two from a total of six essential aspects of heredity that can be said to have received its share of deserved attention.

The *mechanism of distribution* of hereditary characters (*d*) has also been so successfully studied, and the results employed with such brilliant results — its testimony having been brought into striking consonance with that presented by the immediately preceding type of study (foundation in gametes) — that this body of knowledge also stands in no need of emphasis. The mechanism of distribution of hereditary characters is then the second and last of the six essential aspects of heredity that can be said to have received its proper share of attention.

These two last–named aspects of the subject may indeed be considered the mountain of fast accumulating information in the wide otherwise uncultivated province of heredity. To a certain extent our additions to this mountain proceed, at least in many quarters, as though we conceive nearly all else within the horizon as a fallow and negligible area. It now seems in the interest of further progress to question this view, or at least this our actual method of procedure. On the other hand, the inference should not be drawn that all the major facts concerning the foundation of characters and the whole story of the mechanism of their distribution have already been obtained; nor should there be any slackening of effort on the more inviting unsolved problems in these two aspects of the subject. Besides all this there apparently remain many tasks, even within this restricted field (*c* and *d*), for the accomplishment of which present methods of study may prove inadequate. In a large part of what has hitherto been learned (or has taken the form of classifiable knowledge) the chromosomes are principally involved. But in the case of several of the most important features of individual development the "germinal foundation" is still conjectural or quite unknown; and there are features of the organism which are not, and others which probably are not, based upon any familiar form of "distribution or segregation." Only future investigation can disclose the facts for these particular cases.

The cases referred to above are made specific in the following examples; The germinal basis of polarity and bilaterality; the differentiation of the main body regions (head, thorax, body) ; the difficult fact that the effects of a gene are largely confined to localized areas, despite the circumstance that all the cells of the body have a common chromosomal equipment; and finally, the fairly obvious circumstance that the most essential of all the properties of the organism — the fundamental properties of living matter — can not be conceived as at all subject to segregation. In this latter case we must conclude that segregation is impossible, or else we must profoundly modify our

definitions and conceptions of living matter itself; for, if these properties do segregate it follows either that particles of living matter exist with one or another such thing as irritability, respiration and assimilation left out, or that such segregates involve only non–living matter. To urge, for example, that for "protoplasmic respiration" there are too many genes and these too widely represented in all the chromosomes to permit our ever seeing any evidence of segregation; or indeed to assume that any gene whatever exists without itself actively exercising this property, seems to resolve an established principle into an absurdity. Neither segregation, crossovers, non–disjunction nor duplication can apply to the fundamental properties of living matter.

INTIMATE NATURE

Two other and additional aspects of heredity remain essentially undeveloped (*e* and *f* of diagram). It is not easy to make clear at once exactly what is meant by the "intimate nature" (*e*) of a hereditary character (and of its factor basis) — so unfamiliar is this conception to the language of heredity and evolution. But is there not a trace of humiliation in the circumstance that the state of advance in our science is such that any novelty or unfamiliarity attaches to a term like the "intimate nature" or the "properties" of a hereditary character (or factor)? Is there something other than matter or energy, and their various forms and transformations, involved in any such factor or character? Elsewhere in science workers with the forms of matter or the forms of energy, after assurance of their presence or existence, seek *first* to get at the identifiable properties of the bit of matter under consideration. In other fields of investigation iron, sugar, mercury, alanin and adrenin are subjected first of all to disclosure of their properties — their intimate nature. The investigator of heredity now reports variety or differences in his substrates; their localization; and he occasionally refers to the quantities or proportions of his substrates — his sugar and his mercury. But any two of his sugars may be equally regarded as iron and alanin; the effects of any gene being estimated solely on the basis of the total accomplishment of all other genes when that particular gene is present as contrasted with what they do in its absence (or in its alternative representation). As to other intimate differential qualities of the genes we hazard no inquiry. Admitting this procedure, what further might we do about it? A plain suggestion seems to be: First, to recognize this neglect as a real and evident weakness of the present restricted attack on the problem of heredity; a weakness which merits the attention of individual

investigators and of laboratories. Second, to prepare ourselves or some of those trained by us — again necessarily enlisting the cooperation of our colleagues in the requisite sciences — to enter and develop this essential part of the study of heredity.

But are we in a position reasonably to hope for success in this endeavor? To this question most geneticists will now doubtless reply in the negative; and certainly only that reply is possible for those who have not carefully followed other work in heredity than that most prevalent in genetics (*c* and *d*). On this point the writer must state his own conviction that the accomplishment of this precise thing is now becoming clear in the case of one hereditary character, namely, sex. Investigations of the past few years have supplied a large and varied body of evidence that the sex differential, as between male and female, is based upon initial differences of metabolic rate in the gamete or germ stage; that whether ova or sperm are formed within the developing organism depends primarily and continuously upon whether a higher or lower rate of metabolism is maintained in the developing organism from the gamete stage onward through the period of its own production of germ cells; that this intimate metabolic state *can* so definitely dominate the sex factor and the sex character as to determine in fine detail the expression of this most widely expressed character, irrespective of the type of factorial foundation in germ and zygote. The completeness with which this metabolic rate both *replaces* and *supplements* the impulse of the factor itself; and the circumstance that in metabolic rate we are not dealing with an external agent, or with a stimulus whose seat of action is unknown, but with the seat and actuality of action itself — all this provides evidence that this particular factor impulse and metabolic rate are the same kind of thing. In this case, therefore, we now probably have some knowledge of the "intimate nature" of one hereditary character. It is a corresponding or similar type of knowledge that is needed in the case of any hereditary character.

In this connection it may be noted further that, if the above conclusion is correct as to the "intimate nature" of the sex character and the sex factor, we are in this case also in a very favorable position to attain an unusual view concerning one phase of the *origin* of this particular character. It has been pointed out that sex in the living world has originated independently hundreds, perhaps thousands, of times. How does it happen that these numerous independent origins of sex all give us essentially similar pictures of the two sexes? Would it not greatly assist us to an understanding of this matter if we could know the thing out of which sex differentiation arises? And if at the same time we might know

also that this same thing is of wide distribution — as widely distributed in fact as are organisms themselves? It was noted above that these useful facts are becoming available. If all sex rests primarily and fundamentally upon metabolic level or rate, then all the numerous cases of independent origin of sex arose in organisms which necessarily already had one or another rate of metabolism prior to the differentiation of the two sexes from a unisexual condition. All these organisms possessed exactly one and the same thing, or kind of thing, out of which to form or differentiate the sexes. It seems a safe conclusion that it is now possible to undertake a study of the "intimate nature" of some characters and of their factors beyond the effects on development observed in their presence or absence as noted above, and that this fifth aspect of the study of a character is essential — like the preceding aspects of the problem — to a real understanding of any hereditary character.

Since we emphasize the special importance of obtaining adequate knowledge of all the six aspects of heredity on some one character it becomes desirable to inquire whether there is any one single character particularly favorable for all these types of study. In the writer's opinon [*sic*] sex is one of the most favorable characters for this purpose. Something of the status of the sex character with reference to four of the six kinds of knowledge is elsewhere mentioned. Concerning its position in the remaining two types (*c* and *d*) it is sufficient to recall that for no other character so well and so widely as for sex has it been possible to identify a visible "germinal foundation"; and that the "mechanism of distribution" of the factors underlying and normally guiding the development of sex characters is as well understood as that for any known character. It may further be said that experience indicates that in no one animal or plant species may we hope to study advantageously all the aspects of sex or of any other character. Once a particular character is selected for study each of the six kinds of required knowledge should be sought in whatever organism lends itself best to the specific aspect taken for study. It is practically inconceivable that these six radically diverse kinds of problems are all most favorably presented in any one type of organism.

TRANSFORMABILITY

The final and the practical aim in the study of any and all aspects of any hereditary character may be said to be for its control or transformability — in ontogeny at least, in phylogeny if possible. Is this aspect of the problem now amenable to study? Again we note that recent

developments in the study of sex fully demonstrate that this particular hereditary character can be completely transformed to its alternative state, even in adult higher animals. It follows that, since the knowledge acquired on one truly hereditary character (sex) now enables us in the case of some higher animals to force this character to develop into its alternative or opposite form, the experimental control over all hereditary characteristics of this type becomes theoretically realizable and possible. No such character — physical or mental, in man or other organisms — can now be considered irreversible. This can only mean that the full development of a complete science of heredity will have included the control or transformation of characters in ontogeny as a definite part of its aims and attainments.

The application of this control and transformation not merely to ontogeny (the character) but to phylogeny (the factor) in addition might of course put us in a position to control or direct evolution itself — the ultimate goal of our science. Whether in fact this most important power resulted would depend upon the kind of heritable change effected; that is, whether what we succeed in introducing into the race is something abnormal and incapable of further progress, or is a typical and normal fundament as capable as were its precursors of further progressive creative evolution. In the one case we should be taking a magnificent part in creation; in the other, perhaps only facilitating factorial disorder or disease. In the event of a real success here this aspect (*f*) of heredity would meet and be resolved into one phase of the first–described aspect – – the origin (*a*) — of a character. A few attempts to induce one or another heritable change by some specific treatment have been and are now being made, and all recognize that much additional work of this character is needed. The apparently valid heritable changes hitherto found do not seem clearly to involve a particular factor or group of factors, they are probably all of the nature of abnormalities, and they thus far introduce no desirable or promising thing into the heredity of the organism; yet, those very few cases in which the abnormalities can be assuredly associated with a specific procedure or treatment seem to supply a new and most valuable kind of fact. This aspect of heredity, though in all respects quite unsuccessfully studied until very recent years, already promises to receive a share of attention in the immediate future. The same can not be said, however, for the control of heredity in the ontogeny of man and animals.

Many will be inclined to consider lightly this power to control alternative characters in ontogeny. It may, nevertheless, be well for students of heredity to reconsider this matter in the light of a

demonstration cited above. As an aid to such reconsideration it may be suggested that the group of sciences we now call medicine is built upon and takes its value from a measure of control perhaps less far–reaching and less advantageous to the human race than that involved in the control of alternative hereditary characteristics during the development and life of the individual. Medicine also chiefly deals with individual (ontogenetic) life. It sometimes preserves or rehabilitates life during many years; but more often its service — aside from sanitation and hygiene — is limited to aiding our resistance to pain or disease during only hours or days of our life. The complete control of (ontogenetic) heredity, however, would give to all men during all the days of their lives the greater resistance to disease, the predisposition to the longer life, the more advantageous stature, the higher level of intellect, the more desirable of all mental and physical states having allelomorphic representation within them. There is perhaps little that is imminent here; but the range of development of a complete knowledge of this aspect of heredity is the point discussed. It would seem unfortunate if our science should long overlook the great human value and the educative and other responses of mankind to any practical advance in this field.

In conclusion, as workers in a common science — if in fact we are all really aiming at an understanding of heredity and evolution — may we not profitably consider the question which every laboratory, great or small, must raise in determining its policy? Are we as individuals, laboratories and institutions to make our main effort the filling in of details concerning conceptions or principles already fairly established, together with additional conceptions of a similar kind which will doubtless follow? Or shall we consider it equally important, at least of much importance, to wedge our way into essentially new but now recognizable aspects of the general problem which must disclose kinds of fact new and different? It would seem that an adequate development of our knowledge of heredity and evolution requires that at least a few individuals and a few laboratories should now take the latter view and accept the duty and privilege of the development of one or another of the following neglected aspects of the study of a hereditary character: Its complete ontogeny; its intimate nature; its control or transformability.

SUMMARY

Present studies on heredity and evolution offer what is mainly a two–sided attack on a many–sided problem. An attempt to identify the radically diverse aspects necessary to the comprehension of any

hereditary character, together with a concrete examination of these neglected attackable aspects of the subject, brings into clearer view the inadequacy of the present attack. Some of these deficiencies are such as can be adequately met only through a wide interdepartmental cooperative effort. On contemporary students of heredity and evolution and on laboratories devoted to studies in this field rests the responsibility of obtaining this cooperation, and of so directing some of their main efforts that the results of this cooperative effort may soon be attained. Where individuals or laboratories are already prepared to conduct this type of work it should receive immediate, active and encouraging support. Our knowledge of heredity will be more advanced by securing all the kinds of fact necessary to an understanding of some one — any one — character than by a duplication of much information of a few kinds on many characters. At the present time sex is one favorable character for such a comprehensive study. Heredity, as a branch of science, is assuming new aspects which give it an ever–increasing human value and a greatly increased human interest.