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A GENERATION'S PROGRESS IN THE STUDY OF EVOLUTION[1]

By Professor EDWIN G. CONKLIN

PRINCETON UNIVERSITY

THE Penrose Memorial Lecture is not intended to be primarily or chiefly a personal memorial of our munificent benefactor. Such a memorial address was given last year by Professor Waldemar Lindgren, of the Massachusetts Institute of Technology, and although it was my good fortune to have known Dr. Penrose for many years and to have been officially associated with him both in this society and in the Academy of Natural Sciences, I could add little to Professor Lindgren's admirable address. Dr. Penrose was preeminently a gentleman and a scholar. He was a man of dignified modesty, transparent honesty and sincere devotion to genuine science and learning. The form of memorial which he would have most prized was one making for the promotion of science rather than for personal praise or vain show. In the language of Professor Lindgren's address of last year, he said in substance in making his bequest: "Here is the money, take it and use it wisely and well. There are many things I would have liked to do, but could not; life was too short. You try to accomplish them! Carry on!"

This the American Philosophical Society is trying to do, chiefly through its grants in aid of research, its publications, library and meetings. Of the grants made during the past year from the income of the Penrose Fund six were in fields in which he was especially interested, while all of them, we believe,

[1] Penrose Memorial Lecture, before the American Philosophical Society, Philadelphia, April 20, 1934.

are for projects which he would have approved. "He rests from his labors but his works do follow him."

I

If one were searching for the most inclusive subject in modern scientific research, what other topic would touch so many fields as that of evolution? In the non-living world it includes almost everything from the evolution of atoms to that of universes; in the living world practically everything from amoeba to man, from germ cells to developed organisms, from reflexes to reason, from savagery to civilization. Almost all the work of modern science and learning could be classified under some of these fields. The small part of this vast theme which I shall touch upon in this address concerns merely some of the recent work on the methods and causes of organic evolution.

Thirty-eight years ago I, a newcomer to Philadelphia, was introduced to the American Philosophical Society as one of the speakers in a symposium on "The Factors of Organic Evolution." I had been urged by Professor Cope and by the then presiding officer of this society, the late Dr. William Pepper, to take part in the symposium, but being painfully aware of my own inexperience and greatly overawed by the dignity of the society and the distinction of its members I had begged to be excused. Dr. Pepper encouraged me then, and his words have heartened me many times since, by saying, "You know we *can* do what we *have* to do." But when I still plead my inability to take part Dr. Pepper finally said to me, "Well, Professor Conklin, we had hoped to get acquainted with you." This challenge I could not ignore and at once I said, "Very well, I accept." It was the casual recital of this episode that led President Morris to draft me to speak on this occasion on "A Generation's Progress in the Study of Evolution."

The symposium occurred on the evening of May 1, 1896, the speakers being Professor Edward D. Cope, Professor Liberty H. Bailey, of Cornell University, and myself, and since our addresses represented fairly well the methods and conclusions of students of evolution a generation ago, I will briefly state a few of their principal conclusions. Cope[2] maintained the Lamarckian point of view that variations are the materials of evolution and that they are caused (1) by the direct action of the environment on developed organisms (his Physiogenesis), (2) by the inherited effects of use or disuse (his Kinetogenesis), (3) by the energy of growth forces (his Bathmogenesis) and (4) by sensations or consciousness (his Archaesthetism).

On the other side I championed[3] the Weismannian view that (1) acquired characters are not inherited, (2) that inherited characters must be predetermined, but not preformed, in the germ cells, and in particular in sub-microscopic inheritance units, (3) that all hereditary variations are caused by the action of extrinsic forces on the germinal protoplasm, producing changes in its structure, rather than upon developed organisms, and finally (4) that the only way of breaking the deadlock between Lamarckians and Darwinians was by means of experiment. In the light of subsequent events I think I have no reason to regret my immature contribution to this symposium.

Professor Bailey's[4–5] philosophy was neither strictly Lamarckian nor Darwinian, although in general it leaned to the former; it was rather *sui generis* and might be called Baileyan. He maintained that variability is the original law of organisms, that like no more produces like than unlike, but that mutability is a fundamental and normal law, while heredity or permanency is an acquired character. The organism is shaped by its environment, and nature eliminates the non-variable and favors the survival of the unlike.

This account of a long forgotten program in the history of this society is useful merely as indicating some of the opinions and speculations regarding the causes of evolution a generation ago. In what follows I must beg the indulgence of those who are thoroughly familiar with the subject while I recount some of the main points in the more recent developments in our knowledge of evolution.

II

With the beginning of the present century the study of evolution entered upon a new era. Up to the year 1900 it had been based largely upon observations and what were supposed to be logical deductions. Really students of evolution were dealing with probabilities of a higher or lower order and no certainty could be reached on such a basis. What seemed highly probable to one person seemed very improbable to another. Cope accepted all the Lamarckian factors, Romanes rejected use and disuse but accepted the others, Weismann rejected all of them. The fact of evolution was accepted by practically all scientists, but the factors of evolution were

[2] E. D. Cope. He declined to furnish manuscript for publication, but his views were fully expressed in his book "The Primary Factors of Organic Evolution," which had just been published, Chicago, 1896.

[3] E. G. Conklin, "The Factors of Organic Evolution from the Embryological Standpoint," *Proc. Amer. Philos. Soc.*, 35: pp. 78–88, 1896.

[4–5] L. H. Bailey, "The Survival of the Unlike," *Proc. Am. Philos. Soc.*, 35, 1896.

largely matters of opinion, and in general persons believed what they preferred to believe. Indeed this whole subject had become so speculative that it seemed to be a field for the exercise of the imagination rather than of scientific research, and one of the eminent younger biologists, disgusted with this flood of speculation, announced, "I am done with this entire phylogeny business."

Then in 1900 Mendel's principles of heredity, which had remained unrecognized for thirty-five years, were rediscovered and a new science of accurate, experimental knowledge of heredity was born and was christened "Genetics" by Bateson. Almost at once many perplexing problems of heredity were solved; "prepotency" was found to be Mendelian dominance, "reversions" or "atavism" were the reappearance of Mendelian recessives, the results of hybridization were no longer unpredictable and the laws of heredity were at last in process of being discovered.

One year later (1901) De Vries[6] published his great work on the mutations of the evening primrose, *Oenothera lamarckiana,* upon which he had been engaged for fifteen years and in the course of which he observed under rigid experimental conditions among the offspring of this one species the appearance of nine constant mutants, three inconstant and one infertile mutant which differed so much from the parent form and from one another that he called them elementary species, and maintained that they furnished actual, living evidence of experimental evolution. Galton[7] had previously (1892) expressed his belief that "sports," or sudden variations, were the real steps in the evolution of species and Bateson had published his great work on "Discontinuity in the Origin of Species" in 1894, but long before this, Darwin had given it as his opinion that evolution had occurred by means of minute variations rather than by "sports," and in this he was followed by Cope and practically all other paleontologists. Consequently it was not until De Vries had actually demonstrated the sudden appearance of mutations in his cultures that this method of evolution was widely accepted. Since then mutations have been found in almost all organisms that have been carefully studied through successive generations, and in spite of occasional objections on the part of paleontologists or other naturalists who are unable to carry on breeding experiments with their materials, the mutation theory of evolution is now well established, although it is known that mutations may be small as well as great. However, mutations are always inherited, that is, they represent changes in the germ plasm, whereas changes which first occur in developed organisms are not inherited and are called fluctuations. This is indeed the chief distinction between the old evolution of Lamarck and Darwin and the new of Weismann and De Vries; in the old, attention was fixed upon the developed organism and evolutionary changes were supposed to be first made in the adult and then by some mysterious process to be transferred to the germ cells; in the newer views of evolution changes are first wrought in the germ cells and only later appear in the developed organism.

In 1903 Johannsen[8] found that by continued breeding and isolation of self-fertilized beans he could isolate from a so-called pure garden variety nineteen different "pure lines" and that further selection within any one of these lines was without effect. Other similar results in a large variety of plants and animals led to the conclusion that neither artificial nor natural selection could have the effect, which Darwin had postulated, in building up a species from small variations. By some this was hailed as the "death of Darwinism," or natural selection, as a factor in evolution, but it was soon seen to apply only to fluctuations and not to mutations. It is true that selection can not create mutations, but it can act upon mutations that are offered and recent work in the field of genetics has shown that it is a potent factor in evolution.

Almost coincidentally with the rediscovery of Mendelism and the establishment of the mutation theory came the discovery of the cellular basis of these phenomena in the germ cells. The work of certain European biologists had previously furnished evidence that the inheritance material is located in the nuclei of the germ cells and chiefly if not entirely in certain threads, called chromosomes, that are found in those nuclei. When egg and sperm unite in fertilization their chromosomes commingle but retain their individual identity and in the repeated divisions of the fertilized egg, which lead to the developed animal or plant, every chromosome in every nucleus splits lengthwise and its halves separate, going into the two daughter cells; this is repeated at every cell division until every cell of the developed organism has half of its chromosomes from the egg and half from the sperm. Finally when this adult organism in turn forms eggs or spermatozoa the number of chromosomes in these sex cells is reduced to half those present in all other cells. And when the chromosomes of egg and sperm unite in fertilization the full number is again restored. Since on the average organisms inherit as many traits from one parent as from the other and since they receive an equal num-

[6] H. De Vries, "Die Mutationstheorie," Leipzig, 1901, 1903.

[7] F. Galton, "Hereditary Genius," 2d ed, London, 1892.

[8] W. Johannsen, "Ueber Erblichkeit in Populationen und in reinen Linien," Jena, 1903.

ber of chromosomes from each parent it seemed highly probable that the chromosomes contained the inheritance material, but at the beginning of this century no one had demonstrated any genetic relationship between any particular chromosome in a germ cell and any particular developed character.

Then about the beginning of this century Professor McClung, now at the University of Pennsylvania, found that an "odd" or "accessory" chromosome is present in the males of certain grasshoppers, and in one of the last cell divisions leading to the formation of spermatozoa this chromosome did not divide but went into one cell but not into the other and thus two kinds of spermatozoa were formed, one containing the accessory chromosome and the other lacking it. Since these two kinds were equal in numbers, and since on the average males and females are equal in numbers, McClung[9] in 1902 suggested that this accessory chromosome was the determinant of sex.

In keeping with the predominance of men and of male psychology in science it was but natural that it should have been assumed that this accessory chromosome would not be found in females and that its presence in males represented the initial cause of male superiority. But alas for this pleasing fiction! Professor Wilson[10] of Columbia University and Miss Stevens[11] of Bryn Mawr College independently demonstrated in 1905 that there are two such chromosomes in the females of certain insects and only one, or one and a fragment of another, in males. This difference in the chromosomes of males and females was later found in many other species, including man. In short, the male generally lacks certain hereditary materials which the female possesses and instead of woman being the lesser man, as Tennyson expressed it in "Locksley Hall," man was found to be in this respect the lesser woman. Thus the initial cause of sex, which had been a subject of speculation for thousands of years, was found in a difference in certain chromosomes in the two sexes.

A study of the method by which the usual number of chromosomes is reduced to half in the egg and sperm led to the discovery of the causes of Mendelian heredity. In 1901 the late Professor T. H. Montgomery,[12] of the University of Pennsylvania, found that chromosomes of maternal and paternal origin unite in pairs just before the last cell divisions leading to the formation of the sex cells, and in 1903 Sutton,[13] a student of McClung's and Wilson's, discovered that corresponding chromosomes from the father and mother come together in pairs, just as corresponding fingers of the right and left hands meet when the hands are pressed together, thumb to thumb, index to index, etc. In the subsequent cell division the chromosomes of each pair separate so that each germ cell thus formed contains only one of the chromosomes of each pair, or one half the total number. Each of the two cells formed by this reduction division contains one set of chromosomes, like the set of fingers on one hand, but unlike the fingers which are permanently attached to the hands, the chromosomes are free to change hands so that one germ cell may contain a thumb chromosome from the father, an index from the mother, etc., while the other cell contains corresponding chromosomes from the other parent. This union of parental chromosomes into synaptic pairs and their subsequent separation in the reduction division exactly parallels the phenomena of Mendelian segregation of characters, and there is no doubt that it is the cause of Mendelian inheritance.

With these discoveries the foundations were laid for the marvelous developments of cytology in relation to genetics which have characterized the last thirty years. Thus within the first five years of this century were established the Mendelian law of heredity, the mutation theory of evolution, the inability of selection to build up species from fluctuations and the chromosomal mechanisms of sex determination and heredity.

III

Upon these foundations the study of evolution has advanced with giant strides during the past twenty-five years. This is especially true of the correlation between mutations, or inherited variations, and the constitution of the germ cells. Indeed this correlation has given us for the first time an understanding of the mechanisms of heredity, mutation and evolution.

Imagine the amazement and incredulity of the naturalists of a former generation, who thought of evolution only as the transformations of developed organisms under the influence of changing environments, if they could learn that to-day the problems of evolution center largely in the structures and functions of germ cells! And yet this is strictly and literally true. The germ cells are the only living bonds not only between generations but also between species, and they contain the physical basis not only of heredity but also of evolution.

9 C. E. McClung, "The Accessory Chromosome-Sex Determinant?" *Biol. Bull.*, 3: 43–84, 1902.

10 E. B. Wilson, "Studies on Chromosomes. I. The Behavior of the Idiochromosomes in Hemiptera," *Jour. Exp. Zool.*, 2: 371–405, 1905.

11 N. M. Stevens, "Studies in Spermatogenesis," *Carnegie Inst. Wash. Pub.*, 39: 3–32, 1905.

12 T. H. Montgomery, Jr., "A Study of the Chromosomes of the Germ Cells of Metazoa," *Trans. Amer. Philos. Soc.*, 20, 1901.

13 W. S. Sutton, "The Chromosomes in Heredity," *Biol. Bull.*, 4: 231–251, 1903.

In the microscopic chromosomes which are found in the nuclei of all cells and in the ultra-microscopic inheritance units or genes which lie in those chromosomes are found the earliest causes of heredity, sex, mutation and evolution. In biology, as also in physics and chemistry, the ultimate causes of phenomena are found not in gross bodies but in their minutest constituents. What molecules and atoms and electrons are to the physicist and chemist, chromosomes and genes are to the biologist. Present problems of evolution are not how one fully developed organism is transmuted into another, for this never happens, but rather how one type of chromosome or gene is transformed into another—not so much the effect of natural selection in eliminating certain adult forms and preserving others, although this does occur, as its much greater effect in eliminating certain types of embryos, germ cells and genotypes.

No longer do biologists discuss how adult characters can be crowded back into the egg, nor how characters acquired by an adult can be inherited, for they are almost unanimously agreed that these things never happen, but rather how changes in chromosomes and genes are produced and how they give rise to changes in the developed organism. This revolution in the study of evolution had its remote beginnings in the nineteenth century, but its most significant results are confined entirely to the present century, most of them to the past twenty years.

It is impossible in the brief time at my disposal to deal with all the significant advances of these recent years in the study of evolution, and I must of necessity select only a few for presentation. Perhaps the most significant of these discoveries relates to the causes of mutations. In general it may be said that they are caused (1) by changes in the numbers and associations of whole chromosomes, (2) changes in the composition of individual chromosomes, and (3) changes in the genes themselves. De Vries did not attempt to trace the mutations of his evening primroses to the chromosomes, but other younger persons, many of them Americans, did this, and they found that the original form, *Oenothera lamarckiana,* has 14 chromosomes, whereas there are 15 chromosomes in seven different mutants—among them *O. lata, O. albida* and *O. scintillans,* while in *O. gigas* there are 28 and in *O. semigigas* 21. Since there are typically 7 chromosomes in each of the male and female sex cells of *O. lamarckiana* it seemed probable that these mutants were produced from sex cells some of which had more than 7 chromosomes. It sometimes happens that a synaptic pair of chromosomes fails to separate in the reduction division, in which case 8 chromosomes go into one sex cell and 6 into the other. If then a sex cell having 8 chromosomes unites with one having the normal number 7, a form with 15 chromosomes results and if this additional chromosome is from a different synaptic pair in different cases it would account for the differences in those mutants, each of which has 15 chromosomes. Likewise if all the synaptic pairs fail to separate it leads to the production of a sex cell having 14 chromosomes and if such a cell unites with a normal sex cell with 7 it produces the mutant *semigigas* with 21 chromosomes. If both male and female sex cells fail to undergo reduction each would contain 14 chromosomes and if two such should unite it would produce the mutant *gigas* with 28 chromosomes. There are other peculiar modifications of the chromosomes of Oenothera that can not be dealt with here.

Many such cases of supernumerary chromosomes have now been discovered in various plants. The reduced number of chromosomes is known as haploid ($1n$), the usual condition resulting from the union of two haploid sex cells is known as diploid ($2n$), that in which there is one additional chromosome is $2n+1$, etc., that in which a diploid unites with a haploid is known as triploid ($3n$), that in which two diploid cells unite is a tetraploid ($4n$), and cells with still larger numbers of chromosomes are called in general polyploids. One of the most notable of these cases of supernumerary chromosomes has been found by Blakeslee[14] and his associates in the numerous mutants of the common jimpson (or Jamestown) weed, *Datura stramonium.* Here the typical diploid number is 24, but the addition of one or another chromosome ($2n+1$) has given rise to twelve different mutants, while many other types are produced by the further addition or subtraction of chromosomes, as well as by the breaking in two of certain chromosomes and their recombinations, a phenomenon known as segmental interchange, translocation or "crossing over."

Haploid, diploid, triploid and tetraploid plants of one species often differ markedly in appearance and they breed true if the chromosomes from the two parents are balanced so that they can unite in synaptic pairs before the formation of the sex cells. Many true Linnaean species are known that have their chromosomes in multiples of some basic number and they have probably arisen by the multiplication of their chromosomes. For example, many species of roses, and indeed many genera of the large family Rosaceae, have chromosomes in multiples of 7, and in those genera where the basal number is 8, as in plums and cherries, or 17, as in apples, hawthorns

[14] A. F. Blakeslee and B. T. Avery, Jr., "Mutations in the Jimpson Weed," *Jour. Heredity,* 10: 111–120, 1919; A. F. Blakeslee, "Types of Mutations and Their Possible Significance in Evolution," *Amer. Nat.,* 55, 254-267, 1921.

and quinces, Darlington and Moffett have shown that this unusual number has arisen from ancestral species with 7, through non-disjunction of chromosomes at the time of cell division. In wheat, oats and barley the basal number of chromosomes is 7, while different species have multiples of this number. Different species of chrysanthemum have chromosomes in multiples of 9; more than forty species of groundsel (Senecio) have chromosomes in multiples of 10; seven species of docks and sorrels (Rumex) also have chromosomes in multiples of 10. Many other similar cases of wild species with chromosomes in multiples of some basic number could be cited. In other native species, as in the genera Viola and Crepis, chromosomes may be in multiples of some basic number, or they may be that basic number plus one or two, as in some mutants of Oenothera and Datura.

Nearly a score of new species of plants, having all the characteristics of true Linnaean species, have been artificially produced by hybridization or operations under experimental conditions with consequent changes in chromosome numbers and associations. These new species are fertile *inter se,* but are sometimes sterile when crossed with either one or both of the parent species, thus fulfilling the strictest definition of true species as laid down by many systematists. Thus Goodspeed and Clausen[15] crossed two species of tobacco plants, namely *Nicotiana glutinosa,* with 12 haploid chromosomes and *N. tabacum* with 24. The first hybrid generation normally had 36 somatic chromosomes and they were generally sterile, but one partially fertile hybrid produced second generation plants one of which was remarkably large and robust and was found to have 72 somatic chromosomes, that is, it was a tetraploid or *gigas* form. This plant bred true but was sterile when back-crossed to one of the parent species (Clausen[16]).

Another case of the production of a true synthetic species by hybridization and subsequent doubling of the number of chromosomes was described by Newton and Pellew;[17] two distinct species of primrose, *P. verticellata* and *P. floribunda,* crossed and produced a sterile hybrid; this was propagated vegetatively for several years when it suddenly produced a fertile shoot by bud transformation which bore normal seeds and from these arose a new and fertile species, *P. kewensis,* with a tetraploid number of chromosomes.

Lindstrom[18] cut off the tops of young tomato plants of the species *Lycopersicum pimpinellifolium* and in the callus that formed, chromosome doubling took place in some of the cells, and from these cells some tetraploid sprouts arose and bore fruit and seeds. These were highly fertile and have produced plants so different from the original stock that they should be classed as a new species, especially as they are cross-sterile with the parent species.

Another new species produced by hybridization is the pink chestnut, *Aesculus carnea,* from a cross between *A. hippocastanum* and *A. pavia,* the former with 20 small chromosomes, the latter with 20 large ones, while the new species has 20 large and 20 small chromosomes, or 40 in all (Hurst [19]).

Still more remarkable are the results of crossing distinct genera of plants such as the common radish, *Raphanus sativus,* and the cabbage, *Brassica oleracea,* each with 9 haploid chromosomes leading to the production of a new tetraploid genus *Raphanobrassica* with 36 chromosomes (Karpechenko[20]); also the formation of a new genus *Triticale* by crossing wheat, *Triticum vulgare,* and rye, *Secale cereale* (Levitsky and Benetzkaia[21–22]).

All the preceding cases have to do with the production of new mutants or true species by changes in the numbers and associations of whole chromosomes. A second class of mutants are caused by changes in the composition of individual chromosomes. The members of synaptic pairs of chromosomes sometimes twist round each other, break and reunite so that portions of chromosomes become interchanged; this is known as "crossing over"; or portions of a chromosome may become detached and united to another chromosome, which is known as "translocation"; such changes in the composition of chromosomes lead to many complicated mutations which can not be described here.

All changes in the numbers or constitution of chromosomes are known as chromosome mutations or better, permutations. Another and perhaps the most important class of mutations are those caused by changes in the ultramicroscopic genes which lie in the chromosomes. Such mutations have been found

15 R. E. Clausen and T. H. Goodspeed, "Interspecific Hybridization in Nicotiana, II," *Genetics,* 10: 278–284, 1925.

16 R. E. Clausen, "Interspecific Hybridization in *Nicotiana,* VII." *Univ. Calif. Pubs. in Bot.,* 11: 177–211, 1928.

17 W. C. F. Newton and C. Pellew, "*Primula Kewensis* and its Derivatives," *Jour. Genetics,* 20: 405–467, 1929.

18 E. W. Lindstrom, "A Fertile Tetraploid Tomato, Cross-Sterile with Diploid Species," *Jour. Heredity,* 23: 115–121, 1932.

19 C. C. Hurst, "The Mechanism of Creative Evolution." Cambridge Univ. Press, 1932.

20 G. D. Karpechenko, "Konstantwerden von Art- und Gattungsbastarden durch Verdoppelung der Chromosomenkomplexe," *Der Zuchter,* I; 133, 1929; "A Contribution to the Synthesis of Constant Hybrids of Three Species," Proc. of the All-Russian Cong. Genet., Plant and Animal Breeding, 2: 277, 1929.

21–22 G. A. Levitsky and G. K. Benetzkaia, "Cytological Investigations of Constant Intermediate Rye-Wheat Hybrids," Proc. of the All-Russian Cong. Genet., Plant and Animal Breeding, 2: 1929.

in almost all animals and plants that have been bred in large numbers under experimental conditions. The most used animal for these experiments is the little vinegar fly *Drosophila melanogaster*. Indeed in the field of heredity and evolution this is the most famous animal in the world, and the man who has been the leader in its study, Professor T. H. Morgan, has recently received the Nobel Award in recognition of the importance of his work. Scores, if not hundreds, of different workers have been engaged in the intensive study of this little gnat and they are sometimes facetiously called Drosophilists or modern worshippers of Beelzebub, the god of flies. The peculiar advantages of this animal for the study of heredity and mutation are: (1) The ease with which it can be kept and bred in great numbers in milk bottles; (2) the fact that a new generation can be obtained every twelve days; (3) the large number of hereditary characters that can be recognized superficially; (4) its relatively small number of chromosomes, 4 pairs, that can be readily distinguished one from another; (5) finally more than 500 mutations have been found in some 25 millions of these animals that have been studied during the past 25 years. These mutations affect every part of the fly, such as color and form of body, wings, eyes, bristles, length of life, viability, liability to disease, etc. By several ingenious methods, which time does not permit me to describe, it has been possible to locate the particular genes that have undergone mutation in particular chromosomes and even in particular regions of those chromosomes, so that chromosome maps have been constructed giving the locations of these mutant genes in the different chromosomes.

These mutations seem to go in all *possible* directions, but not in *all* directions. Most of these mutant flies are less viable than the wild stock from which they came and many are lethal, that is, they kill their possessor sooner or later, but a few of them are progressive. They may occur in germ cells or in somatic cells. In short, wherever there are genes these may undergo mutation. The fact that most of these mutations are degressive rather than progressive has led some persons to doubt whether they can be the materials for evolution, but it is necessary to remember that much evolution has been degressive and the small number of progressive mutants as compared with the multitude of regressive ones teaches us at what a price progress has been bought.

IV

The nature of the changes in genes by which mutations are caused is unknown, but it seems probable that it is some kind of physical or chemical change. The fact that it may affect one gene and not another similar one that is not more than one thousandth of a millimeter away would seem to indicate that it is not some general environmental influence. This consideration led Muller[23] to the conclusion that it might be due to some form of radiation similar to those by which physicists knock electrons out of atoms. Consequently he subjected *Drosophila* to x-rays and found that the frequency of mutation was increased about 150 times. Some of these mutants were of the same type as were previously known, but many were new. Most of them were detrimental, and more than half of them were lethals, but some of them were carried through 50 generations without reverting. In addition to gene mutations, x-rays cause breaks and translocations in chromosomes, which in turn cause marked changes in the developed animals.

A similar increase in mutation has been caused by x-rays in the case of barley, corn, the jimpson weed, a wasp, *et al.* They have also been induced by radium and possibly by cosmic rays. But mutations are far too common and x-rays and radium far too uncommon to warrant the conclusion that mutations are generally caused by these means.

Searching for some more common cause of mutation Goldschmidt[24] found that by heating the eggs of *Drosophila* to such a degree as to kill most of them he obtained from the survivors new types, and Jollos[25] reports that larvae of *Drosophila* that were subjected to a temperature of 36° C. for 15 to 23 hours produced during eight months more than 100 mutants, while not a single one appeared in his controls. Generally these mutations appeared at least five generations after the experiments, and most important of all some of them were "orthogenetic" or progressive in a definite direction. Thus for the first time, he announced, a progressive series of mutations had been called forth by a common environmental factor. Plough and Ives,[26] who have just this month announced the results of their repetition of the experiments of Goldschmidt and Jollos, find that six times as many mutations occur in the heated lines as in the controls, but while this proves that increased temperature is a fruitful source of mutations there is so far no confirmation that these mutations are directed. Indeed Plough and Ives expressly deny that there is

[23] H. J. Muller, "Artificial Transmutation of the Gene," SCIENCE, 66: 84–87, 1927; "The Method of Evolution," *Sci. Monthly*, 29: 481–505, 1929.

[24] R. Goldschmidt, "Experimentelle Mutation und das Problem der sogenannaten Parallelinduction Versuche an Drosophila," *Biol. Zentralblatt*, 49: 437–448, 1929.

[25] V. Jollos, "Studien zum Evolutionsproblem," *Biol. Zentralblatt*, 50: 541–554, 1930; "Gerichtete Mutationen und ihre Bedeutung für das Evolutionsproblem," *idem.*, 51: 137–140, 1931.

[26] H. H. Plough and P. T. Ives, "Heat-induced Mutations in Drosophila," *Proc. Nat'l. Acad. Sci.*, 20: 268–273, 1934.

any indication of orthogenetic mutations in their experiments.

Hitherto the great objection to the mutation theory of evolution has been that mutations are so generally regressive and that they lead nowhere. The only method of meeting this objection has been to rely upon natural selection to eliminate vast numbers of useless mutations and to preserve the few useful ones and thus slowly to build up the marvelous combinations of useful adaptations that all organisms possess. But there are many indications in the living world that evolution has proceeded in certain directed lines, sometimes even further than was useful, as for example in the enormous size of body and weight of armor of certain Dinosaurs and Titanotheres, and many zoologists since Eimer have insisted that "orthogenesis" or directed evolution is a necessity. If directed mutations can be caused by some common environmental factor, as Jollos suggests, it would solve one of the major difficulties of the mutation theory. Osborn[27-29] in particular has emphasized the necessity of definitely directed variations in a series of publications during the past forty years, the last of which has just been published (1934). He originally called this principle "definite variations" and later "rectigradations." More recently he has stressed the necessity not only of directed mutations, but, much more, of useful and progressive mutations in any explanation of evolution. This principle of the *origin* of the fittest, as contrasted with the *survival* of the fittest, he calls "aristogenesis."

Goldschmidt (1933) has recently emphasized the importance of certain embryological processes in evolution. He concludes that genes control development partly by influencing the velocities of certain reactions, and he suggests that by changing the differential growth rate at an early stage a perfectly new evolutionary line could be started. This suggests a speculation which I advanced before this society in 1903, and published in greater detail in 1905, regarding the origin of major groups, or phyla, of the animal kingdom. The older evolutionists, for example, undertook to show by what transformations of the developed body an annelid or arthropod could be converted into a vertebrate. It was supposed that the invertebrate turned upside down, its mouth closed up and a new mouth formed, and many other changes occurred which would be absolutely impossible in any developed animal. Similar impossible translocations of organs of adults had been proposed to explain the origin of inverse asymmetry, as for example in those rare cases in man where the heart is found on the right side instead of the left and all other asymmetrical organs are reversed in position. When it was discovered that such inversions of all the organs of sinistral as compared with dextral snails could be traced back through the embryology to the early egg cell, it was evident that this inversion was due to relatively slight changes in the locations of substances in a single cell; such changes are now known to be caused, in the last analysis, by genes. Similarly, when it was discovered that the location of the principal organs of several different phyla could be traced back to the pattern of localization of special substances in their eggs, I suggested that relatively slight changes in the localization of these substances would bring about the characteristic differences in the location of the organ systems of vertebrates as compared with invertebrates. Thus instead of turning a developed worm or arthropod upside down, and making many impossible translocations of its organs it would be relatively simple to convert one type into another by translocations within a single cell, such changes ultimately being caused by gene activity. Unfortunately this suggestion, like that of Goldschmidt just mentioned, is at present without experimental proof.

V

Adaptations have always been the chief marvel of the living world, and their method of origin is still the greatest problem of biology. The only natural explanation that has as yet been established is Darwin's principle of the elimination of the unfit and the survival of the fit. There is abundant evidence, both observational and experimental, that this principle is true, but when we load upon it the obligation of explaining all the marvelous adaptations and combinations of adaptations that every living thing possesses the doubt arises as to whether this principle alone can support the enormous burden. I have long felt, along with Cope, Osborn and many others, that some additional factor is needed to explain such universal adaptations. And Darwin himself felt the force of this, for he once said that he never thought of attempting to explain the origin of such a complex and wonderfully coordinated structure as the eye without a shudder. He sought refuge, as did Cope and many others, in the inherited effects of use and disuse as an aid to natural selection, but this refuge is now denied us, for the evidences from genetics are conclusive that such effects are not inherited.

A solution that has found favor with many geneticists lies in the vastly greater duration of past time than was formerly allowed for organic evolution. Darwin estimated that past evolution must have required something like 400 million years. Lord Kelvin, speaking for the physicists of his day, would

[27-29] H. F. Osborn, "Aristogenesis, the Creative Principle in the Origin of Species," *Am. Nat.*, 68: 193–235, 1932.

allow him not more than 100 million years. But the physicists, astronomers and geologists now say that the earth was ready for life at least 1,000 million years ago, and geneticists console themselves with the thought that given almost infinite time and almost an infinitude of mutations almost anything could happen. But after all they can not help feeling that this is not a satisfactory solution of the vast problem of fitness—at present by far the greatest problem of biology.

Another possible solution of this problem was first pointed out by Weismann in his doctrine of intrapersonal selection, and I proposed[30] the extension of the selection principle to many reactions of living things. We know that all organisms are differentially sensitive, that is they move or grow toward certain sources of stimuli and away from others, and in general they respond positively to stimuli which we would call pleasant or satisfactory and negatively to those which we call unpleasant or unsatisfactory. In short, they are generally able to differentiate and select between that which is satisfactory and that which is not. No one can at present explain this property of life, but apparently it is a general characteristic of all living things. It characterizes the behavior of germ cells and embryos as well as adult organisms. It is the basis of that form of behavior known as "trial and error"; it is fundamental to all learning and is the beginning of intelligence and wisdom in man as well as in higher animals. This capacity to differentiate and select is not unlike the "archaesthetism" of Cope and it is at bottom an extension of the selection principle to the reactions of organisms—but with this difference, that whereas in Darwinian selection the selector or eliminator was found exclusively in the environment, in this conception the organism itself also selects or eliminates. There is no mechanistic explanation of this property of life, but the same is true of many other properties of living things. Because we can not at present explain mechanistically the properties of the organization of protoplasm and its capacities of assimilation, reproduction and sensitivity is no ground for denying that these properties exist, and the same is true of the property of organic adaptation. But given these properties, science can explain in a mechanistic, that is, in a causal manner, multitudes of structures and functions and reactions that have arisen in the course of evolution.

It seems to me that recent theories of evolution have too often left out of account these fundamental properties of life. Assigning all evolution to externally caused mutations and to environmental selection neglects the fact that the organism is itself a living, acting and reacting system. Life is not merely passive clay in the hands of environment, but is active in response to stimuli; it is not merely selected by the environment but is also itself ever selecting in its restless seeking for satisfaction. Macfarlane[31] has called this property of organisms "proenvironment" and has assigned to it an important function in evolution. Cuenot[32] has shown that many animals seek and find by a process of trial and error those environments for which they are by nature best adapted, and he calls this "preadaptation." By a similar process, namely, the elimination of unsatisfactory responses, most of the individually acquired adaptations of organisms may be explained. Such acquired adaptations as the repair of injuries, the regeneration of lost parts, acclimatization to high altitudes or temperatures, neutralization of poisons and immunity to disease, which were at one time hailed as a "death-blow to Darwinism," may be explained by an extension of the Darwinian principle of the elimination of the unfit to the multitudinous reactions of organisms.

From my earliest introduction to the science of biology I have been an admirer of August Weismann. Of late it has become fashionable to decry the speculations and theories of Weismann, since they were not based on experiment. But no one can truthfully deny that his logical deductions were a powerful stimulus to research and that many of them have been confirmed in a truly remarkable manner by recent work. He maintained, long before it was demonstrated by genetics and cytology, that the hereditary substance consists of discrete particles, his determinants, arranged in a linear series in the chromosomes. His prediction that one of the maturation divisions in the formation of the egg and sperm must lead to the reduction of the chromosomes in those cells to one half the number present in somatic cells was almost as brilliant an example of scientific prophecy as was the prediction of the existence and position of the planet Neptune. And finally his explanation of the origin of fitness in the living world is still, I think, the best scientific conception that has ever yet been offered. I can not better express my own views on this subject than by closing with these words from the preface of his last book:[33]

> Although I may have erred in many single questions which the future will have to determine, in the foundation of my ideas I have certainly not erred. The selec-

[30] E. G. Conklin, "Problems of Organic Adaptation," *Rice Inst. Pamphlet*, 8: 299–380, 1921.

[31] J. M. Macfarlane, "The Causes and Course of Organic Evolution," New York, 1918.

[32] L. C. Cuenot, "La genèse des espèces animales," Paris, 1911.

[33] A. Weismann, "Vorträge über Descendenztheorie," Jena, 1902.

tion principle controls in fact all categories of life units. It does not create the primary variations but it does determine the paths of development which these follow from beginning to end, and therewith all differentiations, all advances of organization and finally the general course of development of organisms on our earth, for everything in the living world rests on adaptations.

NOTE: In general in the preceding footnotes only the earliest in a series of papers, or a later one which presents a general summary, has been cited.

SCIENTIFIC EVENTS

EXHIBIT AT THE MEETING OF THE BRITISH MEDICAL ASSOCIATION

ACCORDING to the *British Medical Journal,* the Pathological Museum, arranged in connection with the annual meeting of the British Medical Association, at Bournemouth, was housed on the lower floor of the Municipal College. A rare collection of pathological specimens were arranged on benches around each room, with a large number of microscope preparations on tables in the center. The pathological specimens were grouped on an anatomical basis, and consisted chiefly of unusual lesions and "curiosities," many of which excited considerable interest. The nature of each specimen and the name of the exhibitor were announced in the catalogue. The Museum Committee expressed its appreciation in particular to the following colleges and hospitals which lent material for the museum or were responsible for exhibits: the Royal Army Medical Corps, the University of Edinburgh, Bethlem Royal Hospital, St. Mark's Hospital, St. Bartholomew's Hospital, Westminster Hospital, St. George's Hospital, the South Devon and East Cornwall Hospital, and the Cancer Hospital, London. The museum included also, according to the *Journal,* a number of special exhibits, some of which were intended to illustrate subjects discussed in the scientific sections. These comprised a series of specimens and photographs arranged by Dr. C. Lovell, of the Bethlem Royal Hospital, London, showing progressive pancreatitis in relation to mental states. Workers at the Cancer Hospital, London, had on view a series of malignant tumors of skin and connective tissues of mice and rats produced by methylcholanthrene, a transformation product of the deoxycholic acid of bile, and a number of specimens demonstrating the effects of oestrin in the genito-urinary system of mice. Dr. Haddow, of Edinburgh University, arranged a series of sections showing cellular transplantations of fowl sarcoma. Amongst items of more general interest may be mentioned a series of ophthalmological color drawings, instruments and books exhibited by Mr. Arnold Sorsby; the clinical picture gallery arranged by Dr. S. Watson Smith; the pedigree charts of families affected by polyposis intestini, shown by Dr. Cuthbert Dukes, and a series of pulmonary specimens of surgical interest lent by George Mason, of Newcastle-upon-Tyne.

MEMORIALS TO PATRICK MANSON AND RONALD ROSS

THE EARL OF ATHLONE, chancellor of the University of London, on the evening of June 28 unveiled in the library at the London School of Hygiene and Tropical Medicine a memorial tablet to Sir Patrick Manson and a bust of Sir Ronald Ross at a reception to mark the incorporation of the Ross Institute in the school. The tablet was the gift of Lady Manson and family, and the Ross bust was presented by the sculptor, Lady Welby.

The Earl of Athlone, as reported in the London *Times,* said that the occasion was one for the honoring of the memory of Manson and Ross. Manson, after his labors overseas, alone and ill-equipped, had the vision and courage to inspire and mold teaching and research in tropical medicine, and to lay the foundations of a nobly conceived center of education. Ross, inspired in turn by the father of tropical medicine, brought to the teeming millions of the Tropics a wonderful discovery. Manson was a pioneer in the untrodden paths of medicine. After leaving Scotland at the age of twenty-one, he went to Formosa and worked there and in China for nearly a quarter of a century in isolation. He discovered by laborious experiment that the intermediation of the mosquito acted as a nurse in propagating the disease of man—the filaria worm. He made great discoveries and described several new parasites of man and several new diseases. In 1897 Manson set himself to found the London School of Tropical Medicine, and laid his scheme before Mr. Joseph Chamberlain, who appreciated its significance, and in two years' time the original school was built and organized under the aegis of the Seamen's Hospital Society in the Albert Docks.

It was Manson who inspired Ronald Ross and pointed the road along which Ross traveled towards his conquest of malaria, which they recalled now upon the incorporation of the institute which bore his name. When Ross turned to the serious study of disease he concentrated on its prevention, and after his entry into the Indian Medical Service his reaction to the misery of life in India became intensified. He saw that many of the diseases of India were preventible, and that malaria was in many tracts a greater scourge than either plague or cholera. He worked out a technique for examining the mosquito and for how malaria