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THE GERMINAL BACKGROUND OF SOMATIC MODIFICATIONS[1]

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ON the theory apparently that all pleasures must carry a penalty of compensatory pain, some former grim group of zoological Puritans decreed that though this organization may eat, drink and be merry, it must in the end endure a retiring address, so-called presumably because it conduces to the usual result of retiring, sleep. No vice-president of Section F is ever brave enough to break the bonds of this ancestor worship, so you and I, fellow zoologists, are here alike victims of a tradition. Let's be merciful!

In venturing to speak briefly on the germinal background of somatic acquirements, you will observe that I have reversed the traditional order of this combination, the germinal foundation preceding the acquirement. Possibly this is the only novelty you will find in my remarks. But since general topsyturviness is the order of the day, I can at least plead modernity. In these days when children run their parents, freshmen instruct their professors and wives support their husbands, why should not some of our venerable biological riddles be approached backward?

We used to dream of romance, with each yearning soul finding its unerring way to its predestined mate; we now talk of propinquity and endocrines. The dart of Dan Cupid seems slated for replacement by the hypodermic needle and a proper blend of hormones. We used to hear of sin; we now know only psychoanalysis and unsatisfied self-expression. We used to read of prepotencies and pointings, but this lore of the fancier has given place to the chemistry of the gene. So in such precedents of revolution and dis-

[1] Address of the vice-president of Section F—Zoological Sciences, American Association for the Advancement of Science, December 31, 1929.

illusionment I would again justify my means of approach to a very old problem.

The possibility of modifying germ-plasm stands as a perpetual challenge to the biologist because the problem of variability, of the origin of new characters, constitutes the very foundation of both genetics and evolution. Until we know more of the causes of germinal variation than we do to-day, we must remain ignorant of the most essential factor in each of these fields. So it is obvious why, although baffled at almost every turn, the experimenter returns again and again to his attack on the central problem.

Great skepticism prevails among geneticists about interventions of the parental body affecting the germ-cells, particularly in any specific way. Since on the basis of negative evidence at least, the efforts of the flesh seem unavailing in any perceptible modification of germ-plasm, the modern student of heredity almost universally falls back upon the non-committal conception of a directly varying germinal substance, and simply pleads ignorance of the causative stimuli, internal or external, that induce such changes.

The truth is that in the very setting of the problem of the inheritance of somatic acquirements, we are, from one point of view, faced by an apparently insoluble dilemma. For the very fact that a character can be acquired by the body carries with it the inescapable admission that the constitutional capacity for its appearance already exists. It is a commonplace of modern genetics that the characteristics of an organism require for their expression not only an adequate stock of germinal materials which we call genes, but a suitable environment. From this point of view, an acquired character is one in which not the *genic constitution* but the *environment* has been changed.

Such a statement of the problem, however, meets the immediate challenge of explaining how such an acquired character is related to the genes of the germ, but inasmuch as we do not know how any character, acquired or otherwise, is related to the germ, our ignorance is no more dense than it was before. Certainly if our modern knowledge of genetics teaches us anything, it is how little we know about the relationship that exists between the chemical complexes of the germ and the expressed characteristics of the body. We know that any so-called character of the body is the indirect, cumulative product of a long series of interactions of these original chemicals; that great numbers of genes must cooperate to produce even the simplest character; that no one of these genes more than another represents the character in any literal sense, and that any particular gene influences not only one but many characteristics of the body.

There is an increasing amount of experimentation, particularly with X-ray and with radium, which shows that external influences may directly affect germ-plasm and that the resulting changes may become hereditary. The brilliant successes of Muller[2] and his associates in this field through radiation of Drosophila are of so recent occurrence as to be fresh in the minds of you all. Muller, you will recall, by means of X-ray bombardments increased the frequency of mutation about 150 times. Many of the induced mutations were the same as had already been found to occur in ordinary cultures of Drosophila; many were new. As with all observed mutations, including the four hundred odd which have been discovered in Drosophila alone, most were detrimental to the organism. Likewise most of them were recessive. The results seemed to be the random effects of ultramicroscopic bombardments, since even the twin gene of the closely associated homologous chromosome remained unaffected. Since the gene must be a chemical as well as a genetical entity there seems no reason to doubt that the outcome is due to a permanent change in its molecular constitution. As Muller graphically puts it: "The roots of life—the genes—had indeed been struck, and had yielded." He points out, furthermore, the similarity of the X-ray mutations to natural mutations which have been found in Drosophila and concludes that "the minute amounts of natural radiation present almost everywhere in nature . . . some of it of terrestrial origin, derived from the radium and other radioactive substances in earth, water and air, and a smaller part of it of cosmic origin, apparently derived from the diffuse and distant factories of matter . . . all this natural radiation *must* be producing some mutations in the living things on earth."

Within just the past few months Babcock and Collins have announced actual experimental demonstration that short-wave radiations from the earth itself either cause mutation or affect its rate of occurrence. They exposed genetically similar strains of fruit-flies in two different localities, one the university campus at Berkeley, California, the other in Twin Peaks tunnel, San Francisco, where the rock gives off about twice as much radiation as does the campus soil. After five months of culturing in these respective localities a check-up of their records showed about twice as much mutation in the tunnel cultures as occurred in the campus controls. The mutation studied was a "sex-linked lethal" which caused all males to die before hatching, leaving only females in the new generation. The differential percentage in the two localities was found to be constant and consistent. And at the present meeting we have heard Dr. Hanson, although working entirely independently

[2] *Scientific Monthly*, December, 1929, p. 481.

and in a different region, report essentially similar results.

Thus, we can scarcely overestimate the importance of Muller's findings and of the corroborations, extensions and new applications by such workers as Weinstein, Hanson, Dobzhansky, Stadler, Whiting, Blakeslee, Buchholtz, Patterson, Harris, Oliver, Gowen, Babcock, Collins and others, for here at last we have a plausible escape from that hoary fiction, a "spontaneous variation." Whether or not we have the exclusive cause of gene mutations remains to be seen.

To many of us the outstanding perplexity in the field of variation is not so much the mere appearance of changes in the germinal substance as the appearance of the particular kinds of change that eventually lead to that hand-in-glove relationship between organism and environment that we call adaptation. The accomplished facts seem almost overwhelmingly to suggest that environment must play an important part in initiating as well as in conditioning particular kinds of germinal changes.

Time and again in the past, according to paleontologists, whenever conditions arose that would permit of the existence of new types of living organisms, forms admirably adapted to those conditions appeared. In some way the environment molded these new inhabitants to its bounds, and it seems well-nigh incredible—no matter what eons of time are vouchsafed us—to believe that this has been done merely by the negative method of killing off generation after generation of the non-conformists. For on such a basis not only has the adapted organism had to await the accidental occurrence of a favorable germinal variation, but of hosts of them, often highly interrelated, which then must be sifted and perfected by natural selection through innumerable generations to bring about that marvelous fitness which characterizes living things.

Muller himself[3] gives us an interesting argument favoring the view that, together with natural selection, the multiplicative power of mutated individuals, particularly the favored few as against those having disadvantageous or neutral changes, is all that is required for "turning accident into order," and he contends that natural selection need operate with barely enough stringency to permit the multiplication of that rare minority in a generation in which the new mutations have chanced to be favorable.

Not only the facts of intricate adaptation, however, but various facts of geographical distribution likewise incline one to suspect that altered function or environment, if long continued, is directly instrumental in molding the fauna of a given region; yet experimental proof of such direct influence is lacking. Particularly when one contemplates the highly specialized adaptations of many parasites does he feel skeptical of the doctrine of an all-sufficient natural selection based wholly on accidental variations. For the adaptive mechanisms or adjustments of many of these parasites, whether such internal forms as intestinal protozoa or such external ones as bird-lice, must be of comparatively recent origin. Since they are often so highly specific that they can not live on even a slightly different species of host, it is evident that they could have reached their own state of highly specialized adaptation only after the host itself had evolved into a distinct species.

As just the reverse of what appear to be more rapidly or recently adapted forms, we have, on the other hand, our so-called "persistent types" which have remained in sluggish apathy for countless eons while their more versatile brethren have run a wide gamut of evolutionary change. One wonders how their genes escaped this radiant bombardment which set so many of their contemporaries on a course of further adaptation; or if their environment put no premium on change, why they did not at least enter upon a course of non-adaptive evolution through the accumulation of chance hit-effects.

Then again we have to face the problem of what appear to be definite trends in evolution as evidenced by similar changes which have appeared in great groups of separate though allied genera and species of animals since their respective departures from the common ancestral group. I refer to what is sometimes termed orthogenesis, though I hesitate to use this term because it means so many different things apparently to so many different people, ranging all the way from some mystical inner perfecting principle, to merely a general trend in evolutionary development due to the natural constitutional restrictions of the germinal materials, or to the physical limitations imposed by a narrow environment. The impression is held by many students of evolution that certain variations are prone to occur more frequently and more widely than others, in various related organisms, and some believe that such changes, irrespective of whether they are helpful or harmful to the species, tend to accumulate in definite directions. If favorable, it is obvious that their perpetuation is more assured. Since, in a former paper, I have commented rather fully on various lines of this evidence, I shall not review them here. It is sufficient for present purpose to say that many investigators have pointed out parallelisms in variation which tend to appear in different branches of the same large group of organisms.

One of the most recent studies of the kind with which I am acquainted is that of Metcalf[4] called

[3] *Loc. cit.*

[4] *Jour. Morph. and Physiol.* 45: 1, March, 1928.

"Trend in Evolution." In the Salpidae, for example, he finds the same trends in certain characteristics of gut, muscle and eyes appearing in both the solitary and the chain salps. These modifications are most pronounced in the phylogenetically highest groups. While in the colonial types the changes at their inception are probably adaptive or at least not disadvantageous, to the solitary salps they are harmful. Metcalf believes, furthermore, that certain of these evolutionary changes, even though not utilitarian, have been thrown back in the germ-plasm in some way so that they appear far earlier in the individual life cycle than their late phylogenetic origin warrants. Again, he is so impressed with the irregular occurrence of similar characters in subdivisions of such groups as the Opalinidae "along the stem and branches of the phylogenetic tree," as he phrases it, that he sees no reasonable alternative to the conception that the evolution of the family is largely a working out of tendencies inherent in the germ-plasm.

Many other examples of parallelism in related forms will come to the mind of any one who has made taxonomic studies. To take an example from the vertebrates, the same features of color and color-pattern, such as the formation of eye-spots, barring and the like, appear again and again in various genera and species of the pheasant subfamily (Phasianinae). If the original mutations were fortuitous they seem to have instituted a series of changes in definite directions. To be more specific let us glance briefly at the varying stages and types of ocellation to be seen in the interesting group of peacock pheasants (Polyplectron) regarded by systematists as intermediate between the peafowls and the pheasants in the narrower sense. In *Polyplectron chalcurus,* apparently the most generalized species, ocellation does not occur. The only hint of what is to be realized in the more specialized members of the group is found in a pronounced purplish and greenish metallic coloration on certain feathers of the tail. In the male of *P. emphanes,* while there are numerous green metallic iridescent areas on the feathers of the upper wings and back, they have not yet progressed to the condition of being definite ocelli, although on the tail of this same individual there are two transverse bands of ocelli. As a further extension, in the male of *P. thibetanum,* the small feathers of the wings and the feathers of the interscapular region bear distinct small purple ocelli ringed successively with black, light brown and white. The tail is also banded with ocelli. In the male of *P. germaini* the wing-coverts and back bear numerous green ocelli. In the common peacock, which belongs to a related genus, the conspicuous "eye-spots" on the tail are, of course, known to all. Thus this tendency toward the formation of eye-spots in various genera and species of pheasants, apparently hinted at even in the greenish-black iridescence so often visible in the tail-feathers of the common rooster, would seem to be the outcome of a germinal bias which finds different ranges of expression in different species. In some it occurs as eye-spots on the wing-feathers, in others, on the body-feathers; in one species there may be a single, in another two rows of ocelli across the tail. Since these patterns appear in collateral lines, it is obvious that they have not been derived directly one from another but are the outcome of a general tendency present in the group as a whole. One sees in its incipiency in one species a character which may have reached an advanced expression in a kindred group, or finds various more or less intermediate expressions in other related species. The very fact that, instead of existing as a medley of wholly unrelated elements, certain characteristics such as color markings can frequently be arranged as parts of a definite pattern or as stages in a general process indicates directional variation. If one chooses the features of bars and spots and their intergradations in the guinea subfamily (Numidinae) the story is much the same.

The paleontological record also affords many examples of what appear to be directed series of change, even in some cases seemingly to an overdevelopment of structure or to physiological disfunction which has meant final extinction of the species. In such cases possibly for formal explanation we might fall back upon the assumption of some influence of modifying genes or of different equilibria among modifying genes, but then we should have also the problem of accounting for the modifying genes and how they come to operate in seemingly so orderly and determinate a way.

With facts, or what appear to be facts, such as these facing us, then, without denying the probability of fortuitous gene mutations and their initiation by radiant emanations, there yet remains the possibility that mutations may also be otherwise engendered, or that once a gene mutation occurs it becomes more or less subject to other forces within the germ-plasm. Surely genes must be nourished like other living things, since they multiply and grow and apparently display the other characteristics of living matter. They must therefore be open to the vicissitudes which beset other living substance.

Is the gene itself, or that possibly larger vital unit of which it is a part, the fixed unvarying thing we tacitly regard it as being? May it not wax and wane in strength on occasion or may it not have primary and secondary parts like a molecule with side-chains, or be a polymeric particle which may have fewer or more molecular units? Bits of evidence are occurring which suggest some such contingency.

As far back as 1917 Emerson[5] suggested "temporary inactivation" of the gene in certain cases of variegation, and in a similar connection Correns[6] in 1919 conceives of the gene as consisting of a large molecule with variable numbers of duplicate side-chains attached so that "to each number of these side-chains would correspond a definite ratio of white and green in the mosaic plant." This idea of a central molecule and side-chains has a very familiar sound to the speaker inasmuch as he discussed such a conception at some length before the American Society of Naturalists, at Ithaca in 1910.[7] Again, in 1924, in attempting to explain variegation, we find Eyster[8] postulating *genomeres,* gene elements which can segregate during development. According to him these may or may not be chemically identical. Likewise in 1927 Lillie[9] questions the view that genes are always present in the same quantity. Earlier, in 1916, Sewall Wright[10] speaks of "four quantitative gradations of one factor, which determines the amount of the basic color-producing enzyme."

Perhaps the most elaborate and consistently worked out theory of quantitative gene differences is that of Goldschmidt[11] who, in his theory of balanced action of the gene, discusses at much length the effects of the same gene in different quantities. He has been led to his present position through his attempts to analyze cases of intersexuality which he is able to initiate at will in the gipsy-moth.

Experiments and studies in sex determination and sex control all tend toward the conclusion that each sex in addition to its own determiners also contains the genes for the production of the other sex. The actual sex of the individual, leaving out the question of sex hormones and of other possible modifiers, is determined by the quantitative relations between these two sets of genes. According to Goldschmidt one of these sets resides within the sex chromosome, the other outside it. Under ordinary conditions two doses of the gene within the sex chromosome, or in other words, two sex chromosomes, produce the sex represented by the chromosome, but with only one sex chromosome, the outside determiners prevail. Where the male is heterozygous for sex as in Drosophila the sex chromosome carries the determiner for femaleness, and where the female is the sexual heterozygote, as in Abraxas, the sex chromosome bears the determiner of maleness.

5 *Genetics,* 2, 1917.
6 *Sitzungsber. Preuss. Ak. Wiss.,* 34, 1919.
7 *Am. Nat.,* 45, May–June, 1911.
8 *Genetics,* 9, 1924.
9 SCIENCE, 66, 1927.
10 Carn. Inst. Pub., 241, 1916.
11 *Quart. Rev. Biol.,* September, 1928.

Goldschmidt succeeded in isolating different races of the gipsy-moth, of different sex-determining potencies; that is, different ones of them had different but typical quantities of the female- and male-producing genes respectively. By selecting his races Goldschmidt could get ones with quantities of maleness or of femaleness which, in the resulting cross, no longer balanced the quantities introduced from the other parent, with the result that, at will, any predictable degree of intersexuality up to and including sex reversal in either direction could be secured. In the gipsy-moth, since the female is heterozygous for sex, ordinarily two sex chromosomes indicate male, and one, female. However, by choosing a race with high quantities of the outside female-determining substance and crossing it with an individual in which the two sex chromosomes came from a race which possessed in these chromosomes a very small quantity of the male-producing gene, Goldschmidt secured what were actually females in spite of the fact that their gametic constitution (with two sex chromosomes) was that of males. He asserts, "If a given race is crossed in one direction with another test-race we can predict every result of crosses with all other races in every direction." And he goes on to say, "It is claimed as a fact that in our work on intersexuality different quantities of one gene have been studied."

Digressing from these special instances, Goldschmidt enlarges his conception to make it apply to all genes, drawing on such fields as multiple allelomorphism, irregular chromosome distribution and the like as the chief sources of his argument.

He conceives of the gene as operating through "the production of chains of reaction of definite velocities which are a function of the quantity of the gene in question." As to the nature of any given gene, he regards it as a "definite quantity of something (of course qualitatively different things in many different genes) linked with a chain of reactions with a velocity proportional *ceteris paribus* to its quantity." He believes with many others who have arrived at much the same conclusion that in the present state of our knowledge we can best regard it "as a type of enzyme and specifically as an autocatylist."

Again, such remarks about chains of reaction and catalysis have a familiar sound to the present speaker because in his 1910 paper[12] before the naturalists, already referred to (and even in an earlier paper,[13] 1907), he discussed at some length the probable functions of the chromosomes as the source of enzymes which initiate series of progressive reactions that result in chemical interactions. The following excerpts are as valid to-day as when they were written:

12 *Am. Nat.,* 45, 1911.
13 SCIENCE, June 28, 1907.

It is a well-known chemical fact, moreover, that when two or more progressive reactions are going on simultaneously, a quickening or retardation of the velocity of either, with the consequent precocious development of certain stages in the sequence, may lead to a partial or complete deflection of the original trend of the reactions and the formation of entirely different end-products than would otherwise have resulted. And velocities may be varied greatly by such factors as temperature and catalytic agents.

If in the comparatively simple cases of associated simultaneous reactions with which we are acquainted in non-living matter, relative velocities may so modify the results, we can readily realize of what tremendous importance regulation of this matter must become in living protoplasm where doubtless vast numbers of chemical reactions and interactions are going on at the same time. In fact, could we locate such a time-regulating factor in the germ-cell it would seem that we had accomplished a long stride toward an understanding of the controlling and coordinating mechanism which insures the appearance of just the proper substance at the right time in morphogenesis. It would constitute a qualitative as well as a quantitative regulator, for by determining quantity at any given time it determines what the next chemical reaction will be, and hence in the very doing of this, it necessarily conditions the chemical outcome of that reaction. As we have seen, temperature and catalytic agents are important factors in modifying the velocities of reactions in ordinary chemical processes, and inasmuch as under normal conditions of development the temperature factor is a fairly constant one, we are left to face the question as to whether in protoplasmic phenomena there is anything to correspond to catalyzers. Such substances we find in the enzymes.

In any epigenetic conception of the germ-cell—and this in greater or less degree seems to be the only plausible one to-day—we are forced, in explaining morphogenesis, to postulate the existence of some time-, quantity- and quality-controlling mechanism. The one evident class of substances in the germ-cells which can fulfil the necessities of the case are the ferments. For since they will determine the velocities of chemical reactions they must in consequence control the quantitative relations of the cell chemistry at any given unit of time. But from the very fact that where a large number of associated reactions are going on simultaneously, these quantitative relations at given stages of the chemical interchanges must profoundly influence qualitative results, we can not but conclude that this initial control of velocities must condition the qualitative results.

If we regard the chromosomes as centers of such a series of velocity-controllers, or, in other words, as sources of various enzymes, we can at once appreciate the necessity for having them so accurately balanced off in size and particularly in their quantitative relations one to another. For since the velocity of the reaction in a fermentable substance is determined not only by the presence of the ferment, but also by the amount of it, the quantitative relations of the ferments to one another would have to be very accurately maintained.

There is no obstacle in the way of supposing, furthermore, that if we regard ferments as of nuclear origin, the cytoplasm of a given tissue may not modify the ferment, as it itself takes on the necessary modifications for its own specific functions. We have good evidence that the production of ferments can be modified by even the substratum on which living organisms grow, and such a relation as this, close as it is, is certainly less intimate than that existing between nucleus and cytoplasm. For example, certain molds cultivated upon starch form diastase, but if provided with albumin they will produce instead a proteolytic ferment. Moreover, by gradually altering their other nutriments, yeasts can be made to utilize after a time various foreign compounds.

If, as all evidence indicates, ferments operate as catalyzers, then we must not forget that it is the very general belief among chemists that catalytic agents do not initiate the chemical reactions with which we find them associated, but that they only tremendously accelerate such reactions, or in a few known instances retard them. Since the nature of the building material must determine fundamentally the nature of the thing built, we must look outside the enzymes for much that will determine the peculiar individual outcome of the developmental processes. Leaving out of consideration for the present other functions the chromosomes may subserve, we might regard them as a sort of gauge for the feeding out of enzymes at the proper rate to bring about proper velocity reactions in the other cellular constituents, and perhaps regard the whole matter of mitosis and exactness in chromosomal distribution as a mechanism by which a quantitative metabolic regulation is maintained.

Looked at this way, the physical basis of heredity could not be considered a series of equipotent units, but rather it must be regarded as being composed of systems of units of different orders of organization and different degrees of coordination. Alterations in the configuration, constitution or relative positions of the unit constituents which represent the links of the main protein chain or ring, for instance, would precipitate much deeper-seated changes than would replacement of side-chains by those of different type, and such replacements would, in turn, doubtless appear objectively as differences of greater degree than those resulting from shifts in the composition or configuration of the individual side-chains.

If we consider that the supplying of the proper amounts and kinds of ferments is one of the important functions of the chromosomes, then we may suppose that in biparental inheritance each set of chromosomes is operating, probably catalytically, on a series of fundamental cell constituents that are largely common to both lines of ancestry; and that slight constitutional or configurational differences in corresponding enzymes bring about individual differences such as we recognize in the adult. We have already seen that different ferments within certain limits may act on the same substance and yield different results; consequently, in the intrusion into the egg of slightly altered enzymes in the chromosomes of the male, we should expect corresponding structural modifications to result.

Any influence which could effect constitutional or configurational changes in other essential constituents of the germ-cell would doubtless produce corresponding alterations in the adult. It is probable that not only changes of nuclear origin are reflected on to the cytoplasm, but that, conversely, cytoplasmic alterations may affect the nuclear constituents, for we have already seen how even the substratum may modify the enzyme factors in entire organisms such as molds and yeasts. Furthermore, there is no reason apparent why if the differences, no matter how produced, are modifications in the fundamental constitution or stereometry of the material affected, they should not persist permanently in the new germ-cells.

It would seem, in fact, that in the permanent effects of such reciprocal influences as here depicted for nucleus and cytoplasm, we might be able to account in large measure for the accumulations which have step by step been grafted on to the primitive protoplasm in its epigenesis toward the complex conditions of to-day, or in other words, in its racial evolution. Moreover, it is conceivable upon this basis how in later stages of phylogeny, as new chemical configurations or new chemical substances were developed, some of these could bridge back into relations with more primitively established substances and thus bring about ontogenetic short-cuts in development, or how, on the other hand, these abridgments might result in part from alterations in the more primitive molecular configurations.

I may seem to have run on to great length aimlessly, but I would simply point out that if a mere shift of tags is made, what in this earlier paper I regarded as chromosomal enzymic forci become "genes," and the account sounds much like a modern attempt to explain the action of genes through enzymic behavior.

I have not carried you through all this repetition, however, merely for the satisfaction of dressing up old stuff in new guise, but because I think that in its line of argument one may find some germ of thought about what I started to discuss, the germinal background of somatic acquirements. Among other things the citation of the relations of yeasts and molds to their substrates and the possibility of one eventually radically modifying the other may not be without significance in the chromosome-cytoplasm relation.

In what respects the germinal predispositions which permit of the appearance of so-called acquired characters under special conditions differ from the predispositions that lead to the appearance of inherited characters under usual conditions, no one knows. About all we can say is that in case of what is commonly regarded as the inherited character, the character is usually capable of reappearing in successive generations without being called forth each time by a specific environmental factor. But since, as we have seen, the potentiality of acquired as well as of inherited characters must in some manner exist in germinal protoplasm, the difference would seem to be one of degree or of fixation rather than of kind.

We have no reason to believe that the living substance of the germ-cells has any mysterious powers that are not shared by any or all of the somatic cells. In tissue cells we know that changed internal relations or unusual environmental stimuli may result in such diverse modifications as those of growth, hypertrophy, atrophy, hyperplasia, metaplasia and what not. Just as excessive exercise leads to overdevelopment of a muscle, so increased strain in bone leads to increased growth of bony tissue; if one of a pair of organs (lung, kidney, thyroid) is lacking or is destroyed the other soon adjusts and performs the function of the pair combined.

In many compensatory adjustments, as of enlargement of the hemolymph glands and bone-marrow following removal of the spleen, the compensating organ is not in direct connection with the one which is disturbed or missing. It seems probable that the inciting agent is carried by the circulating fluids of the body, although in higher animals one may have to reckon with the nervous system. If, however, a serum-borne agent may incite compensatory hypertrophy or other changes in tissue-cells, may not some serum-borne agents stimulate germinal protoplasm to additive functioning or other changes? It seems improbable that the germ-cells, bathed in the same fluids, nourished by the same food, stand wholly apart. If we had but a single side-chain in common between a protein of a somatic tissue and a protein of the germ, then anything that could affect one might well be expected to affect the other. In the endocrinal secretions alone one sees a series of powerful substances circulating through the body and producing profound effects in any or all of its parts. Both clinical and experimental evidence reveals that increase or diminution of an endocrine gland may be followed by marked alteration of bodily structure or function. When one sees how sex endocrines may experimentally be made to override genetic constitution itself in determining sex, he is tempted to regard the very male- and female-determining genes as possibly intracellular endocrinal structures. Since change in an endocrine gland may produce permanent changes in various tissues, may there not be germinal homologues of such tissue which may likewise be modified, particularly if repeated generation after generation? In an earlier paper[14] I have expanded upon this theme, especially as it might have significance in orthogenesis. Any

[14] *Am. Nat.*, 56, March–April, 1922.

internal or external agent which could affect particular constituents, nuclear or otherwise, of the somatic cells should, on the face of things, be able to influence homologous elements in germ-cells.

My own experiments in this connection, with immune sera, have already been laid before this society and I shall not subject you to the tedium of recounting them again. All I wish to say at present is that the experiments both on the effects of lens antibodies and on transmission of induced immunity are being repeated, this time with inbred stocks, and in the case of the lens work, with individual lens proteins. A small though sufficient number of successes are being secured from time to time to keep me encouraged and of the same opinion as that expressed in my earlier work. I still believe that the serological reactions of the body afford one means of breaking in upon the germ.

What apparently would have to happen to have an acquired become an inherited character would not be the germinal creation of the capacities for its appearance—these must already exist or it could not appear—but some sort of germinal fixation that establishes it as part of the more habitual expression of the germ-plasm. We commonly conceal our ignorance of the matter, to be sure, by talking about the "plasticity" of the organism, but this very plasticity must have genic implications, for the fact remains that the organism has the inherent capacity for acquiring the somatic modification.

That profound shifts in the organization of the germinal protoplasm may occur, particularly in the order of the appearance of characters in individual development compared with the order of their evolutionary acquisition, is evident when one regards the frequent precocious appearance of an adaptive mechanism far in advance of the conditions under which it is to operate. The eye of the unborn mammal, for example, develops long before it encounters the external agent light upon which it depends for its very significance. Yet, if our conceptions of evolution mean anything, the vertebrate eye must originally have developed in some functional cooperation with light, no matter whether we regard light as a causative or merely as a selective agent. Likewise the mammalian placenta, though among the latest of acquisitions in phylogeny, is one of the first things established in ontogeny. The point I would make is that, as time goes on, adjustments do come to pass in germ-plasm which may alter the chronological relations of hereditary acquisitions, and that this indicates that germ-plasm is not a fixed, inadaptable thing.

It would seem not improbable that any acquired adjustment, based on the casual potentiality of the genes of the organism, repeated generation after generation, would foster successive adapted generations of individuals until such casual reactions of the genic complex became its customary reaction. Obviously both types of potentiality must reside in germinal protoplasm. At present I see no explanation of how casual potentialities of the germ-plasm which permit of the somatic acquirement of characters become ingrained in the mechanism which underlies the more independently recurrent characters called hereditary, unless it is to be found in the quantitative changes in genes or of genic potencies. Evidence of such changes seems to be slowly accumulating. Once concede that the constitution of the gene can wax or wane and the way is open to the conception of how this might be induced through nutritive, toxic or functional means. It may be that when we learn more about the protoplasmic basis of ordinary hypertrophy, atrophy and habit-formation we may also see our way toward an understanding of the origin of inherited adaptations. Until we do so possibly we shall remain in ignorance of this most elusive attribute of all living things.

THE NATIONAL ARBORETUM[1]

By Dr. FREDERICK V. COVILLE

ACTING DIRECTOR

THE National Arboretum is an institution for the increase and diffusion of knowledge concerning trees. The National Arboretum Act, approved by President Coolidge on March 4, 1927, states that the purpose of the arboretum is research and education concerning tree and plant life and that in order to stimulate research and discovery the National Arboretum shall be under scientific direction.

To study the living tree, to breed new kinds, to select the best among them, to develop methods of propagating them, to show to what soils and to what situations and to what special purposes they are best adapted, such is the field of experiment and discovery to be occupied by the National Arboretum. The human race has bred sheep and cattle and horses, but not elephants. The elephant is too big, too wild, too long-lived. The human race has bred wheat and potatoes and apples, but not timber trees. They also have seemed too big, too wild and too long-lived. But the time has come to begin.

A strange case of the superiority of an individual

[1] Address delivered on January 17, in Washington, D. C., before a meeting of the American Society of Landscape Architects.