THE PHYSICAL BASIS OF PERSONALITY

PRONOUNCED PERSONALITIES

These types are often hereditary but in all cases are associated with peculiar reactions of the glands of internal secretion.

THE PHYSICAL BASIS OF PERSONALITY

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PREFACE

THE personalities exhibited by our friends and acquaintances are various, no two of them are quite the same, although one may frequently show traits that remind us of another and thus some are more alike than others. Some of these personalities are agreeable to us and some are not. If it were possible to determine from appearance those persons who in the long run would be generally congenial, many unpleasant experiences could be avoided. For this reason there is a very useful purpose in understanding persons on the basis of their individual characteristics. Although such an accomplishment may not be widely nor readily attained yet it leads towards an appreciation of the relationship between a definite physical constitution and its characteristic functions and behavior. The ways in which individuals react in the community, some arriving at success and many failing, their different susceptibilities to ordinary disease, many succumbing during early life and some surviving to old age—all indicate significant differences in physical constitution which result from variations in inheritance and development among human personalities.

The present volume is an attempt to give a general conception of the recent state of our knowledge *concerning the physical determination of individual personalities*. This, of course, is a somewhat complex subject not altogether easy

to present in a simple and engaging fashion. However, an endeavor has been made to discuss the matter in not too technical language which should be readily intelligible to all interested readers. The special sciences have a considerable language of their own often not fully understood even in other scientific fields; nevertheless, many of the useful terms in connection with the subjects of inheritance and development are becoming familiar in the general language of today.

During the spring of 1930 the writer delivered the series of Lane Medical Lectures at Stanford University in California. The problems of inheritance and development as related to personality were discussed and this book is primarily an outcome of those lectures. The lecture audience was familiar with the technicalities of the subject and the matter was presented in a more specialized way than is given here. As a matter of fact, it has been necessary to rewrite and rearrange the entire text in order to adapt it for presentation to the more general reader.

The treatment adopted is somewhat comprehensive in so far as the various aspects of the subject are concerned, yet no attempt is made to enter into a complete or detailed consideration of all its phases nor to give specific references in the discussion of minor points—the limits of a single volume necessarily prohibit this. My aim has been to make clear the physical factors underlying the origin of personality, and from this origin to carry the individual through the processes of development producing finally the finished person. The work and experiments of many investigators have been drawn upon freely. The literature is as volumi-

nous, however, as the subject is broad and it has been only possible to mention certain important discoveries connected with particular facts while other equally important works have been necessarily omitted. Much of the discussion is concerned with the author's own investigations; this is not due to an exaggerated sense of their value but rather to familiarity with their place in the field as a whole.

Many of the considerations are based on experiments which are no longer new to those acquainted with the subject. Yet most of the work discussed is quite recent, and the breeding experiments on the structural types among dogs as reviewed in the last few chapters are published here for the first time. There is no example among higher animals of such great diversity in size, shape, general behavior and, therefore, in personality, as that exhibited by the well-known breeds of dogs; and it is of great significance that certain human freaks practically parallel in their growth and form these diversified canine types. The growth of such distorted types and freaks is associated with modifications in the structure and function of their internally secreting glands. Investigations of these problems are being conducted on the Cornell University Experimental Morphology Farm, the first of its kind to be established.

It is a pleasure to acknowledge my gratitude for the efficient coöperation of my associates in this work and particularly to Miss Emilia M. Vicari, scientific associate, and Mr. Norman R. Speiden, manager of the experimental farm, whose help with the experiments has been invaluable.

Finally, my thanks are due the publishers, W. W. Norton and Company, Inc., for their personal interest and for their

many kindnesses and great assistance in the preparation and presentation of this book.

C. R. STOCKARD

Cynobia Farm
January, 1931

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THE ASPECTS OF PERSONALITY

THE personality of an animal or thing depends primarily upon its nature or constitution. What is meant by constitution? The answers differ. One may say, the make-up or composition of a thing. Or again, its chemical composition under the existing physical conditions. Constitution depends not only upon the composing elements, but also upon the physical states under which the composition exists.

The physical state of existence is frequently as important in determining the nature of non-living things as are the elements of which they are composed. Common iron ore has no peculiar magnetic qualities, but when its molecules assume a certain arrangement it becomes a lodestone —the earliest magnetic instrument found by man. Not every piece of iron would be useful as a magnetic needle; for this it must assume a definite constitution, which results in a peculiar behavior expressive of a new personality.

Free water in nature is a very different physical stuff from the fixed water of crystallization. It is well known, for instance, that crystalline copper sulphate contains a number of molecules of water to which it owes its crystalline character and its blue color. Yet water in such a crystal

fails to show its fluid properties—it is neither wet nor soft; no one knows exactly its condition. We simply know that when crystals of copper sulphate are heated free water is given off and the copper sulphate loses its blue crystalline appearance and is left a non-crystalline white powder. If this white powder be put into water the blue color appears in the solution.

The living stuff of which our cells are composed contains fixed or combined water and, in some cases, also free water. But here again the way in which the water is held or combined is a mystery, and we simply know that if water be driven out and the protoplasm dried, it usually dies, though this does not always or necessarily follow. The physical state of the contained water affects the constitution of a thing, just as the presence of combined water differentiates the crystal from the amorphous powder. These well-known elementary facts need to be kept in mind and applied in thinking of the more complex problems of organic or living constitutions.

What have these facts to do with biological constitutions or with human personalities? We may think of an organic or a living constitution as comprising definite chemical substances existing under peculiar physical states and in definite quantitative proportions and arrangements. Life is a property of certain peculiarly arranged compositions. But even in such a complexity the constitution may be somewhat modified by varying the chemical proportions, changing the physical conditions under which they exist, or by disturbing the given qualitative arrangement. Any one or all of these types of alteration are frequently occurring.

The Revival of Interest in Investigations of Personality

A century or more ago a great deal was written regarding animal and human constitution as related to personality, but very few facts bearing on the subject were accurately applied, although some were available. The paucity of facts and their inexact application no doubt had much to do with the gradual breakdown of the discussion and the diversion of attention to other equally obscure questions. After a certain interval the subject of individual constitution and personality has again become a popular one. What has awakened this renewed interest in individual differences or human constitutional variations? Has a new set of facts fallen into our hands which makes the riddle of personality more readily soluble than it was during the earlier agitation? If so, what are these facts newly at the command of biological knowledge? I venture to assume that the new so-called facts have been largely gathered from studies on the glands of internal secretion, which have been in progress on the modern basis for almost half a century. The juices from these internally secreting organs often exert a marked effect on the structure and function of the bodily organs, and at times on the body as a whole.

These secretions seem to initiate the change in nature of the individual from a child into a man, and, later, they may modify the health and happiness of the man. With little knowledge many have exclaimed: "Surely the glands of internal secretion are the keys to human constitutional differences!" Thus many persons have rushed in to explain the good constitution, the bad constitution, the strong constitution, the weak constitution, and susceptibility to dis-

ease, insanity and crime, on the basis of this one grand underlying mechanism of control—the internal secretions.

Where in the animal kingdom did endocrine secretions come from? When during the individual's evolution do they begin to exert control? And, above all, what determines their constitution? These are the questions which few of the interpreters of the constitutional personality have asked themselves. Yet they are fundamental questions in an analysis of constitution, particularly in constitutions modifiable by internal secretions. With these questions unanswered, how can we expect to know the relations of internal secretions to human personalities? How, for example, does growth depend upon certain of these specific secretions, as is generally claimed, when we see growth occurring in splendid fashion among plants and lower animal forms where such specific secretions are not known to exist?

Where are the answers to such questions to be found? Are they evident in complex adult human individuals on which nearly all the personality studies are now being made? This scarcely seems probable. A comparative analysis of simple constitutions might be a logical method of approach; the origin and development of individual personalities would certainly be a necessary study in the solution and final understanding of any such intricate problem. These approaches, however, have scarcely been suggested and certainly have not been seriously used in any of the present-day treatises on human personality.

The constitution of a man should at least deserve as careful and as comprehensive a study as the constitution of any lower form of animal life. Yet I venture to think that

a zoölogist would not seriously impress his fellows by an attempted analysis of the constitutional differences among the adult population of a given animal species without having considered the ancestral or germinal history and the individual development of these animals. It is equally necessary for an understanding of human constitution that we consider the nature of human germ cells and the development and growth of the embryo, foetus, and child. Without such considerations we cannot be certain of conclusions based alone on adult constitutional changes. This developmental analysis may not be possible or practicable to do; if not, then we must resort to comparative studies on other mammalian species and to that most productive of scientific methods, controlled experimentation, which also is usually impossible on human beings.

The Limits of Personal Existence

The medical consideration of constitution and personality has largely centered around the adult as a single peculiar or diseased individual; there has been some thought of the family in a general way, but with very few actual examinations of parents, grandparents, and collateral lines, and with only slight comprehension of the group or race to which the person belongs. Adult individuals have been subjected to various physical measurements in order to determine whether those suffering from a given disease would exhibit similar measurements. A little light and some confusion has been derived in this way. The light consists mainly in the repeated rediscovery of the existence of two well recognized physical types among human be-

ings: in simple designation the *linear* or long-headed type and the *lateral* or broad-headed type.

But physicians, like most other people, are inclined to think of the existence of the individual as extending from birth to death; that is, only the period of visible life and common acquaintance from birthday to the deathday of the ordinary man. And further, within this arbitrary span, childhood is often thought of as a least important period. History is written on such a basis, the dates of birth and death are the limiting marks. But the heroes of history were biologically superior individuals long before they were born or named. The biologist very well knows that the most important part of individual existence for man is passed and over before birth. The maturation of the germ cells, the gametes, in the two future parents—the union of a particular two of these gametes, a male cell or spermatozoön from the father and an ovum or egg from the mother, to form the new person—is the supreme consequence in individual existence. No other two germ cells from the same two parents would, as they unite on the basis of chance, make quite this individual person, but rather a brother or sister.

We must further understand the evolution of the new individual through the various embryonic stages, to the foetal condition with its development and growth, and finally to that sudden physical metamorphosis—the event we call birth, a change from endoparasitic to free existence. By means of these stages which have been attained within a short period of only a few months, the individual has passed from a single spherical cell of microscopic size to a fully formed human baby of seven pounds weight and

the complexity of millions of cells. Comparatively little remains to be accomplished during the following twenty years of the person's developmental history. The chief events,

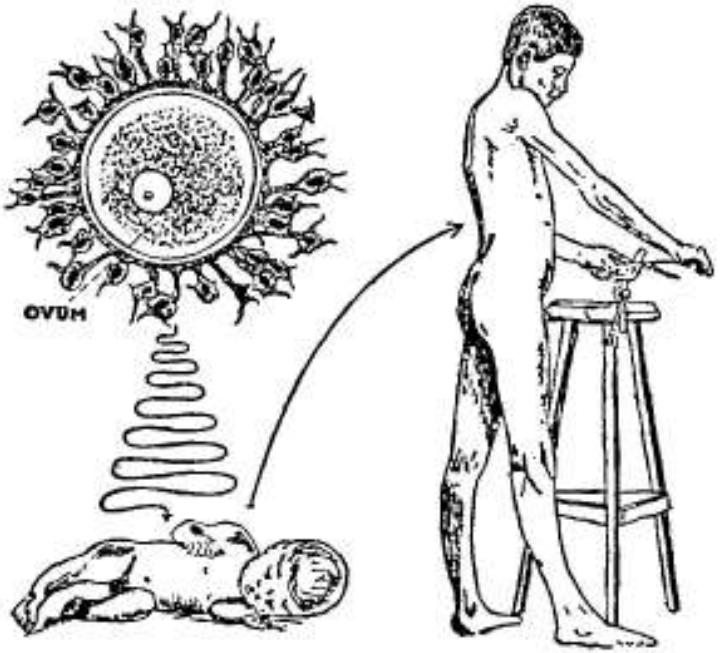


Fig. 1. The single-cell ovum of microscopic size undergoes an enormous evolution in producing the seven pound baby composed of millions of cells while a comparatively small change is yet to take place increasing the baby into the only twenty times heavier adult man.

probably more than ninety-five per cent of the entire development, and the dangerous steps when any mishap may cause organic deformity and future malexistence, are passed before the day of birth.

The individual as a member of a species, its relation-

ships, its method of origin, and its developmental processes—these are what we need portray! Therefore, a considerable portion of this book will be devoted to a very general discussion of this ordinarily neglected period which so shortly precedes the free-living existence commonly recorded as all of life. Let us think for a little of the life of people before they were born. What are their physical requirements during this prenatal life-time? They are much the same as during postnatal existence; but the responses of the individual to variations in these requirements are quite different, and usually much more pronounced in their modification of personality.

The Personal Demands on the Environment Before and After Birth

What are the common things in our external environment upon which we, adult individuals, most critically depend? The four best known to be of vital importance are oxygen from the air, temperature limitations, water, and foodstuffs. None of us could survive a temporary cut-off of oxygen for longer than a small number of minutes. Free oxygen is critically essential for our existence. If, however, one of us was deprived of oxygen for a short time and was practically dead, as in the case of drowning, he might with the aid of artificial respiration and heart stimulation be successfully revived. After revival the individual would be constitutionally much the same as before this experience. The egg and embryo are as fully dependent for their development upon a free oxygen supply as are postnatal persons. Let us, then, suppose that the oxygen

supply be cut off from the embryo; it also will die. But if the supply be merely temporarily stopped and then restored with sufficient promptness, the embryo may revive and continue development. In this case it frequently happens that the constitution of the individual is decidedly altered. Not only is this true, but the alteration differs in quality depending upon the developmental stage or time at which the interruption in oxygen supply occurred. In general, the earlier the accident the more severe the constitutional modification. Figure 2 illustrates marked alteration in form and abnormal eye development in the embryo which may result from early lack of oxygen. We find that an accident from which the postnatal individual may recover without lasting effect may in the embryo introduce radical and permanent disturbance. In order to insure normal development the embryonic environment must continually supply free oxygen. Has nature made provision by which this oxygen supply may be guaranteed? To this question we shall return later.

The second necessity from our environment is temperature limitation. Human life or personal existence is constitutionally adapted to a very narrow range of temperature variation. Without provision of clothes or shelter it is doubtful whether human beings could long survive in a temperature only so low as 50°F. Without artificial protection we are uncomfortable even at 60°F, and would probably be happiest only in the short range between 70° and 80°F. As the temperature rises above 80°F and reaches the limit of slightly above 100°F, we become depressed, unfit for strenuous effort, and finally feverish and sick. Our normal behavior and life functions are definitely

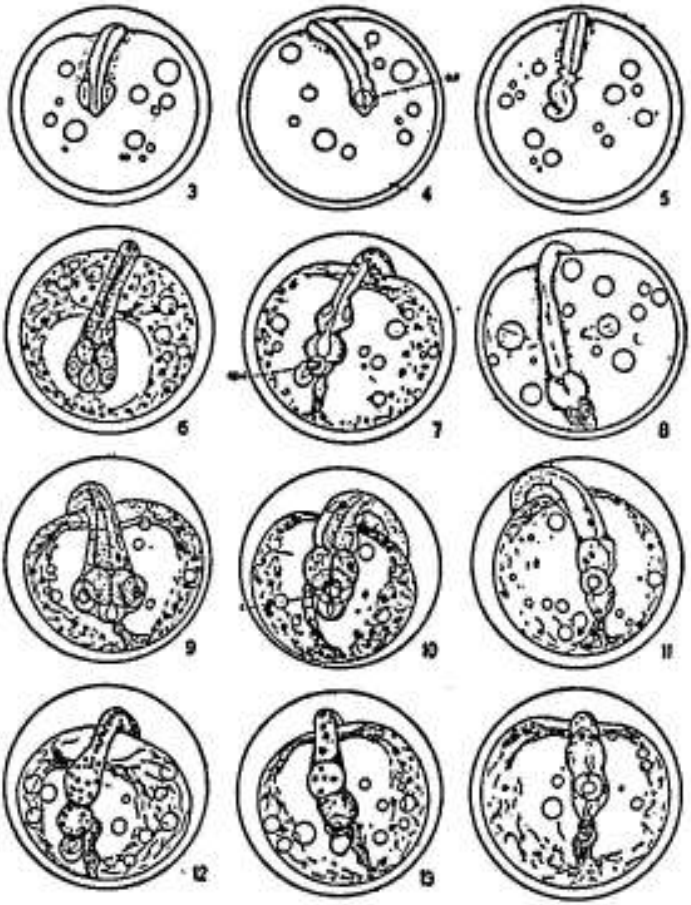


Fig. 2. Modifications in the development of the eyes and body form in unhatched fish embryos; these may result from temporary deprivation of oxygen supply. Specimens number 3, 6 and 9 are normal embryos of different ages for comparison; op. c. the embryonic eye.

designed to play their rôle within only a short range of temperature variation.

These necessary limitations in temperature are also strongly demanded by the developing embryo. Here again, as in the case of variations in oxygen supply, the response to temperature change on the part of the embryo may be most hazardous for normal constitution. When the temperature is lowered below the normal limit the internal chemical reactions, or metabolism, of the developing embryo are slowed, and development moves at a less rapid rate. This modified rate tends to disturb the usual balance and coördination of the growing parts, and abnormal responses result. Even though the proper temperature be again restored, the constitutional modifications may persist and a defective or deformed individual is produced. Altering the temperature is one of the readiest and most commonly employed methods of experimentally modifying embryonic development and thereby artifically producing various monstrous types. Figure 3 shows structural alterations in individuals that arise from eggs subjected to unfavorably low temperatures. Nature must definitely provide a proper temperature for the developmental environment of her higher organisms. Has any provision been evolved for this temperature regulation?

The third acutely necessary element both for adult life and also for the development of the embryo is water. The deprivation of free water supply will stop the life of human beings within a few days. Living protoplasm is a watery substance and drying or driving out the water disrupts its constitution. All vertebrate animal eggs require a moist condition for their development. Drying stunts and

retards development. However, modification in the watery content of protoplasm is a very difficult thing to manipulate and the experimental embryologist has rarely resorted to such disturbances as a method for carrying out his analyses.

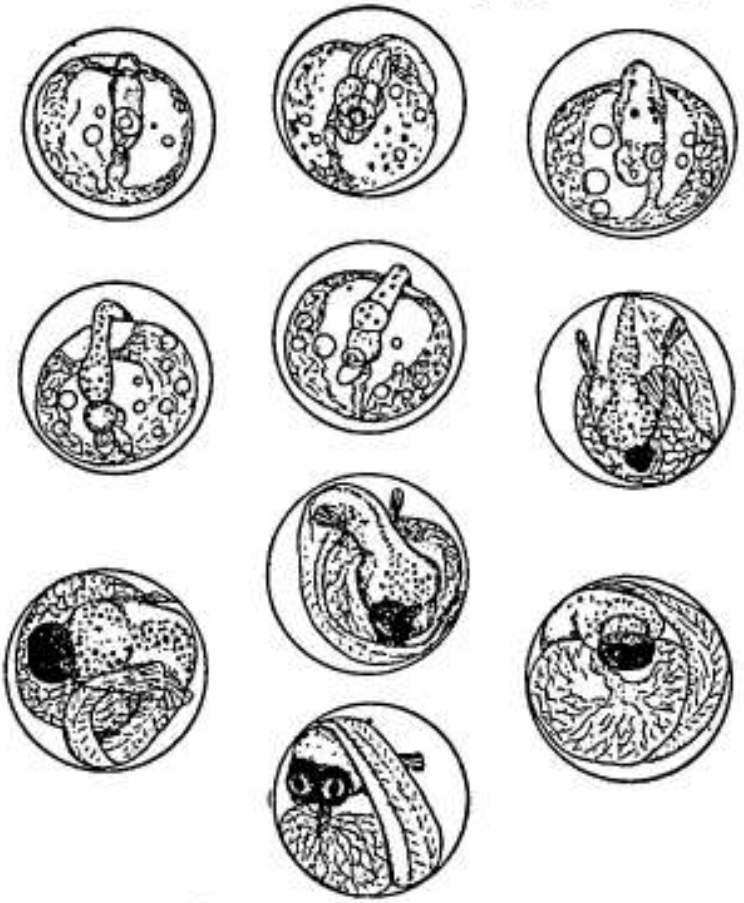


Fig. 3. Gross alterations in structure of body and eyes in fish embryos. These may follow unusual temperature conditions during early developmental stages. Several show a single cyclops-like eye and the lower specimen has the two eyes fused into a double eye.

In the case of water, the external environment and the internal conditions become so intimately continuous that they are difficult to separate. We become more and more impressed with the fact that the so-called external environment actually extends far into the egg and embryo or into the protoplasm itself and there is no clear distinction between external and internal environment or actually between environment and living stuff.

The embryo must be provided with a moist environment in order to retain its own water and to proceed with normal constitution and development. The water of protoplasm has recently been discussed by Dr. E. F. Adolph as "living water." Has nature evolved any provision for insuring the presence of this moisture to the embryo?

Finally, our fourth necessity is food. Food is a more complex stuff than the three afore-mentioned essentials for life and development. Human or animal food includes in the main a mixture of proteins, fats and carbohydrates. These are the stuffs which animal organisms use in building up their own tissues. Self-synthesis is the characteristic property of living protoplasm. Persons have the power of storing food to a considerable extent and under certain conditions of starvation they may actually use their own tissues in maintaining life. Lack of food in the outer environment, therefore, does not so acutely affect immediate existence as disturbances in the supply and regulation of the three other necessities.

We may exist for many days without intake of ordinary food. The egg and embryo are similarly provided with a limited food reserve, and violent changes in developmental constitution rarely result from deficiency of food during

the early embryonic period. Lack of food tends in general to stunt or retard the increase in size of the developing embryo and foetus rather than to cause gross deformities. Not infrequently, however, severe constitutional changes and modified personalities may later develop as a result of faulty, unbalanced and insufficient nutrition of the foetus and young individual—a fact well known to most physicians. Several essential and active substances called vitamines, as well as certain inorganic salts, may be classed as foods and these are highly necessary for normal development.

Growth of the human embryo and foetus from the minute egg naturally involves increase in size and the materials for this increase must be available. Finally, in animal evolution, what, if any, provisions have been developed in order to insure the quality, supply and delivery of food?

Not only biologists and physicians as students of living things, are concerned with the problems of our early environmental necessities, but all intelligent persons should be awake to these constitutional requirements as they are to other ways and means of maintaining their good standing in the community. We shall, therefore, in the next chapter, consider briefly the evolution of the habits and mechanisms which have arisen among the vertebrate animals as means of controlling and insuring the environments under which their embryos and, hence, their personalities are to develop. For unquestionably these processes of development are of most fundamental importance in a consideration of the basis of human personality.

II

THE EVOLUTION OF MECHANISMS FOR REGULATING DEVELOPMENTAL ENVIRONMENTS

A COMPARATIVE survey of all classes of vertebrate animals will show that a most striking evolution of arrangements has come about which tends to insure for the developing egg and embryo a properly regulated environment. We may question whether highly complex structural evolution ever could have been possible without the provision of means for protecting and insuring the surroundings of the delicately sensitive stages of development. In other words, the highly differentiated personalities of man and mammals are only possible of attainment under protected and regulated environments, since the helpless periods of development have been necessarily so greatly prolonged and complicated.

Environmental Hazards and the Aquatic Eggs of Fishes and Amphibia

The lowest vertebrates spend their lives entirely in that archaic and homogeneous environment in which life probably first arose—the sea-water. The fishes as a rule spawn their eggs freely into the water and leave them to develop.

But there are various provisions which tend to insure the four necessities of environment for the development of the eggs. In the first place, the fish itself only exists in water containing a sufficient oxygen supply; yet further to insure this supply the eggs are deposited in shallows where oxygen is even more likely to be abundant, or if spawned in the deep sea, they are commonly provided with an oily yolk which not only serves as food for the embryo but also causes the egg to float near the freely aërated surface. Such pelagic eggs are probably in this way more certainly exposed to a rich oxygen supply.

The temperature favorable for development varies with different species and the spawning season is probably in some way adjusted to this. Certain species only spawn during the warmer seasons and their eggs are thus unlikely to be arrested by cold. Other species, such as the trout and the cod, for example, spawn in the wintry waters and their eggs develop normally at almost a freezing temperature and die if the water becomes warm.

The problem of sufficient water or moisture for the embryo is rarely presented to these aquatic animals. Only at times when the ponds or streams temporarily become dry do their eggs suffer or actually die for want of water. The eggs of fish are provided with sufficient yolk or foodstuff to nourish the embryo until it becomes able to feed upon outside food.

Low water-living vertebrates apparently need only little and simple provision for regulating the developmental environment. But with the exposure of their eggs to the accidents of nature, dangers are great, mortality is high, and thousands of eggs produce only a few adult fish to main-

tain the piscine population. The chief insurance for development is the production of excessively large numbers of eggs.

There are, however, a few specialized cases among the fishes in which the eggs develop within the body of the mother, thus being well protected. These viviparous species produce comparatively few eggs, since the body of the parent can adequately accommodate only a small number; and the hazards of development are so reduced that a proportionately greater number survive to reach adult life.

One grade higher in the animal scale we find vertebrates that have partly freed themselves from life in the water. Most amphibia spend the adult stages of their lives as air-breathing, land-living forms. Still, these animals have evolved no provision for developing their embryos on land and so they must return to the water for spawning their eggs in order that the embryos may not die from drying. The egg-yolk supplies a food reserve and the spawning time usually occurs during a season of proper temperature requirements. The eggs of amphibians, like those of the fish, are freely preyed upon as food by other aquatic animals and large numbers are necessary to insure the development of a few.

We conclude in general that the eggs of fishes and amphibians deposited in the water are liable to death from want of oxygen due to stagnation of the water, from changes in temperature in cases of either extreme chilling or overheating of the water, and from evaporation or flowing away of the water. The parent animal has evolved no mechanism or habit for effectively avoiding or greatly lessening these dangers. The storage of yolk in the egg as a food reserve

is the only endowment in the way of regulated environment that is bestowed upon such embryos. A higher order of constitution than that of an amphibian has not been evolved under these scanty provisions for protecting development.

The Reptilian Egg as a Mechanism for Regulating Environment

The next class of vertebrates above the amphibia, the reptiles, are completely equipped for life on land and may even exist in the arid wastes of the desert, although many species still tend to be marsh-land feeders. The reptiles are capable of a continuous life on land because of the fact that they have evolved arrangements for the development of their embryo away from the water. Such an attainment is just as necessary for land-life as is an arrangement for locomotion on the ground. The reptiles produce a comparatively larger and more complex egg than do the lower vertebrate forms. The yolk-laden ovum is surrounded by a quantity of albuminous material which insures a moist environment throughout the earlier stages of development and then serves as an additional amount of food during the later time. The albumin surrounding the yolk is itself enclosed in either a porous leathery or calcareous shell which permits the passage of gases and the intake of free oxygen from the air.

The mother has developed an instinct which causes her carefully to bury these eggs in warm sand or, in other cases, in decaying vegetable humus, where a sufficiently high temperature is ordinarily provided. In some cases

the mother actually covers and guards the eggs against the dangers of being trod upon or devoured by their enemies.

The reptiles have thus evolved arrangements for supplying food, moisture and oxygen to their developing embryos, and they have only failed to furnish the proper temperature for the incubation process. Under such conditions they need produce only a limited number of eggs. Thus reptiles have been enabled to evolve a far more complex constitution than has been possible in the unregulated developmental environment of the amphibian and fish.

The two highest vertebrate classes have probably arisen from reptilian ancestors, yet the birds and mammals have each evolved quite different means for insuring the development of their young.

The Protection of the Bird Embryo.

The birds have retained much or all of the reptilian method and have only improved upon this arrangement by providing the temperature which guarantees the development of the egg. Here again we find the very large ovum laden with food-yolk and surrounded by the watery albuminous coat, which is now covered with both a porous membrane and a chalky shell, facilitating a free exchange of gases between the embryo within and the air without, a highly perfected nurturing mechanism.

The bird carefully deposits the egg in a nest of her own construction or on a well-selected spot. She then sits almost continuously over the egg, her warm body supplying the

necessary heat for incubation. Thus with the birds we find an arrangement for transmitting oxygen to an embryo surrounded by constant moisture, supplied with an abundant food reserve, and warmed by the temperature of the parent's own body. The accidents of nature are greatly reduced and only a small number of eggs are necessary to produce the adult population. Under these regulated conditions of development a marvelous delicacy of constitution has been attained by the bird.

The Intra-uterine Environment of the Mammalian Embryo

One might think that the birds had left little to be improved upon in protective arrangements for the nurture of the embryo. Yet we, as mammals, are sufficiently conceited to imagine that the course of embryonic protection achieved by us, in the general evolutionary ascent from the reptilian state, is far superior to that slight modification acquired by the birds. The males of our class may doubtless be considerably prouder and more enthusiastic about the internal mode of development than the multiparous females who at times may not have been completely persuaded as to the superiority of the mammalian method.

Examining in general the means evolved by the mammals for controlling the environment of the developing egg and guaranteeing to the embryo the four elementary necessities, we find an almost unique departure from the direction of the more primitive methods. The laying of the egg into the outside world is discontinued except among the lowest of the mammals; the higher orders have com-

pletely discarded the entire reptilian method of embryonic protection.[1]

The mammalian ovum has become the smallest and least provided with food-yolk to be found among the vertebrate eggs. This egg, scarcely visible without the aid of a microscope, begins its development within the oviduct and then travels through the duct, very soon to become attached in a somewhat parasitic fashion to the uterine wall. The uterus responds to the presence of the fertilized ovum in a manner so effective that the developing embryo becomes placed near enough to the maternal blood stream to be supplied by it with oxygen, water, food, and a definite degree of temperature. Under normal conditions these necessities are as completely provided for the embryo as for the body tissues of the mother herself. Such an arrangement is *par excellence* nature's guarantee to the embryo of the four essential environmental requirements for life and development.

The contrast in size and structure between the eggs of the bird and mammal is illustrated by Fig. 4. Little yolk is present in the mammalian egg since food is supplied indirectly from the blood of the mother. The coat of albumin of the reptile and bird eggs is dispensed with, being no longer necessary as a reserve of available water, which the maternal blood now far better provides. The pervious coats of membrane and shell which permit free passage of air to the embryos of reptiles and birds are needless in mammals since here there is a free exchange of oxygen and gases between the maternal and embryonic bloods through

[1] The few sporadic cases of internal development among the fishes and reptiles are accomplished by a quite different order of arrangement from the mammalian pattern.

the permeable vascular walls. The dependence upon an external temperature, which may at any time vary, is replaced by the permanently uniform internal body temperature of the mammalian mother.

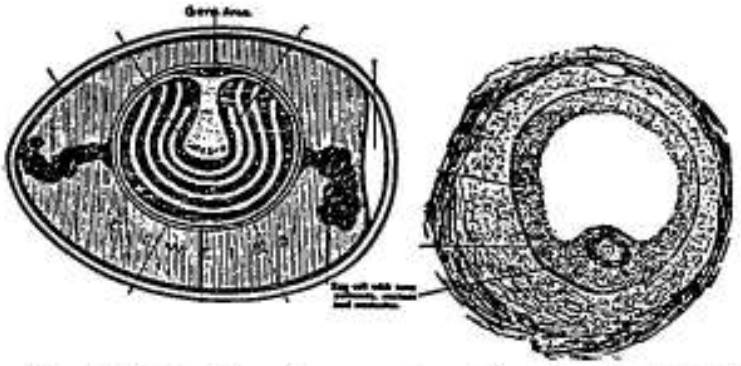


Fig. 4. On the left a diagrammatic section through the hen's egg showing the shell, white and yolk; the germ of the embryo lies on top of the yolk sphere. This tiny germ corresponds to the entire egg of the human being as shown by the small cell labeled in the right figure. (After Ziegler and Bremer.)

It would seem that injuries due to environmental irregularities could no longer occur and that development must be perfect except for possible defects that might arise from constitutional deficiencies within the original germ cells from which the embryo was derived. Closer examination will convince us, however, that unfortunately this is not always the case and accidents of the environment are still possible even under such perfect conditions.

Although theoretically the mammalian arrangement seems perfect, the uterine reactions to the early embryo are very delicately balanced responses, and defective placentation or attachment with poor communication between

mother and embryo is a common occurrence. Defects in placental reaction vary from harmless deficiencies in limited regions of the placenta to entire failure of the communicating arrangements and the death of the embryo. Many, probably most, of the spontaneous abortions in human and other mammals occur near the time of the first menses or oestrus after conception, and they probably result from faulty uterine reaction and consequently poor implantation of the ovum. The deficient responses may be due to a subnormal reaction on the part of the uterus, as a result of disease, or of poor physiological tone, or of improper ovarian secretion; or, on the other hand, the abnormal implantation may result from a defective reaction on the part of a poorly developing embryo derived from bad germinal stock. The proper placental arrangement depends upon both the mother and the embryo; it is actually a mutual affair, and a dead egg does not become implanted.

The Environmental Factor in Abnormal Human Development

In studying the abnormalities of embryos and foetuses collected from a large number of human abortions, something of the consequences of poor communication between the embryo and mother has been learned. For this knowledge we are largely indebted to the extensive and careful studies of F. P. Mall and Arthur W. Meyer, in this country, and to a number of European investigators, particularly the German pathologist Schwalbe. The types and kinds of embryonic defects in these human cases are often the same as those resulting from experimentally produced

arrests in lower animal forms. The probable cause for both groups of developmental defects would logically seem to be a deficiency in the supply of one or more of the four above-mentioned critically essential demands of normal development. Reducing the oxygen supply and altering the temperature are the most effective artificial means of modifying embryonic development and inducing monstrosities.

Which of the necessary factors is most probably concerned in defective human development? The character of the defects would seem to indicate that they are not due to simple food deficiencies; sufficient food is probably obtainable. Again, it is rather improbable that the defects in the mammalian embryo could be attributed to lack of water as this is almost necessarily present in the internal environment. The temperature regulation is very probably uniformly adequate in the mammal since the embryos of animals which may be studied experimentally are actually capable of withstanding a wider range in temperature variation than would be possible within the body of the mammalian mother. The placental arrangement and the internal mode of development seem then entirely adequate for temperature regulation, and largely sufficient for a proper supply of water and ordinary food. The one essential element that may be critically deficient on account of poor placental communication is oxygen; and we know from illustrations previously cited, that a reduction or cut-off, even temporarily, of the oxygen supply may give fatal or decidedly pronounced results. On the basis of a large array of evidence which need not be given here, one is justified in the conclusion that improper placentation is most dangerous because of faulty communication between the

maternal and foetal circulations and, consequently, a diminution in oxygen supply to the embryo.

Imperfections and "weak spots"

In conclusion, we recognize that deficiencies and alterations in the embryonic environment are most serious in their effects in modifying prenatal constitutions. And we shall later examine evidence which shows that the effects of unfavorable conditions are the more severe the earlier in the individual's life they chance to occur, and, conversely, they become less severe as maturity is reached. For example, a treatment with a given dose of substances such as ether, alcohol, or various salts may actually cause the egg during the earliest stages of development to give rise to a non-viable double-headed monster; a little later, the same dose of the same substance may induce various defective conditions in the development of the central nervous system; still later, abnormal growth and twisted body form may result; while in the early infant a comparable dose may cause only disturbed function and temporary illness, not necessarily leaving any permanent effect; and finally the adult individual may actually employ comparable amounts of the same substances to produce only pleasurable sensations with no harmful results.

In the light of such facts as these one realizes how nearly correct the embryonic environment must be in order to insure perfect development from a perfect egg. Individual eggs differ in their quality and thus in their susceptibility to slightly unfavorable environmental conditions. One egg

may develop vigorously and well in an environment which a weaker sister individual cannot successfully withstand. Many of these facts are to be discussed more fully in the chapters to follow, but at this time we may appreciate the difficult problem with which nature is confronted in her effort to escort the delicate egg and embryo through the varying mazes of environmental change, to deliver finally a normally constituted personality. If the environmental alterations referred to above may give rise to severe developmental disturbances, then minor changes in environment of even short duration may possibly induce blemishes or slight defects in great numbers of so-called normal young animals.

It would not be altogether erroneous to assume that most individuals are finally born with some imperfection due either to lack of quality in the germ cells from which they arose or to a lack of exactness in the environment under which they were nurtured. These imperfections are our "weak spots," which are so commonly known to the layman as well as the physician. Too often on their account a person breaks down in illness or actually dies, while the rest of the bodily make-up is sufficiently strong to have survived for years. Few are built on the plan of the wonderful "one horse shay" depicted by the anatomist and physician, Professor Oliver Wendell Holmes. As he refers to the "weak spot":

"Find it somewhere you must and will,
Above or below, or within or without,
And that's the reason, beyond a doubt,
A chaise breaks down, *but doesn't* wear out."

One may go far in defense of the thesis that the human personality finally dies from some defect, "weak spot," that was present at birth. In other words, the individual dies of a disease (faulty construction) with which he was born.

Actually length of life itself is, therefore, largely a genetic and a congenital affair, particularly for the species. The rat is old and often dies before the end of three years, the mouse at two, the dog at from eight to twelve, and human beings are old or dead before three score and ten years with rare exceptions. Something in the personality of the animal determines its deathday as well as the length of its prenatal life and its birthday. The sturdiest individuals of the species live the longest, and natural selection insures this fact even among men and in spite of modern sanitation and the mechanical age. The susceptible and less fit individuals that formerly died of the one-time prevalent infectious diseases are now in the absence of such diseases killed by automobiles and other modern devices. The less well adjusted persons are unable to negotiate the traffic and run miscalculated chances or are willing to risk their lives with reckless and incapable drivers. Their constitutional defects handicap their behavior.

Natural selection in complex modern communities seems to be playing more on the nervous traits and mental capacities than upon the old-fashioned brute strength that counted so highly in savage combat. The onslaught of environment has somewhat changed its base of action towards the higher nervous centers. Yet still, the individual personality is the chief determiner of its fate, and death only by sheerest accident is unrelated to the constitutional state.

III

THE CONSTITUTION OR PERSONALITY OF THE GERM CELL

IN what form does the individual person exist in the germ? Or, phrased in a more general way, what is the constitution of the germ? This question has given rise to much guessing and heated controversy throughout the ages of medical and biological history. And yet even today it is being feverishly studied by the ablest investigators with the most refined and complicated methods of genetics and experimental biology. No question could be of more fundamental importance to living beings. Something of an insight into the importance of this subject I shall attempt to develop in the next chapters.

Early Conceptions of the Individual in the Germ

More than two centuries ago, and before microscopic structures were studied, there had developed a distinct school of opinion regarding the manner in which the structure or character of the future individual existed in the germ. The members of this school held that the embryo was preformed in the germ simply as a tiny or invisible individual with all its organs and parts already present, and that development was merely the enlarging and unfolding

of this minute bud into the newborn baby. This doctrine was first known as the theory of unfolding or *evolution*, and was later better designated the preformation theory. It was soon found to present a peculiar difficulty on account of the fact that among the higher animals every individual is developed as the result of the coöperation of the two sexes. The individual could not be in both the male and the female germs; it must be in only one. Therefore, when the Dutch microscopist, Anthony van Leeuwenhoek, announced the discovery of the male germ cell, the spermatozoön, by his student Stephen Hamm in 1677, an active controversy arose as to whether it was the egg or the seminal filament which contained the preformed germ. This controversy was begun with particular vigor since Leeuwenhoek himself, in one of the papers reporting the discovery of the seminal filament, declared it to be the preformed germ of animals: at fertilization it entered the egg which served only as a nutritive medium necessary to the growth of the spermatozoön in evolving the person. This declaration gave rise to the school of *animalculists*, while those who had already contended that the preformed germ existed in the egg were known as the *ovists*.

Numerous treatises and early texts on embryology pictured the spermatozoön containing within its nuclear or head-part the tiny homunculus or imaginary man with knees upbent and arms folded in a somewhat prayerful attitude. The designation *animalculists* was doubtless derived from the free swimming animal-like activity of the sperm cell; and after the refutation of the preformation theory the seminal filaments were long held to be independent parasitic organisms comparable to certain protozoa, while the

seminal fluid itself was then thought to be the fertilizing medium.

The two opposing groups of preformationists were doubtless equally satisfied with the clarity and simplicity of the developmental problem on this naïve unfolding basis, until their enthusiasm led them to follow the line of preformation reasoning to its logical conclusion. If the entire future individual lies folded in the germ cell and if its development is simply growth and unfolding, then it must also contain germ cells from which the next generation would be derived, and these cells should have folded within them the second generation to follow, and so on. The germ cells of mother Eve according to their calculations must have contained 200,000 million human germs.

Such a proposition seemed to necessitate enormous volume, no matter how minute the buds, to represent all the future generations of the human family. This box-within-box doctrine, or as the Germans termed it, *Einschachtelungslehre*, was probably the most pronounced *reductio ad absurdum* which the history of biology affords. It is gratifying, however, that whenever in the history of science progress seems blocked by error, an unusually bright flash of truth gleams forth to light a new way.

And so, in the midst of these preformation doctrines, there opened a new epoch for embryology, when, almost 170 years ago a young German medical student presented in a thesis for his doctor's degree overwhelming evidence in proof of the step-by-step or epigenetic process of animal development. Casper Frederick Wolff in 1759, exactly one century before Darwin published his *Origin of Species*, presented facts which showed how the organs of the em-

bryo were developed from undifferentiated material, that each stage of the developmental process prepared the essential way for the following stage, and that organ preformation could not be demonstrated in the animal egg. This contribution ranks as an epochal classic in the advance of our knowledge of animal constitution and the origin of personality.

However, this early epigenetic point of view, although marking a great step forward, was by no means the same as our modern conception of embryonic development. Seventy years were yet to pass before the great German botanist, Schleiden, and the equally distinguished German zoölogist, Schwann, were to make the still more fundamental contribution to an understanding of organic constitution through their discovery of the cell and the realization of the cellular composition of the bodies of animals and plants. This great discovery of the cellular composition of living things was made only a little less than a century ago. And after the establishment of the cell theory embryonic development necessarily became recognized as a far more clearly epigenetic process.

This brief introductory statement is necessary in order properly to place the actual significance of our specific topic, germinal constitution. We are now prepared to begin with the germ as a cell and shall undertake to consider the possibilities of influencing it as such, and of further analyzing its inner nature and structural constitution.

The Relationships of the Germ Cells to the Body Cells

The egg and spermatozoön are truly animal cells, although they differ from the general body cells in possessing

the potentialities necessary for giving rise to a complete new individual. Questions occur as to what relationships or connections may exist between the body or *soma* cells and the germ cells of the animal. Is it possible for the body cells to give rise to germ cells or in other ways to influence or impress their experiences to any degree upon the germ cells? Or, are the body cells and the germ cells completely set off from one another, the body merely serving as a temporary harbor for the germ cells which have been continuously passed on from generation to generation since life began on this world? These are most significant questions in any consideration of human constitution.

The fact that many of the structures and arrangements in animals seem to fit so exactly into the natural environments in which they exist has long forced certain observers to believe that the efforts of the body parts to adapt themselves and fit the environment are in some way impressed on the germ cells and are transmitted through these to the next generation. Such a conception is commonly known as use-inheritance, or the inheritance of acquired characters.

The great French naturalist, Jean Baptiste Lamarck, first presented this idea of the transmission of acquired characters in elaborate detail as his conception of the manner in which organic evolution had been brought about. In his *Histoire Naturelle* Lamarck proposed that "All which has been acquired, laid down, or changed in the organization of individuals in the course of their life is conserved by generation and transmitted to the new individuals which proceed from those which have undergone these changes." It was held that the effects of vigorous use of an organ in any definite way, such as the action of the front feet of

moles in burrowing, would be transferred through the body to the germ cells and these would respond by producing a next generation of animals with front feet already at birth better adjusted for the burrowing performance. It was thought that in this manner the beautiful harmony between the structure of a part and its life function had been induced. The theory was widely appealing, and even today, with a complete lack of experimental demonstration of its truth, it is not altogether dead.

The inheritance of acquired characters, or somatic experiences, was accepted by Darwin and frequently used by him in explaining many adaptations. This belief in the influence of the activities of the body organs, or soma cells, on the germ cells was partly responsible for leading Darwin to propose the hypothesis of *pangenesis* in his classical treatise on *Animals and Plants under Domestication*. Darwin assumed that the cellular units of the body throw off minute granules which are dispersed throughout the whole system; that these, when supplied with proper nutriment, multiply by self-division and are ultimately developed into units like those from which they were originally derived. These granules he termed *gemmules*. They are collected from all parts of the system to constitute the sexual elements or germ cells, and their development in the next generation forms a new being. They may likewise be transmitted in a dormant state to future generations and may then be developed. Hence, Darwin stated, it is not the reproductive organs or buds which generate new organisms, but the units (or cells) of which each individual is composed. These assumptions constitute Darwin's provisional hypothesis of pangenesis which is actually, as the name indicates, the

idea of genetic particles from all parts being finally focussed to constitute the reproductive cells.

Darwin recognized that views in many respects similar had been earlier propounded by various authors—Buffon's "organic molecules," Herbert Spencer's "physiological units," and others. But it may safely be said that no theory could have gone further in making the germ cells entirely secondary to the somatic units or body cells than did the pangenesis hypothesis. In such a scheme the body cells in variation, use and disuse, and all modifications, are readily able to transfer their reactions to the central germ and thus to the following generation.

This was the climax and also the culmination of significant theories which proposed that influences passed centripetally from the soma to the germ. Soon after the proposal of pangenesis a great tide of discoveries chanced to occur, all of which swept strongly against these ideas. Each new fact seemed to emphasize the independence of the germinal constitution and investigators began to think of variations and new qualities in the individual as being derived only in a centrifugal way from their centers of origin in the germ.

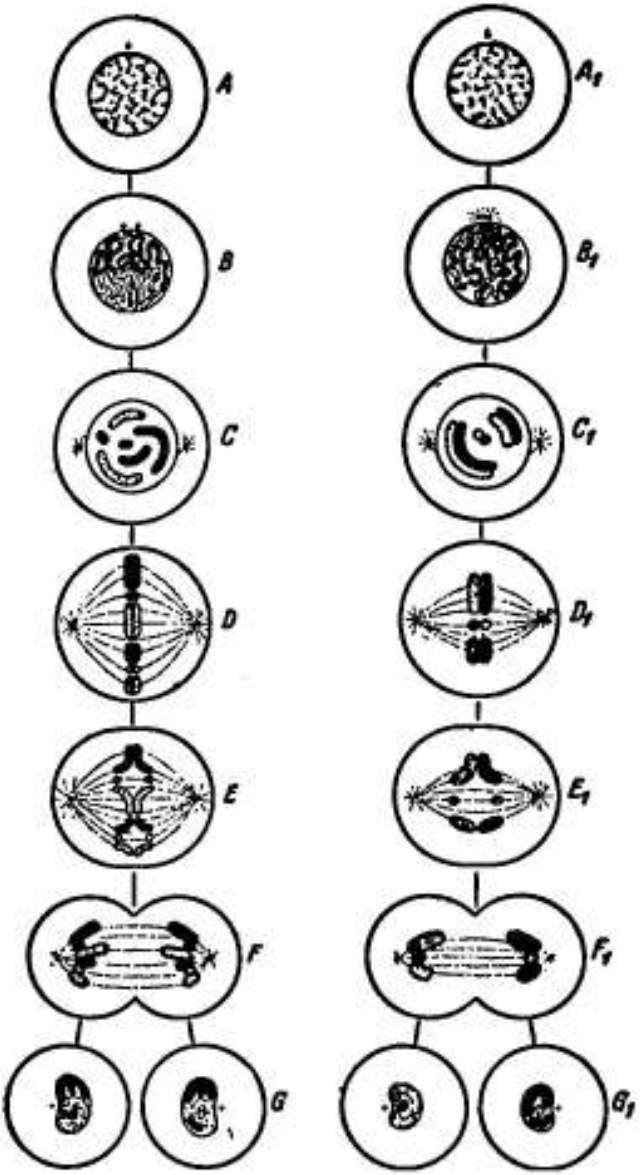
This turn of the tide accompanied the progress of investigations into the structural constitution of the germ cells. During the last quarter of the nineteenth century the chromosomes were discovered as the chief nuclear elements of the cell, and their peculiarly consistent behavior during cellular reproduction attracted the interest of a host of able investigators with the result that important facts of cellular constitution were rapidly accumulated.

Independence and Purity of the Germ Plasm

It was from this atmosphere of cellular investigation that the eminent German zoölogist, Weismann, crystallized his conception of the continuity and purity of the germ plasm. His idea really started our modern analysis of development and inheritance. Weismann emphasized the independence and separateness of the germ cells from the influences of the body cells and probably did more than any other biologist to overthrow the then prevalent belief in the inheritance of conditions acquired through individual body performance.

During this period the recognition of the chromosomes as definite cell parts and the history of their behavior during nuclear division laid the foundations for a modern conception of germinal constitution. Today, we may tentatively say that the constitution of the chromosome is actually the constitution of the germ.

A characteristic number of these chromosomal bodies are present in the cell, and each of them is equally and consistently split during cell division, so that half of every chromosome is passed to one daughter cell and half to the other, as may be seen in Fig. 5. As long ago as 1883, Wilhelm Roux, in his study, "*Über die Bedeutung der Kernteilungsfiguren*," had supposed that the formation of chromosomes in long threads brought about an alignment in linear series of different materials or "qualities." Then by longitudinal splitting of the chromosomes as an early step in nuclear division all of these "qualities" are split equally or divided and passed to the two daughter nuclei


A
B
C
D
E
F
G
A1
B1
C1
D1
E1
F1
G1

which arise from this division. In the light of our present knowledge, Roux's early interpretation is astounding in its minute accuracy of conception.

A few years after this interpretation of nuclear division Weismann, in 1887, predicted on theoretical grounds that in order that the number of chromosomes in the species remain constant from generation to generation there must be a time somewhere during the maturation of the germ cells at which the chromosome number is reduced to half, as is shown in Fig. 5 on the right, and in bisexual reproduction the original number is again restored at fertilization by the union of the egg and the sperm. When different species are crossed the proper number is not restored and confusion results as is shown in Fig. 6. This is the primary reason for failure of development on crossing different animal forms.

A year later another zoölogist, Boveri, advanced a somewhat similar conception of reduction in chromosome number. And only three years after the phenomenon of reduction was first observed by Henking in an insect, *Pyr-*

Fig. 5. A diagram illustrating the cells in a species having six chromosomes, the three black chromosomes derived from the father and the three homologous gray ones from the mother. During ordinary cell multiplication, shown on the left, each of the six chromosomes divides equally and thus the two new cells in F and G each have a group of six chromosomes. In the maturing germ cells the number of chromosomes is reduced to half as seen on the right. The similar maternal and paternal gray and black chromosomes unite to form three pairs. The chromosomes now do not divide but the members of the pairs separate from one another and the two resulting cells each receive only three instead of six chromosomes. The number is thus reduced, but on uniting with a germ cell from the opposite sex it will again be raised to six. (After Karl Belar.)

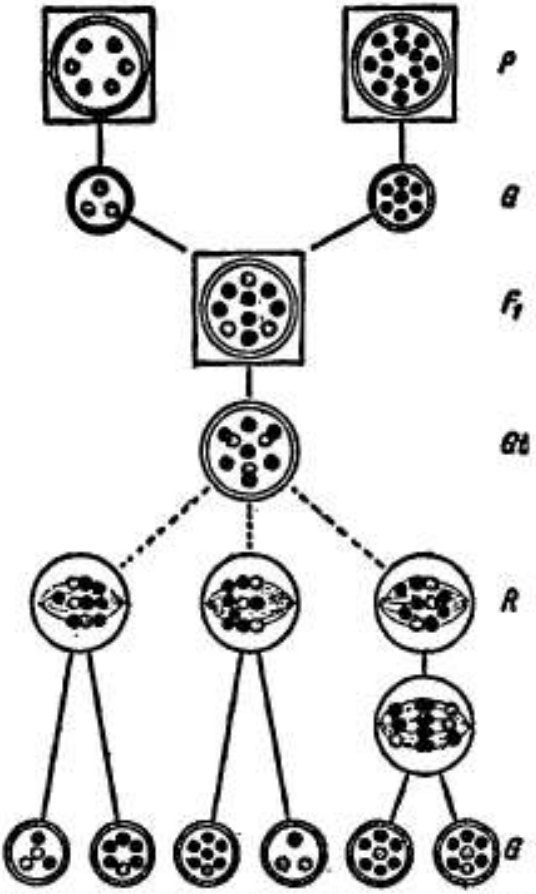


Fig. 6. Diagram to illustrate the chromosomal difficulties in crossing two different species usually having different numbers of chromosomes. The union of the two germs, G, one with 3 and the other with 7 chromosomes, gives confusion and makes pairing of similar maternal and paternal chromosomes impossible in the germ cells of the hybrids. The last line of circles shows the confusion in combination and chromosomal numbers which results. (After Karl Belar.)

rhocoris. Following this, reduction was found in a number of other animal forms by Haecker, vom Rath, Rückert and others. The chromosomes now became the bodies of greatest interest in the constitution of the germ cells and they were recognized as the basic material carriers in heredity. Thus far had the modern conception of the constitution of the germ advanced in 1900.

The Mechanism for Inheritance

In the year 1900 the rediscovery of Mendel's laws of heredity was announced by three botanical investigators, Hugo de Vries in Holland, Correns and Tschermak in Germany and Austria. These laws brought into biological science an understanding of such profound significance that every phase of our present investigations are probably in some manner illuminated by it. The laws of heredity, in their modern and refined form, have served enormously in facilitating a minute analysis of the physical constitution of the germ plasm. Almost immediately following their rediscovery these laws were interpreted in association with the already known facts of the behavior of the chromosomal structures in the germ cells. The segregation of characters and their independent transmission in inheritance exactly paralleled the segregation and transmission from generation to generation of the chromosomes in the germ cells.

We now, at last, have the necessary tools for actually breaking down and building up different animal constitutions at will and in accurately predictable fashion with these genetic laws. Figure 7 illustrates in a most striking

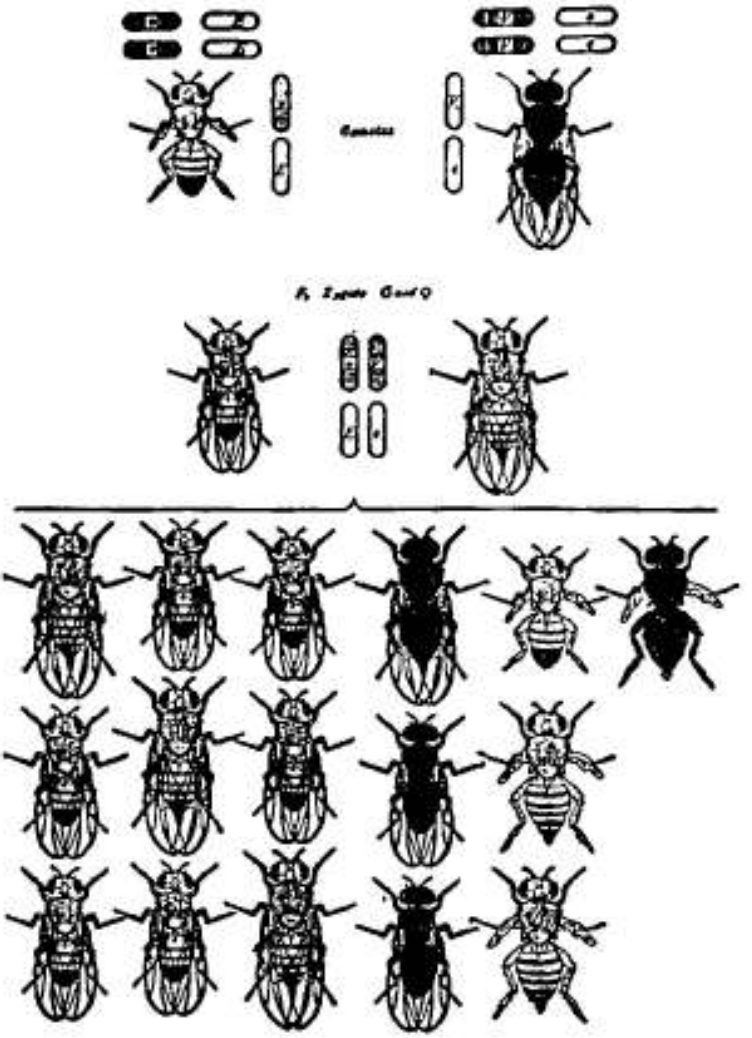


Fig. 7. Cross between vinegar flies with a recessive wingless character and a recessive ebony color. The F_1 hybrids all have full wings and the wild color pattern. But the offspring from these, the F_2s, show all combinations of the original four characters; 3 show the dominant wild color to one ebony color, 3 show

manner the process of bringing together four separate characters from two different individuals and the outcome in the second generation. How can such facilities be ignored and, still more urgently, how can they be applied in a comprehensive analysis of human personality and constitution? Yet if we confine our study and attention to adult individuals in constitutional clinics it is impossible to imagine how we are to work back for the analysis of the fundamental principles of personality. The final study of personality must necessarily be made on the developmental and comprehensive basis.

To understand more clearly the problem of germinal constitution we may consider in some detail an individual case. Let us for illustration analyze the plan shown in Fig. 8. At the middle of the two side diagrams are shown groups of bodies arranged in pairs. These represent chromosomes in the act of undergoing the reduction division. In the left diagram 14 chromosomes are seen arranged in 7 pairs of different shapes: one chromosome of each pair is black and the other striped. The black chromosomes, we assume, were all derived from the mother, and the striped chromosomes came from the father, of the individual containing this cell. These chromosomes thus represent the two sets of genetic contributions which the parents supply to the child. In all the body cells the chromosomes exist as a number of pairs of similar unit chromosomes. Each maternal

the dominant long wings to one wingless, and only one in sixteen shows the combination of the two parental recessive characters, ebony color and wingless. The F_2 generation in the figure is arranged to show the expected 9:3:3:1 Mendelian ratio for such four factor combinations. (After Morgan.)

chromosome has its paternal mate and comparable genetic elements exist in both. This well-recognized condition is spoken of as the duality of the chromosomes. Each pair of chromosomes is distinctly different in genetic quality from every other pair, and in several forms the genetic significance of the chromosomal pairs have been accurately followed. In many forms a particular pair is in some way associated with sex determination, and these are designated as the X-chromosomes. The two large bar-shaped chromosomes on the inner side of the left figure of the diagram are the sex chromosomes and since this cell contains two such chromosomes it constitutes a female individual.

After the two chromosomes of each pair have come together and fused, which is designated as synapsis, they pull apart, the maternal derivative of the pair going toward one of the newly-forming daughter cells and its paternal mate going in the opposite direction to enter the sister cell. Neither all of the maternal nor all of the paternal chromosomes need go towards one or the other daughter cell, but each pair of chromosomes seems to separate independently of the other pairs, as Dr. Eleanor Carothers so clearly demonstrated, and, therefore, an enormous variety of sortings are possible in the two daughter cells. The moving apart of the members of the pairs gives one chromosomal group to one daughter cell or egg and another to the other. In the left diagram the egg, A, at the top has obtained a different combination of chromosomes from the egg, B, at the bottom. The one at the top has the black maternal X-chromosome along with three other maternal and three paternal chromosomes, while the egg, B, at the bottom, has the striped paternal X-chromosome along with an opposite

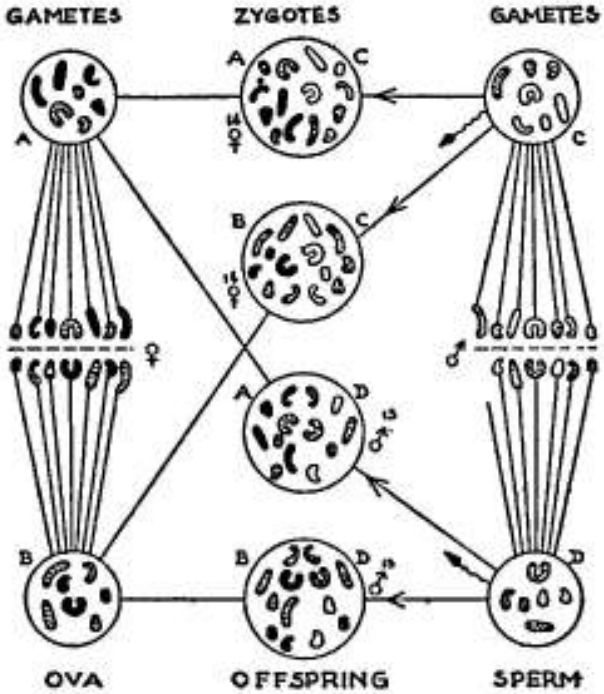


Fig. 8. A diagram to show the sorting of the chromosomes in two female germ cells and two male cells and the subsequent result of combining these germ cells to form four possible new individuals. The female cell on the left separates the two members of each of the seven pairs of chromosomes to form two eggs each with seven, the black chromosomes from maternal and the striped from paternal origin; the two ova are not alike in their chromosomes. The male cell on the right has only 13 chromosomes and sends 7 into the upper sperm-cell but only six into the lower; these two sperm-cells are also different in their chromosomes. If each sperm could unite with each egg the 4 possible combinations are shown in the middle circles. Every circle has a different combination of chromosomes derived from the four grandparents as indicated by the black, the lined, the dotted and the white chromosome bodies. No two pairs of chromosomes are the same in any two of the offspring.

combination of other chromosomes. These two eggs differ from one another in the qualities of these chromosomes. Thus there has been established a different segregation of genetic stuffs in each of the two eggs and, therefore, they are constitutionally different from one another.

The right side of the diagram in Fig. 8 illustrates a similar reduction division occurring in a male individual. There is here only one X-chromosome, the maleness being associated with the absence of the other X. The other chromosomes are all in pairs as in the female; the maternal members of the pairs are stippled and the paternal members are white. The male in many animals has a small so-called Y-chromosome derived from his father and this pairs in a not altogether consistent way with the maternal X-chromosome. For simplicity this Y-chromosome is omitted from the diagram.

The members of the chromosomal pairs in this maturing sperm-cell again move apart to give two male germ cells each with half the original number of chromosomes. The upper cell, C, contains the bar-shaped X-chromosome and the lower sperm-cell lacks an X-chromosome. It thus has only six instead of seven chromosomes. The two sperm-cells, C and D, are clearly constitutionally different in their chromosomal qualities, although both are derived from the division of a single spermatocyte. We may conjecture that by chance either one of the sperm-cells C or D may fertilize either of the eggs A or B and give rise to a *zygote*, the new individual.

Suppose for the first case that the sperm, C, fertilizes the egg, A, to give the offspring, A–C. The chromosomal combination in this individual contains two X-chromosomes

and the person is, therefore, a female. In the second case, allow the same sperm-cell, C, to fertilize the egg, B. Again we have in the combination two X-chromosomes and a female offspring, B–C. However, these two females, A–C and B–C, although we have allowed them to be derived from the same sperm-cell, making them more closely related than any two ordinary sisters could be, are yet constitutionally different. A–C possesses the factors carried by the X-chromosome from the paternal grandmother in genetic competition with corresponding factors in the X-chromosome from the maternal grandmother, while B–C has the same X-chromosome from the paternal grandmother matched against the X-chromosome from the maternal grandfather. Comparable differences exist between every chromosomal pair in A–C when these are compared with the pairs in B–C. Since the chromosomes carry the actual factors which determine the physical characters of the individual these two females, though almost as closely related as is biologically possible for two persons to be, are yet genetically different individuals. These genetic differences will appear in the later developmental expressions of these two persons.

Returning to the diagram, we may now examine the results if sperm-cell, D, be allowed to fertilize each of the eggs, A and B. When D fertilizes A, the individual, A–D, is derived. The chromosomal combination contains only one X-chromosome and is, therefore, a male. When D fertilizes B we have the offspring, B–D, which again has only one X-chromosome and is a male. These two brother individuals are more closely related than any two ordinary brothers could be, since they are both derived from one and

the same sperm-cell in union first with one egg, then with the other. Yet again we find decided differences in genetic constitution. The male, A–D, will develop characters determined by the X-chromosome handed down from his maternal grandmother, and the brother, B–D, may develop none of these characters while deriving a correspondingly different set from the maternal grandfather.

It is quite evident that still more pronounced differences in chromosomal constitution will be met if we now contrast the chromosomes in the two brother circles at the bottom of the middle diagram with those of the two sister circles at the top. The examination of this diagram conveys a general idea of the genetic backgrounds for many of the differences in physical appearance and functional behavior found among groups of children derived from the same two parents. We could on this basis imagine the possible case of the formation of an individual deriving all its chromosomes from only three of the four grandparents, and thus receiving nothing in its entire genetic constitution from one of the grandparents.

The Uniqueness of a Personality

A detailed examination of the chromosomal complexes derived from two parents, such as we have followed in the last section, finally impresses one with the extraordinary uniqueness of every individual personality. It is, of course, common knowledge that no two individuals are exactly alike, although we frequently find ourselves treating a number of them in much the same way and erroneously expecting the same response to the given treatment from all of

them. Should not more attention be paid to differences? Some such feeling as this probably has to do with the present renewed interest in human constitution and personality studies. The interest is really in constitutional differences. And taking this to be true we are in the present discussion attempting to analyze the basis for these differences. Nothing is more convincing of the profound and fundamental truth of individual uniqueness than a consideration of germinal constitution, when one realizes that differences in the chromosomal complexes are the foundation for differences among adult individuals.

A phase of this subject was presented most dramatically in an address, almost twenty years ago, by Professor H. S. Jennings, from which we may quote: "Myself, my personal identity, has as a matter of fact arisen in connection with a particular union of two germ cells each bearing a certain combination of the strands that determine characteristics. The essential question is: Could any other combination have produced *my* personal identity?

"We find that other combinations are formed in great number, but that none of these do as a matter of fact produce *myself*, not even when they are combinations of germ cells from the same two parents. Suppose that my particular combination of germ cells had never been made, then seemingly those other combinations that *are* made *would* produce the same results that they now produce, namely, individuals that are *not*—I. And my personal possibility of experience would have been forever non-existent!

"On this basis, what are the chances that *I* should ever have existed; that the particular combination which produced *me* should ever have been made? According to

competent authorities, one of the two preëxisting combinations from which my combination was derived possessed somewhat more than 17,000 germ cells, while the other produced the very considerable number of 339 billions of germ cells. So far as conditioned by the characteristics of these germ cells, any one of the 300 billions might have united with any one of the 17,000; any combination was *a priori* as probable as any other, and the chance that my particular combination should have been formed was therefore but one in five millions of billions! . . .

"But this gives but a minute fraction of the real odds against my existence, or your existence, if each of us depends on the occurrence of some particular combination of the strands. We have taken my two parents and their union as given. But the chances were equally many thousands of billions to one against the existence of each of them, and even existing, they might have mated otherwise, absolutely precluding the possibility of that combination to which my identity and experience are attached; and if we go back many generations, applying as we must the same considerations, we see that the system of notation which humanity has devised would be quite inadequate to express the odds against the formation of the combination from which I was derived, or you were derived. The chances were infinite against my existence and your existence."

IV

THE GENES, DETERMINERS OF PERSONALITY

In the previous chapter we went only so far in our analysis of the germinal constitution as to consider the gross form of the chromosomal bodies in the nucleus and their general behavior in the maturation of the germ cells and the fertilization of the egg. We have also assumed that the chromosomes are the important carriers of the hereditary factors which give rise during development to the characters of the individual. We now arrive at the question: what is the nature of the constitution of the chromosomes? What manner of stuffs in them are these factors which determine the different characters of the individuals? These questions introduce a modern particulate theory in biology which T. H. Morgan, the leading exponent of this principle, has called "the theory of the gene."

The chromosomes are composed of *genes*, the genetic elements. A single gene has not been seen, but today with ions, atoms, electrons, protons, and most deadly ultramicroscopic and filterable viruses, unseen is no longer unreal. In fact, the trend of modern physical sciences is to study the ultimately small and unseen as the most fundamental objects in nature. And, strangely enough, it is only the estimated number and arrangements of the ultimately small and unseen electrons to which are attributed the differences

in character which distinguish the chemical elements from one another.

What we do see are the effects initiated by these unseen things; observing constantly characteristic effects one becomes acquainted with particular electronic arrangements and with definite complexes of genes. The arrangement of certain genes in the chromosome are probably as clearly worked out, in a few cases at least, as are the arrangements of the electrons in some of the elemental atoms. Disarrangement or structural disturbance changes the nature and character of the element and of the chromosome. The morphologist may indeed derive considerable satisfaction on finding that the ultimate nature of things seems so dependent upon physical arrangement.

The Arrangement or Linkage of Genes

On the basis of a large amount of evidence we may define a chromosome as *a linear arrangement of genes*. The location of the invisible genes in the chromosomes has been determined entirely through experimental analysis of inherited characters. No other biological knowledge has been acquired on a more radically experimental basis than that concerning the points of location of certain genes in certain chromosomes. The nature of the chromosome depends upon the number and quality of its composing genes. Genes seem to be distinct and unique units and are not known to become contaminated by association with one another. The gene is remarkably stable, although like all other organic things it may change or mutate. After the mutation of the gene the characters which it influences are also changed. By

the employment of mutant characters in genetics, or studies of heredity, almost all our understanding of the function of the chromosomes and the mapping of the gene positions within the chromosome have been brought about.

In studying the inheritance of a number of characters that were transmitted according to Mendelian expectations, the late Professor William Bateson and his brilliant coworker, R. C. Punnett, discovered the fact that two characters in the individual may be linked together in their manner of inheritance. For example, in crossing varieties of sweet peas a purple blossom and elongate pollen grains were inherited together in a definite Mendelian way, while a red blossom and round pollen grains were likewise definitely linked together. Following this initial discovery a great number of linked characters were found in both animals and plants.

It was soon recognized that a number of characters were linked with one sex, occurring, for example, only in the male and not in the female of the species. These were called "sex-linked" characters. It was thought that this linking together of certain characters must be due to the fact that the genes upon which they depended were contained in the same chromosome—that the genes for all sex-linked characters, for example, were contained in the sex-chromosome. Through linkage, or grouping, of characters Morgan and his associates have been able to unravel many of the most difficult problems in inheritance. Figures 9 and 10, from Morgan's experiments, illustrate very clearly the sex-linked inheritance of white and red eye color in the common fruit-fly, Drosophila.

The extreme importance of the genes as factors which de-

termine the characters of the individual impresses us with the significance of the chromosome as the carrier of a linked series of the genes throughout mitotic divisions. Consistent and usual behavior of the chromosomes becomes essential

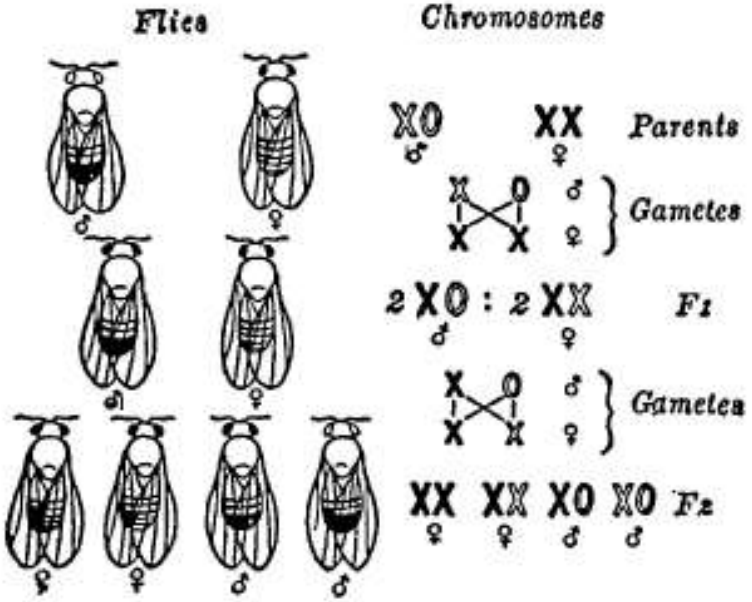


Fig. 9. The sex-linked inheritance of red and white eyes in the common fruit-fly. The animals on the left and a diagram of the chromosome combinations on the right. A white-eyed male with the white X-chromosome mated to a red-eyed female with two red X-chromosomes gives red-eyed males and females in the first generation since each offspring receives one dominant red X-chromosome from the mother. When these F_1s, are mated together they produce the second generation with all the females red-eyed since each female must receive either one or two red X-chromosomes; half the males are red-eyed and half are white-eyed since they receive only one X which comes from the mother, and half of the mother X-chromosomes are red and half are white. (After Morgan.)

for the consistently normal expression of individual characteristics.

Is there likelihood, on the other hand, of unusual or abnormal occurrences in chromosomal behavior? If so, how

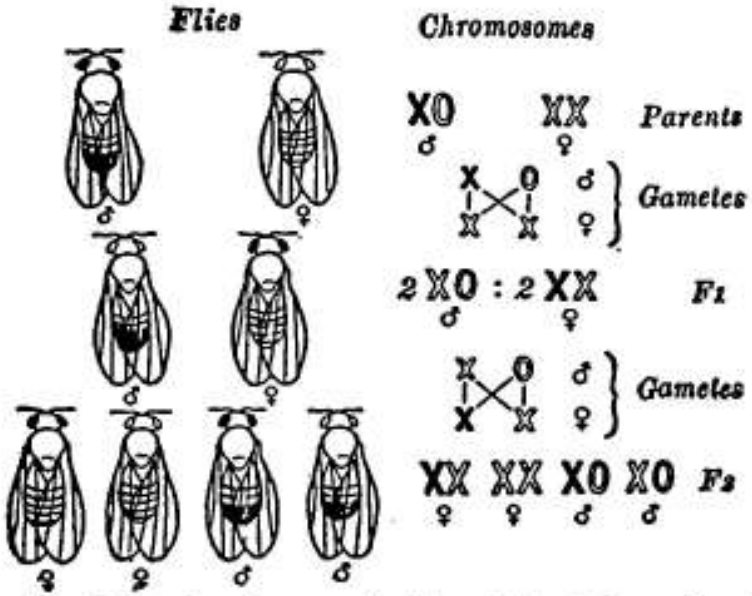


Fig. 10. Reciprocal cross of white-eyed female by red-eyed male, gives in the first generation white-eyed sons like the mother and red-eyed daughters like the father ("criss-cross inheritance"). In the second generation there are both red- and white-eyed females and males; compare with Fig. 9. (After Morgan.)

do such occurrences modify the chromosomal make-up and arrangements and what are their consequences on the characters of the person?

It has been mentioned in a previous chapter that the members of the chromosomal pairs fuse with one another

during the maturation divisions of the germ cells before their number is halved. This pairing or synapsis is usually a very orderly coming together lengthwise of each two homologous chromosomes—the one from maternal and the other from paternal origin. When chromosomes are thus paired in synapsis, it is thought on the basis of considerable evidence that corresponding, or so-called allelomorphic, genes in the two lie immediately opposite one another. During this period of synapsis peculiar reactions sometimes occur. The most common of these has been termed crossing-over.

Crossing-over of Genes between Chromosomes

In crossing-over the two fused chromosomes probably become twisted around one another at some one point so that the part of each chromosome beyond this point lies in line with the other portion of the opposite chromosome. In pulling apart on the division spindle after such twisting, each two pieces of chromosome lying in line become joined, making a single chromosome, and these newly joined pieces move away together. By this process the two original chromosomes have exchanged comparable parts of themselves and the pieces thus exchanged are said to have crossed-over. Chromosomal twistings and arrangements necessary for such an occurrence have been seen in the germ cells but the actual proof of crossing-over has been derived from genetic evidence, see Fig. 11.

As has been pointed out the hereditary characters are transmitted not as single units but in definitely linked groups. The number of linkage groups corresponds in a

given animal species with the number of chromosomes. Much evidence indicates that the characters in a group are linked together on account of their being determined by the

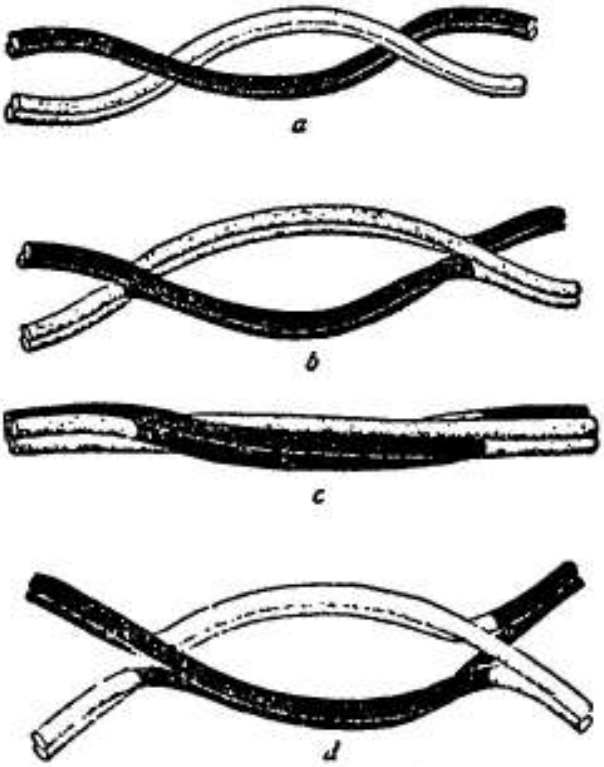


Fig. 11. Diagram showing pairing and crossing-over of two chromosomes at the four-strand stage. (After Morgan.)

series of genes within one chromosome. Therefore, the effect of crossing-over is the breaking away of some of the characters from one linked group and their new association in another group. For example, if a chromosome containing genes A, B, C to Z is in synapsis with an homologous chro-

mosome with genes a, b, c to z, and crossing-over occurs at the points Ee, then one chromosome will become A B C D e f g and so on, and the other will become a b c d E F G and so on. In this case, if we suppose all capital-letter genes to be dominant factors and all small-letter genes recessive, then before crossing-over the capital-

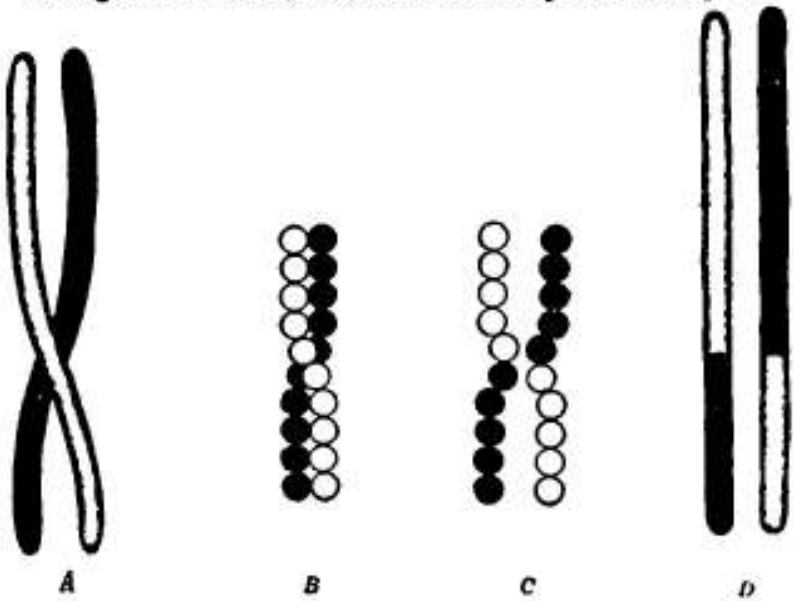


Fig. 12. Diagram of crossing-over. At the levels where the black and white rods cross in A, they fuse and are united as in D. The detail of gene crossing-over is shown in B and C. (After Morgan.)

letter group of linked characters was completely dominant over the other, but after crossing-over the groups are mixed and each contains both dominant and recessive characters. Figure 12 is a diagrammatic illustration of the supposed crossing-over between two strings of genes.

Morgan and his associates, particularly Sturtevant and

Bridges, have found in the small fruit-fly, Drosophila, that large numbers of characters are linked or grouped into four sets, corresponding to the four pairs of chromosomes in the cells of these flies. Such sets of linked characters are not absolutely consistent in their groupings. It occasionally happens that a character which is ordinarily associated with a certain set of other characters becomes dissociated from these and links itself with another set through crossing-over.

Crossing-over is a frequent phenomenon, and on the probability that those genes or particles furthest apart in the chromosomes are more liable to become separated from one another when the crossing-over occurs, than other particles lying closer together, much has been learned of the exact serial arrangement of the genes along the line of the chromosome. The probability that the arrangements of genes are serial has been determined through the breaking up of the usual linkage of character groups in inheritance. The results finally make it possible to plot the relative loci of the genes and thus chart the chromosomal maps.

Figure 13 from Morgan's experiments shows how two characters usually linked in inheritance may become separated and independently inherited following crossing-over. White eyes and yellow body color are usually linked in the sex-chromosome of the fruit-fly but as the figure shows they become separated in a small percentage of cases.

Nondisjunction or Fusion of Chromosomes

A second peculiar occurrence may arise during the synaptic pairing of the chromosomes. One of the pairs may

fail to have its members separate and so remain double. In this case, the two fused chromosomes must both pass into the same cell at division, instead of each unit of the

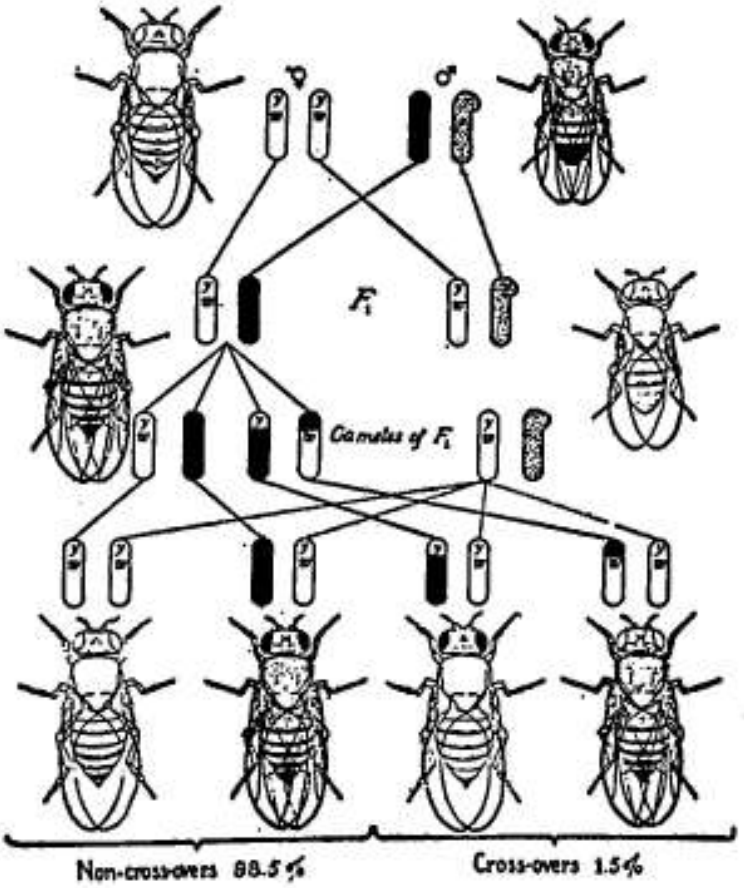


Fig. 13. The effects of crossing-over on body characters. White eyes and yellow color are linked in the sex chromosome of the fly, but after crossing-over the yellow and white become separated and yellow flies with red eyes and gray flies with white eyes are shown in the lower right group of the diagram. (After Morgan.)

pair going into one of the two sister cells. To this phenomenon the term *nondisjunction* is applied. In such a case the egg or the sperm-cell will contain an extra or duplicate chromosome. When this cell unites with another cell at fertilization, an individual is formed having three instead

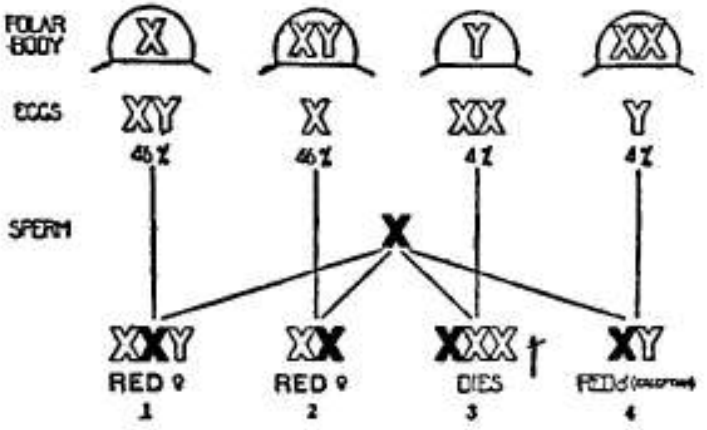


Fig. 14. Nondisjunction causing an excessive number of similar chromosomes. In the upper part of figure the four possible modes of reduction of the sex-chromosomes in XXY eggs are shown; the results of their fertilization by an X-bearing sperm from the normal red-eyed male is shown below; XXY and XX red-eyed females and XXX animals which die and exceptional, XY, red-eyed males are produced. (After Morgan.)

of two or a triploid instead of the proper diploid condition, of this particular chromosome. There is, therefore, an accessory set of factors, and, as a result, a peculiar and confused expression of the involved characters occurs. Or, at times, the presence of this additional chromosome may actually prove fatal, a successful development of the individual seeming to be impossible under such an arrangement.

The presence of an accessory or additional chromosomes may possibly be associated at times with abortion and prenatal death in human beings. Again Morgan and his coworkers have been the chief contributors to our knowledge of these phenomena. An examination of Figs. 14, 15 and

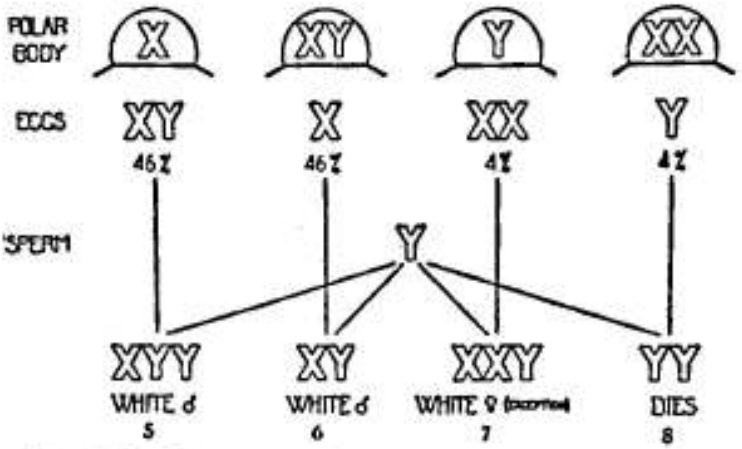


Fig. 15. Nondisjunction. The same as in Fig. 14, but followed by fertilization with a Y-bearing sperm of the male which gives white-eyed males, XYY and XY, exceptional white-eyed females, XXY, and complete absence of X with double YY which dies. (After Morgan.)

16 will serve to make clear the peculiar chromosomal arrangements in nondisjunction.

The fact that one cell may receive both members of a chromosomal pair during reduction also makes it evident that the other cell may lack entirely a certain chromosome, and its later history is likewise peculiar. The absence of the small fourth chromosome has occurred in *Drosophila melanogaster*, the fruit-fly, so extensively studied in modern genetics. Peculiar compound individuals that may arise

through abnormal fertilization and strange chromosome reactions are illustrated by Fig. 17.

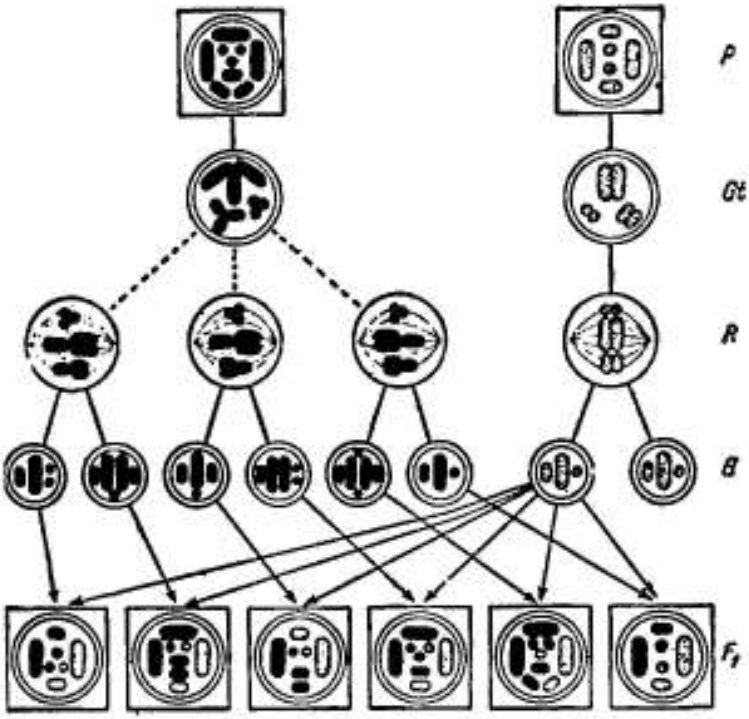


Fig. 16. A diagram of nondisjunction and the following triploid condition in three chromosomes. Eggs of this kind fertilized by normal sperm, shown on the right give the combinations in the lower line with five abnormal groups with irregular chromosomal numbers to one normal group of six chromosomes at the right end of the line. (After Karl Belar.)

Translocation of Portions of Chromosomes

A third type of occurrence may disturb the integrity of the chromosome. Either an entire chromosome or a part

of it may become attached to a non-homologous chromosome and be carried by it during cellular division into a cell in which it does not properly belong. Here we have a combination of two separate groups of genes and, resulting from this, a peculiar linking together of characters that are

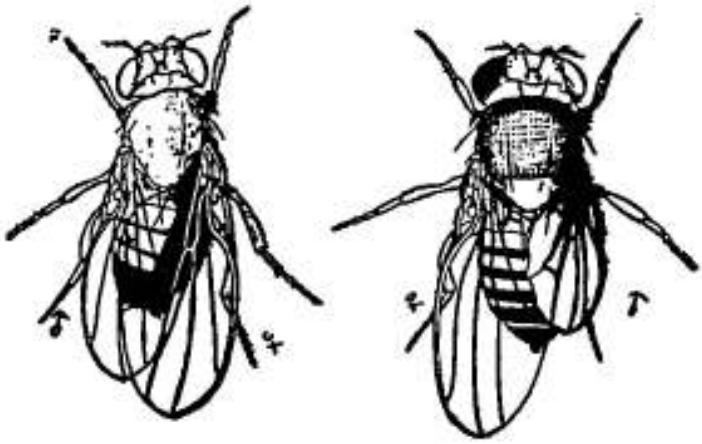


Fig. 17. Abnormal sex-chromosome reactions in the germ giving rise to specimens which are male on one side and female on the other and with different sex-linked characters on the two sides. Such specimens illustrate vividly the effects of the genetic basis on body character. (After Morgan.)

usually transmitted separately. This unusual attachment of an entire chromosome or a part of a chromosome to a dissimilar chromosome has been called *translocation* by Bridges, who first became aware of it from genetic evidence in the fruit-fly, Drosophila. Mrs. L. V. Morgan, in 1922, described one X-chrdmosome attached in this manner to another X. Mrs. Morgan also clearly showed the peculiar genetic effects which resulted from this condition. It was

later found by Stern, in Morgan's laboratory in 1926, that a portion of the Y-chromosome of the male might become attached in a similar way to the X-chromosome. Stern found through genetic studies that the presence in the cells of this attached piece of the Y-chromosome was not sufficient to prevent sterility in the male but it was able to do so when another incomplete Y-chromosome was present. Stern presented both genetic and cytological evidence proving that the Y-chromosome had broken and that one of its pieces had become attached to a dissimilar chromosome.

Muller has more recently shown that translocations, or "breakage with reattachment of a fragment to a non-homologous chromosome" frequently occur following exposure of germ cells to the X-ray. The use of X-rays provides such an abundance of these cases that among them many of a suitable nature for both a genetic and a parallel cytological analysis are to be found.

Muller has reported translocation from chromosome III to II, see Fig. 18, and from III to Y in the well-known fruit-fly. A study of the various breaks and reattachments has enabled him to supply valuable physical proof of the correctness of the gene sequence in chromosomal maps which had been plotted from the frequency of crossing-over in genetic studies.

Deletion in the Chromosome

The X-rays also produced in Muller's experiments another type of chromosome modification–*deletion*, or the elimination of middle pieces of chromosomes. This has been produced by irradiating adult male fruit-flies and

then crossing them to females of the so-called attached X-race. When this procedure was followed, in approximately one per cent of the cases the X-chromosome from

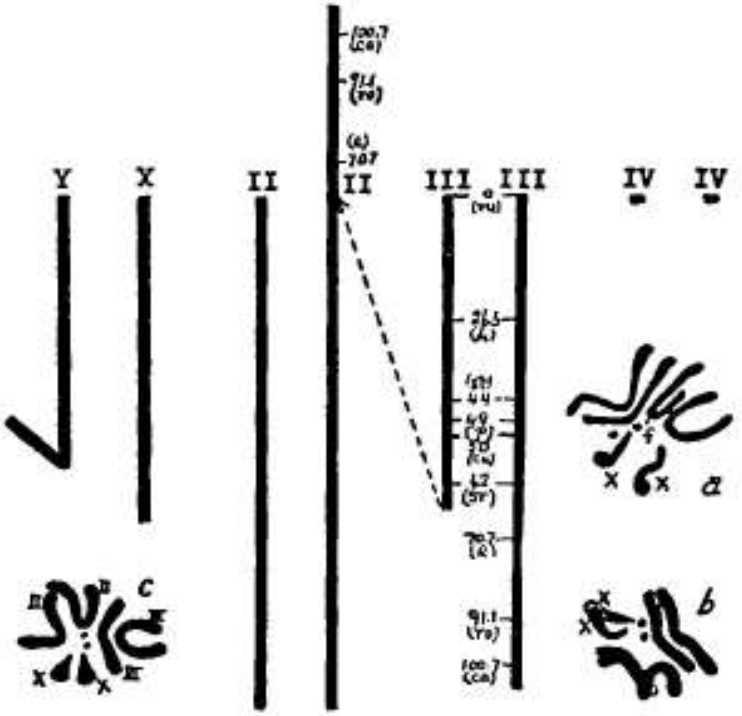


Fig. 18. Diagram of the translocation of a part of III-chromosome to II-chromosome. The "right hand" end of the third chromosome has broken and become attached to the "left hand" end of the second chromosome. (After H. J. Muller.)

the male underwent a deletion of its middle part, leaving a small piece from one end attached to a small fragment of the other end. Various deletions of the X-chromosome of this general type were analyzed, and it was found that the size of the remaining fragment varied genetically and

cytologically. One coherent section of the genetic map had been deleted, including every one of the genes tested in that section, while in the remainder of the chromosome all

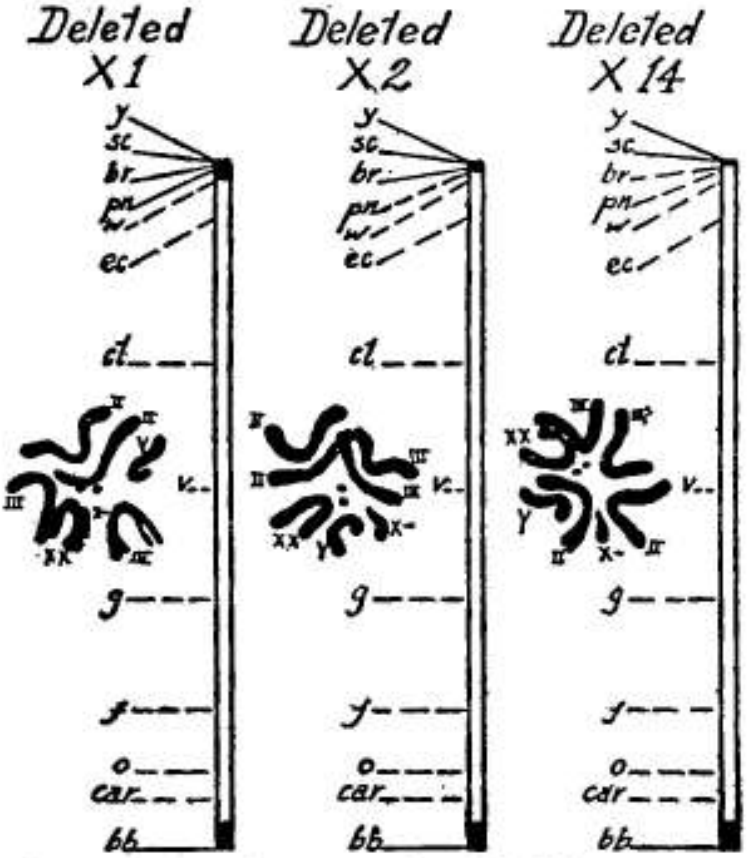


Fig. 19. Deleted chromosomes. One of the X-chromosomes in these cases has dropped out a large portion of its mid-region, leaving only the two small black end pieces. The three sketches show the exact microscopic picture of these chromosomes. (After H. J. Muller.)

of the genes that should have been there were still present. Figure 19 is a diagram of this condition.

These cases of deletion furnished illustrations of the fact that the genes, which the calculated chromosomal map represents as lying together, really do lie physically together.

In biological constitution the genes may be considered the ultimate structural units or atoms through the influences of which our physical personality is determined. This much seems highly probable, concerning the nature of these important cell particles.

V

WHAT CHANGES IN GENES CAUSE CHARACTER ALTERATIONS OR MUTATIONS

WHAT has occurred in the genes when a mutation, or sudden modification of a character, appears in the individual? Are genes ever lost, or do new genes ever arise in the chromosomes? No direct answer to such questions is yet possible. How does evolution come about, or what initiates the progressive changes in the complexity of animals in so far as this depends upon the genes? Here also our answers become very uncertain; extremely little is known of the exact mechanisms which lie back of these evolutionary changes in character.

Something of the nature of such processes may possibly be learned through studies of the inheritance of rudimentary and disappearing organs. It is commonly agreed that the degeneration of certain parts, such as the gills from our neck, and the changing over of their remains, in forming, for example, the middle ear as a sound conductor, has been occurring in evolutionary processes. And since these changes bear directly on the subject of constitution and personality as well as on modifications in constitution, a case in point deserves consideration.

The Specialized Feet in Mammals

Among the mammals there are various types of specialized or modified feet in which the one common feature is the reduction in number of digits or toes below the primitive five-toed condition. It is generally accepted on evidence from paleontology and comparative anatomy that the early mammalian foot was five-toed, and as a rule a reduction in number of toes has taken place on the median or thumb side and then on the little finger or lateral side first of the foot, then of the hand, alternately. The most median, or first digit of the foot, the big toe, has probably been the earliest toe dropped out by many mammals.

The extreme condition at present exists among the family Equidae, including the horse, with only the axial or third digit of both the front and hind feet remaining to form the actual hoofed foot for contact with the ground. In the *Artiodactyla*, or cleft-hoofed mammals, such as the sheep and cow, the two middle digits, the third and fourth, are retained while the border or side digits are either absent or functionless rudiments. Lesser degrees of reduction in number of digits occur among almost all the orders of mammals.

We are still quite ignorant of the hereditary processes through which this reduction in number of toes has taken place. Yet one may suppose in general that certain mutations or germinal changes have brought it about. If such a supposition be correct, we may ask whether in these mutations the genes, or factors for the development of those toes which have disappeared, are also lost, or permanently modified, so as to render it impossible for the old five-toed

pattern to reappear. Or are the original factors for all five digits still present in the germ cells in their primary condition, even though certain toes are lost, and thus have the mutations that eliminated the toes involved other genes which may prevent the toe factors from indicating their presence through the development of the digits? There is evidence which would seem to indicate that the latter possibility may be correct. If so, then one might under proper conditions find, or even be able to bring about, a reappearance of the lost digits.

Studies of these degenerating toes are important on account of their bearing on the origin and progress of other evolutionary changes in structure. Many of these changes are present in our own bodies, such as the general disappearance of hair over the skin, degeneration of the third molar teeth, modification of the ancestral gill structures in the larynx, the well-known rudimentary appendix, and so on, to a list of far more than a single hundred.

The Loss and Reappearance of Digits

The author has studied two species of mammals, belonging to two quite different orders, which seem to throw light on the question of the evolutionary loss of toes and the inheritance of a reëstablished original digital number.

In most breeds of dogs, and in the wolves and jackal which are probably ancestrally related to them, there are five digits on the front foot and only four toes on the hind foot. Only one species of the family Canidae, *Lycaon pictus*, the African hunting dog, has only four toes on each foot, as is the case with the Hyaenidae, the family which in-

and other mammals would probably show next the loss of the little finger of the front foot, and so on with this alternating scheme, until only the axial or third digit remains, as in the case of the horse.

Evidence has now accumulated which indicates that when an atavistic return of digits occurs in these mammals the digits reappear in the reverse order from that in which they disappeared. In the guinea-pig the first digit to reappear is the small toe on the hind foot, as Castle found, and the next is the thumb on the front foot (which has reappeared in one of my specimens as reported in 1927). But until now no guinea-pig is known to have redeveloped a great toe, this being probably the earliest digit lost in the history of their digital reduction.

The dog, however, is apparently just finishing the process of losing the great toe from the hind foot, and this toe still occasionally reappears. In the dog the thumb also has become a high-placed, small, degenerate digit, functionless and probably in its earliest stage of disappearance. Thus the guinea-pig and the dog furnish very instructive stages in the evolution of the *digitigrade* or toe-stepping foot, showing the accentuation of central toes and the degeneration of those from the borders of the feet.

Inheritance of the Great Toe in Dogs

In order to understand the inheritance of the above described conditions I have studied the results of hybrid matings between pedigreed pure St. Bernard dogs having the great toe present and pure line great Dane dogs which completely lack the big toe. I have never seen a great Dane in

which the big toe was visibly present, although a large number of them have been examined, but a rudimentary first metatarsal bone, with which this toe normally articulates, is present in the foot skeleton of the Dane. The eight pure-bred St. Bernard bitches which have been used in our experiments all possessed the great toe on both hind feet. One of these, "Hercuveen Helmar," not only has the great toe, but has it doubled on both hind feet. This animal has been cross-mated four times with three great Dane males. Figure 20 shows in outline the toes in dogs.

Two cross-matings between "Helmar" and the champion Dane male "Argus von Berkenhof" have given litters of seven and two pups respectively, all nine of which have a great toe on each hind foot.

This female produced by the Dane male "Prinz" fifteen pups, seven males and eight females, all possessing great toes on both hind feet. She was finally mated with the Dane male "Franz" and gave birth to a litter of thirteen pups. Two males and one female among these pups had a double great toe on both hind feet, the same condition as that shown by the mother. Two other male pups had a single great toe on their right hind foot and double great toes on their left feet. The other eight pups, six females and two males, all possessed a single great toe on each hind foot.

Thus this female St. Bernard, when crossed with male Danes lacking the great toe, has given thirty-seven pups all possessing great toes. This would seem to indicate that she is pure or, technically speaking, *homozygous* for the factor for great toe development, since it is expressed as a dominant character in all of her hybrid offspring.

The reciprocal cross has also been made between three

great Dane bitches and three St. Bernard sires. These bitches like all great Danes were without the large toes, and the St. Bernard males all had a single great toe on each hind foot.

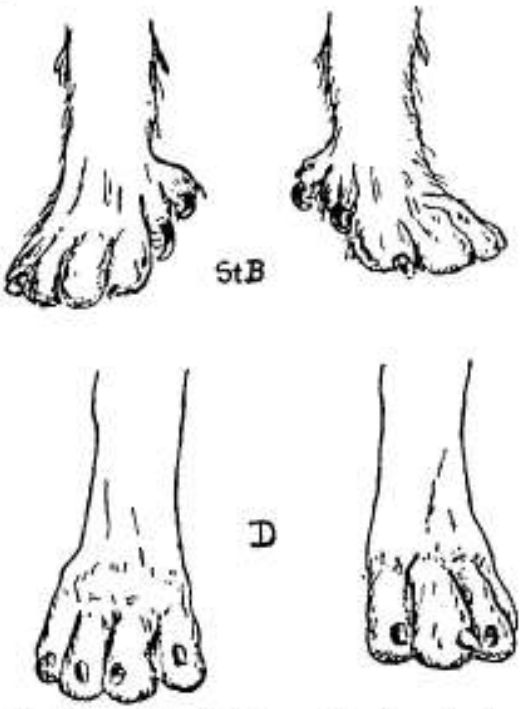


Fig. 20. Outlines of the hind feet of the dog showing above the presence of a big toe in the St. Bernard feet and below the absence of this toe in the feet of a great Dane. The big toe is not only present but frequently doubled in the St. Bernard as the outline shows.

From all of these cross-matings, which have produced seventy-eight hybrid pups, it would seem that the presence of the great toe in the dog is inherited as a dominant char-

acter in spite of the fact that this digit has almost been eliminated in the evolution of the feet in the entire family Canidae.

At this time only two litters of F_2, or second generation, pups from *inter se* matings of the St. Bernard-Dane hybrids (both male and female possessing great toes) are available. The first litter of eight contains four pups with great toes present on each hind foot and four pups without great toes. If the great toe is inherited as a single factor dominant character it would be expected to appear among the second generation pups in the ratio of three animals with the toe to one without. The other litter of second generation puppies has great toes present in six of its members and absent from one. The present numbers are so small that an exact ratio could not be hoped for, but it is of interest that in this generation individuals both with and without the toe do occur, the majority possessing it.

The back-cross between the St. Bernard-Dane hybrid and the recessive parent, the great Dane without a big toe, happens, however, to give a better numerical result. A single litter has been derived from a Dane mother, without great toes, by her son, a Dane-St. Bernard hybrid with great toes. Among the six members of this litter, three possessed great toes on both hind feet and three did not. This is exactly the expected one-to-one ratio which should result when the hybrid, impure or, technically termed, *heterozygous* dominant, is back-crossed on the pure recessive parent type.

A back-cross in the other direction, between the dominant great-toed St. Bernard parent and a St. Bernard-Dane hybrid, with great toes, gave thirteen pups all, as expected, possessing the great toe. In this mating the St. Bernard

mother had double great toes on both hind feet. Six of the back-cross pups also had double great toes on both hind feet, and one of the pups had five toes on the right foot and six toes on the left. Thus, strangely enough, exactly half of the hind feet in this litter of thirteen pups have double great toes (six-toed feet) and half have the typical single great toe.

The presence of the great toe and the doubling of this toe seem to be inherited as entirely separate characters. The inheritance of the great toe follows the expected behavior of a single dominant factor, while the doubling of the toe in the single case just cited has followed exactly the expected behavior of a simple recessive factor. This result is probably quite accidental since the double toes in some of the first hybrid generation are clearly out of line with the expression of a recessive character. But there is the more likely possibility that the St. Bernard bitch here used as the mother may be homozygous or pure for the dominant great toe, and at the same time heterozygous or mixed for a possible dominant doubling factor, a condition which would be expected to give exactly the toe composition of the litter described above. This interpretation is supported rather than opposed by the appearance of double toes among the first hybrid generation. More data are necessary for a final analysis of the double toe.

Inheritance of Reappearing Toes in Guinea-Pigs

Among guinea-pigs an extra toe, in the place of the small toe, is occasionally developed on the hind foot. In each of eight different stocks observed in our laboratory for more

than fifteen years, little toes, fifth digits, have occurred on the hind feet of a few individuals.

This reappearing ancestral little toe varies in development from a structurally perfect digit through all degrees of imperfection to an attenuated fibrous outgrowth tipped with a malformed toe-nail; such a remnant is often lost at birth or soon after, see Fig. 21. The percentage of expressed inheritance for the extra-toed condition varies directly with the perfection of development shown by the parental extra toes. Thus by mating only animals with perfectly developed extra toes, 100 per cent of the offspring show extra toes, but in various degrees of perfection.

Within this carefully selected group of guinea-pigs with 100 per cent little toes, a single guinea-pig has appeared with thumbs on the front feet. This specimen is highly important and its toes are shown in Fig. 22. Here the evolution of anatomical structures has been reversed through a selected concentration of non-mutant factors and a return to the ancestral five-toed condition in the front foot and to the four-toed stage in the hind foot. The germinal or hereditary basis for five digits is, therefore, still present in guinea-pigs although structurally unexpressed in racial evolution for long generations and probably for centuries of time. The evolutionary loss of the toes has been due to something other than a simple loss of toe-determining factors from the germ.

The toe arrangement is less modified in the dog than in the guinea-pig, and the genetics of the reappearing great toe in dogs is correspondingly much simpler than the reappearance of the small toe and the thumb in the guinea-pig.

Strangely enough, as we have seen, the rarely present big toe in dogs is frequently doubled; and this, with certain

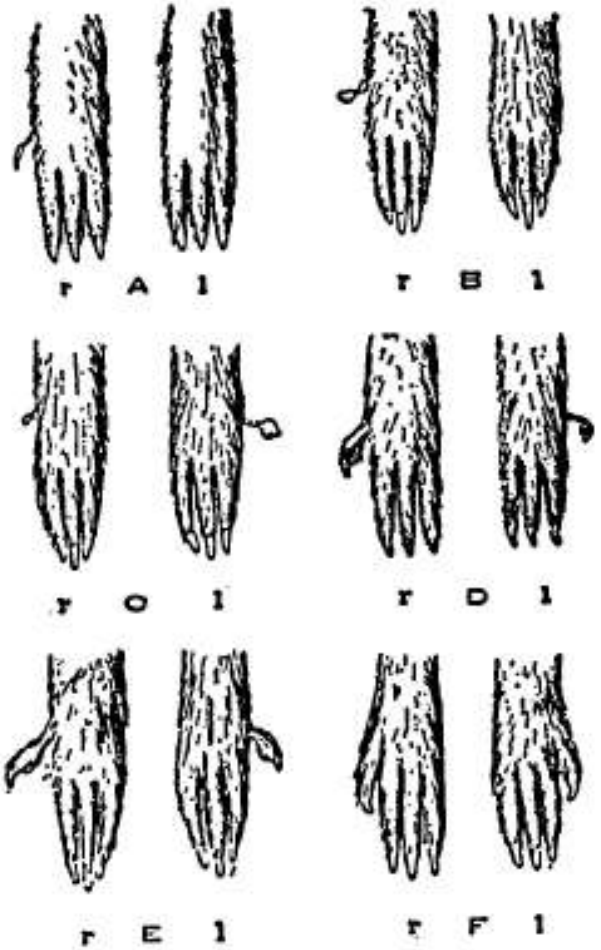


Fig. 21. The reappearance of the small toe in the guinea-pig. Great variation is shown in the degrees of its development from a fibre-like process in A to a perfectly formed toe in F.

Fig. 22. The reappearance of a thumb on the front feet of the guinea-pig after being absent for probably hundreds of generations. A reversal of the evolutionary processes.

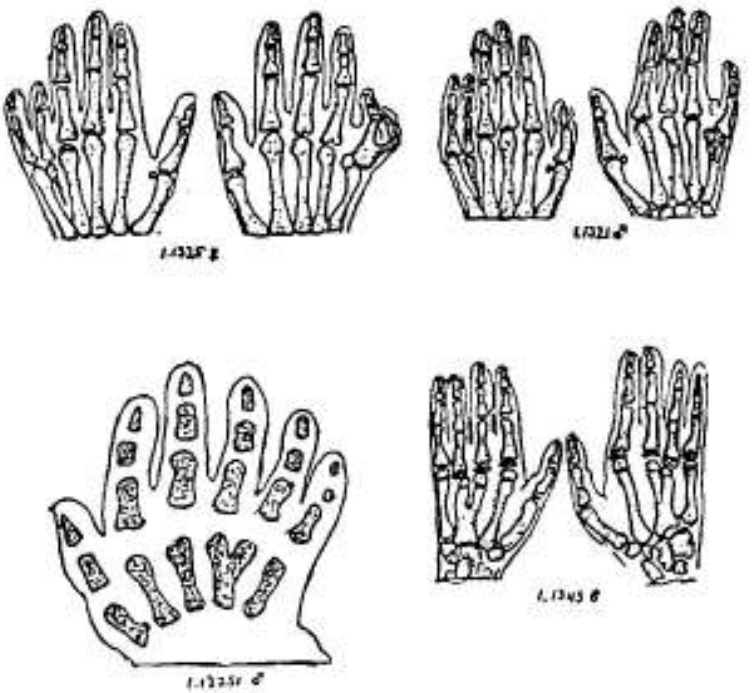


Fig. 23. Outlines of X-ray photographs of the bones in polydactyly or extra digits on the human hand. (After Sverdrup.)

conditions of the digits in six-fingered or polydactylous human hands (see Figs. 23 and 24) suggests the possible interpretation of human polydactyly as an early expression of the mutant conditions which, when further progressed, tend to cause suppression or loss of the border digits from the hands and feet. If this be a possibility the future human hand may possess fewer fingers, since the presence of accessory border digits is by no means an uncommon phenomenon.

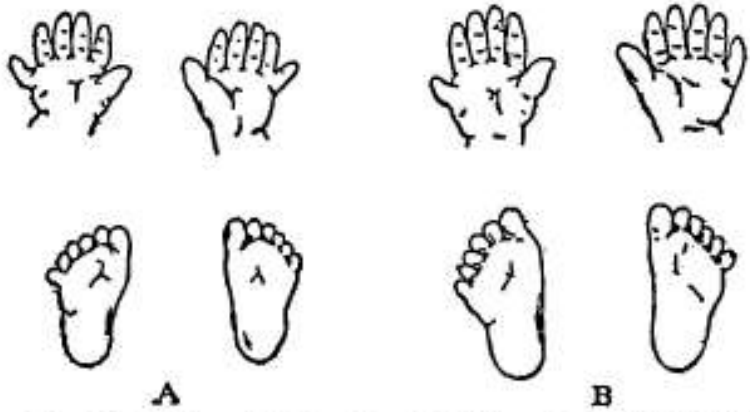


Fig. 24. Outlines of the hands and feet from two human identical twin brothers. There are six fingers, an additional one on the little finger side, on the four hands, and six toes on each of the four feet. These two individuals very probably arose from a single human egg.

Genes and Character Changes

The reappearance of the long lost digits in dogs and guinea-pigs demonstrates the fact that the germinal basis for such lost and rudimentary characters has not disappeared: the genes for the determination of these characters are still present. If these genes are still present, then what manner of change has caused the loss of parts in the individual? In the above cases it might be conjectured that changes or mutations occur in certain genes or gene arrangements which merely permit one part, in this case certain digits, to gain an advantage over other parts in their developmental competitions. This could bring about the result just as well as a mutation which actually destroyed the genetic basis for a given digit or structure. Mutations may have served

simply to accentuate the growth and size of the axial or middle digits at the expense of the marginal ones.

The inheritance in the female of uterine modifications might in itself be sufficient cause to account for many species differences on the basis of resulting modifications in the developmental processes under a changed environment. The inheritance of quadruplet young in the Texas armadillo may probably be the result of some such cause. In other cases, changed characters in the progeny might appear and remain constant while the germinal mutation that induced them may have acted only on the character of the reproducing females. In this way, a character might appear to be definitely inherited without actually being directly inherited as such.

The origin of many new parts may have come about slowly on account of the inheritance in the race of new or mutated developmental environments, while the genes or determiners for the parts themselves may not have been affected. In such a manner the modification of the useless first gill-pouch in land-living vertebrates may have become metamorphosed into our complex middle ear, and the left-over drainage apparatus from the embryonic kidney or mesonephros may have been changed into the well-adapted genital ducts. Many similar examples of functional change, or *functionswechsel*, as the German zoölogist, Anton Dohrn, expressed it, are found among higher vertebrates, although the actual genesis of such modifications is quite unknown.

Hybridization frequently brings out atavistic characters from one or both of the parent stocks, as is seen in the frequent striping of the legs of mules from the combination of the horse and ass. This may be due to the weakening, or

breaking down through out-crossing, of dominating complexes in the germ, if our above supposition of the modification of competitive advantage among the developing parts is possibly valid.

It is very probable that inbreeding and domestication, as contrasted with the wild natural processes of breeding, does much to bring about new conditions of constancy in composition of germinal complexes, without modifying the genes themselves. These somewhat artificial combinations give rise to the modified domestic forms which transmit their type under careful selection but tend in certain cases of multiple breeds, such as the dogs, to return to the wild type when allowed free mating in nature. It is also a fact that a single genetic character may be expressed under one environment but not under another; such a phenomenon we shall later discuss.

Reappearance of Lost Ancestral Structures in Man

Finally, we know among human beings of ancestral conditions reappearing to the individual's great disadvantage. The gill-pouches which are present in the early embryo may, for example, persist and form an open fistula on the side of the neck communicating with the cavity of the pharynx. From such cases we surmise that the genetic basis for a gill-breathing arrangement is still present in our germ cells, although in evolution we have lost the gill-breathing apparatus millions of generations ago. One may wonder whether the gene or genes for the determination of any character are ever lost from the germ. The reappearance of archaic structures would make us rather think that a shift-

ing of gene arrangements with consequent changes in their interactions might possibly be the mechanism for mutations which cause the alteration and falling out of structures and characters.

All these phenomena have a significant bearing on the problem of human personality and constitution, and the fact that their analyses are not yet sufficiently well-developed to be readily interpreted makes their recognition none the less necessary for a truly scientific understanding of human personality. Any other so-called understanding is, of course, no understanding at all!

VI

DEVELOPMENTAL OR EMBRYONIC PERSONALITY

THE germinal constitution has a long path to follow in evolving the mature individual. This germinal make-up, or genetic complex, acts as pilot, steering and directing the developmental processes towards a specific goal —we might better say, towards an ideal goal, since we shall find that it is questionable whether development ever does produce a full expression of the actual hereditary background. The pilot in this case is never completely able to master all the pressing currents of the environment. The mature individual is the final product of a definite germinal complex expressing itself through development under a particular set of conditions. In other words, the development of the person depends, on the one hand, on the exact nature of the original germinal composition, and, on the other hand, upon the varying elements which the environment may present.

The inheritance or genetic basis may be defined as the complete complex of factors which the individual receives through the union of the egg and spermatozoön from which it arises. Certainly no other factors except these can ever be present in this individual. Most individuals must carry, therefore, hereditary basis for a large number of characters quite different from those they express: in part these are

the recessive antagonists to the dominant characters which do develop. For example, all children born from the union between an albino mother, lacking skin pigments, and a normally pigmented father will show their father's pigmentation, although they will have inherited the albino character from the mother as an unexpressed recessive. Anyone seeing such children and not knowing their parentage would fail to realize that they carry the factor for albinism in their germ cells. But if these albino carriers should ever produce children by albino mates, half of their offspring would be albinos and half of them would be pigmented—a very different result from that derived from the union between the ordinary pigmented person and an albino!

Again an individual may be said to have inherited a type of nose from his father or from his mother, and yet he may develop entirely without a nose! A son may inherit his father's mouth-shape and yet show a harelip and cleft palate, his mouth in no sense resembling that of his father. In such a case, the inheritance for the character would have been perfect but the developmental conditions must have been such as to inhibit its growth and expression. It is often difficult to say what we actually have or have not inherited. We simply see the characters which have been able to express themselves out of the fundamental genetic basis with which we started. Individual constitutions are truly a combination of inheritance and development, and the possibilities of neither are expressed to their fullest extent. Jennings has clearly epitomized the situation as follows: "Characteristics are not inherited at all; what one inherits is certain material that under certain conditions will pro-

duce a particular characteristic; if these conditions are not supplied, some other characteristic is produced."

Environment and the Expression of Characters

Some years ago, Morgan found that among certain stocks of the common fruit-fly, Drosophila melanogaster, reared in an unusually humid environment, a germ change or mutation occurred which showed itself in the form of an abnormal or deformed abdomen, see Fig. 25. This definite genetic character bred as a sex-linked dominant: that is, it first appeared in one sex and not in the other, and it was dominant over the normal condition, so that all individuals of one sex had an abnormal abdomen and no individuals of the other sex had the defect. When flies carrying the abnormal abdomen were transferred to a dry environment they ceased to give rise to offspring with the abnormal abdomen; all developed into perfectly normal specimens. This line of

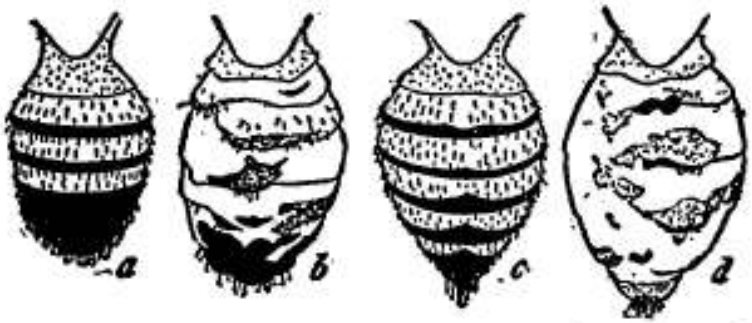


Fig. 25. Drawings of normal and abnormal abdomens, in a and b, males and, c and d, females of Drosophila. The abnormal abdomen is inherited but only occurs under certain environmental conditions. (After Morgan.)

individuals was bred in the dry environment for nine generations as perfectly normal flies. They were then again transferred to the humid environment and immediately gave rise to the abnormal abdomen in the expected fashion. The ordinary strains of fruit-fly of course do not give abnormal abdomens when bred in the humid environment. This particular line of flies possessed a distinct hereditary quality or mutation for abnormal abdomen which only expressed itself in the humid environment. When a generation was bred in a dry environment they failed to exhibit the mutant condition. This case is particularly interesting since it shows that animals with a definite genetic composition may under certain conditions develop perfectly normal bodies, while under other conditions they develop only abnormal bodies. The so-called *genotype*, or germ composition, may be abnormal and yet the *phenotype*, or body composition, may develop perfectly normally under given conditions; or the reverse may also be true: a normal genotype may give rise in a peculiar environment to an abnormal personal constitution.

Another occurrence of a comparable nature was recorded by Miss M. A. Hoge in 1915, showing a striking influence of low temperature on the expression of a Mendelian character. When a definite mutant line of fruit-flies was kept at low temperature, accessory and double legs were inherited in an exact Mendelian ratio. In the double legs the flexor surface of each component faced toward the other, each leg thus being a mirror image of its double, and the two constituted a typically twinned extremity. When this strain of flies was later bred at normal temperatures the double legs did not occur in the Mendelian ratio. The slow development

at low temperature was necessary in order to bring about the full expression of this hereditary character! Of course the ordinary lines of Drosophila lacking this mutant character do not develop accessory legs when kept in the low temperatures.

These environmental influences over the development or expression of a character in an individual only emphasize the important fact that the absence of a character in a person does not at all mean the absence of the necessary hereditary factors from the germ. There is always, as we have seen, the double problem of transmission and expression; a character may be inherited or transmitted but because of unfavorable developmental surroundings it is suppressed and does not develop. As Morgan has stated it: "In cases where, on the factorial hypothesis, a certain factor is expected to be present in an individual, then, even if the individual fails to develop the character commonly taken as indicative of the factor, the actual presence of the factor may be demonstrated by breeding tests." If circumstances are provided similar to those in which it previously appeared, a character will show itself again.

A number of years ago it was discovered that if the eggs of a common fish, the Atlantic Coast minnow, *Fundulus heteroclitus*, be developed in sea-water to which had been added certain salts or other substances, a considerable percentage of the embryos will exhibit peculiar eye conditions, the most striking of which are shown in Fig. 26. Many of the young fish show a typical median cyclopean eye, so termed after the single-eyed Cyclops of mythology, instead of the usual two lateral eyes. Other individuals develop only a single lateral eye on either the right or the left side

of the head. We might surmise from such occurrences, as Professor Goodrich, the British zoölogist, suggested some time ago, that had the ocean water chanced to have this arti-

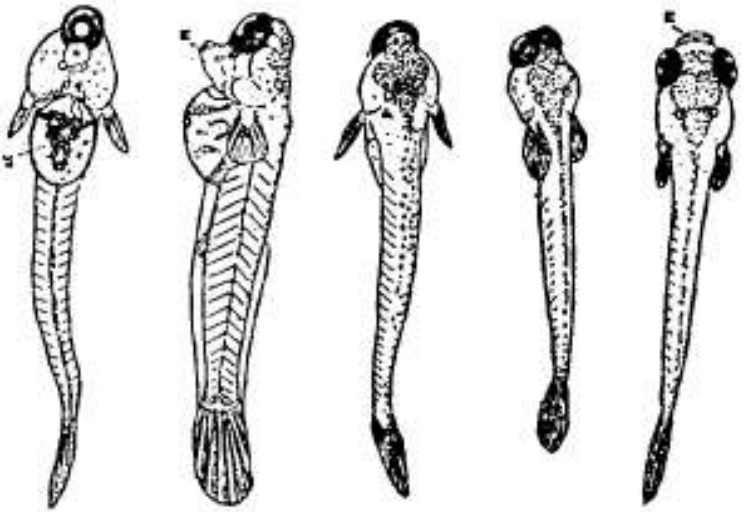


Fig. 26. A series of one-eyed cyclops fish produced from normal eggs developed in a modified sea-water environment. The right specimen is a normal two-eyed fish for comparison.

ficial composition as its usual state, fish would normally be single-eyed cyclopean animals. In other words, the genetic composition of these fishes causes them to develop two eyes in normal sea-water, but the same genetic composition gives rise to a single cyclopean eye when an excess of magnesium chloride is added to the sea-water. If sea-water normally had the composition which causes fish to develop with the cyclopean eye, and an experimenter should develop the eggs of fish in a solution of the same composition as our now ordinary sea-water, he would find them giving rise to

fish with two lateral eyes instead of the median one; and these two-eyed specimens would appear to this imaginary investigator as monsters.

What we consider to be normal animals are simply animals normal for the present-day environments in which they develop. If the earth had evolved a somewhat different condition of soil, water, or air, the organic population of the world would have been quite other than what we see today.

Twin Formations or Doubling of Persons and Parts

A single fertilized egg usually develops into a single individual animal, but it has been known for a long time that the single egg may form double or twin individuals.

One of the earliest accomplishments in experimental embryology was the production of two embryos, or twins, from a single egg. This was done by Driesch, Wilson, Morgan, Zoja, Loeb, Schultze and others almost forty years ago. The phenomenon was first induced by separating the two primary cells in the dividing egg so that they were no longer in their usual intimate relationship; each then developed independently and produced a complete individual. In the light of this striking experiment, the occurrence of twins and double monsters under natural conditions was apparently explained as being the result of an undue separation of the first two cells, or *blastomeres*, during the first cleavage of the egg. This separation might have been caused in a mechanical way, the two cells having been pressed or squeezed apart, or something unusual in the chemical nature of the environment may have reduced the normal degree of cohesion between the first two blastomeres, allowing

them to fall abnormally far apart and finally to become entirely separated from one another (see Fig. 27, B).

But it is dangerous too readily to interpret occurrences in nature on the basis of simple results from experiments. This clear-cut experimental production of twins, and its

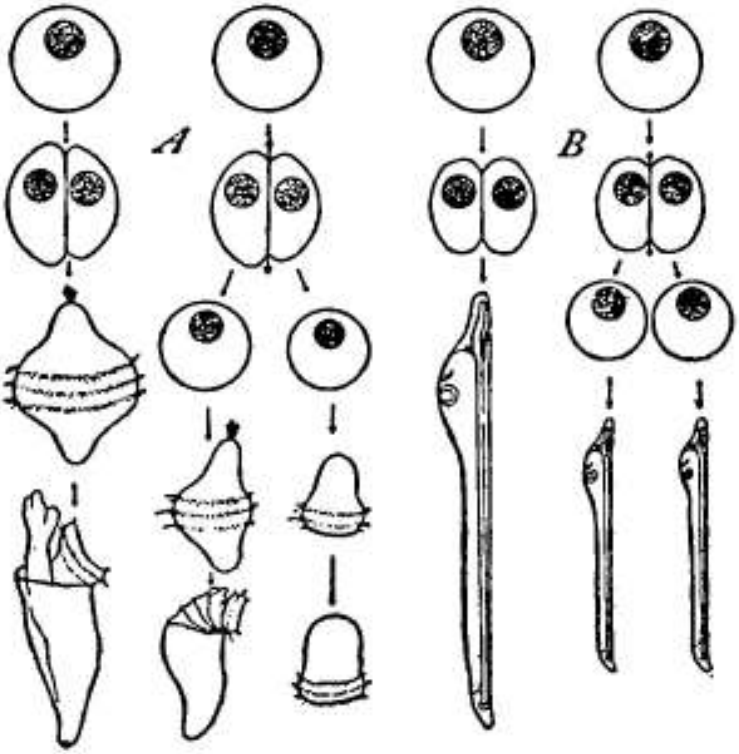


Fig. 27. Diagrams illustrating the results when the first two cells of the developing egg are cut completely apart. A, snail's egg, to the left developing normally, to the right one of the two separated cells develops into the head region only, and the other into the body portion. B, the lancelet egg, to the left developing normally, to the right each of the two separated cells develops into a perfect animal although a dwarf in size. (After Wilson.)

ready application and acceptance as an explanation of the *modus operandi* for a well-known natural phenomenon undoubtedly held back the general understanding of the phenomenon of twinning.

For very soon after the production of double development from the two blastomeres evidence began to accumulate which questioned the interpretation of the separated cells as an explanation for natural twin formation. The significance of this evidence was not at once appreciated, but from our present state of knowledge its bearing is very readily seen. Wilson, Conklin, and others, discovered that, on separating the primary blastomeres, or first two cells, in certain species of eggs, complete twin embryos do not result. Yet there is no reason to believe that in nature twins and double monsters do not at times arise from the eggs of such species. Twin formations are certainly not due to the separation of the first two cells in these particular species, since each of the blastomeres developing independently gives rise only to a partial, not to an entire, embryo. In these eggs "organ-forming stuffs" are early differentiated and localized and these stuffs are unequally distributed to the two cells, even at the first cleavage. The individual blastomeres, or early cells, in such cases are not totipotent, being capable in their later development of giving rise only to certain parts of the embryo, not to the whole (see Fig. 27, A). The eggs of a number of worms and molluscs show this very early localization of differential stuffs, yet in some of these animals various types of double individuals are not uncommon. Such double individuals as these, in the light of present evidence, are the results of a simple process of budding as we shall explain presently.

O. Schultze found that double embryos would arise from the frog's egg by simply holding it in an upside-down position, see Fig. 28.

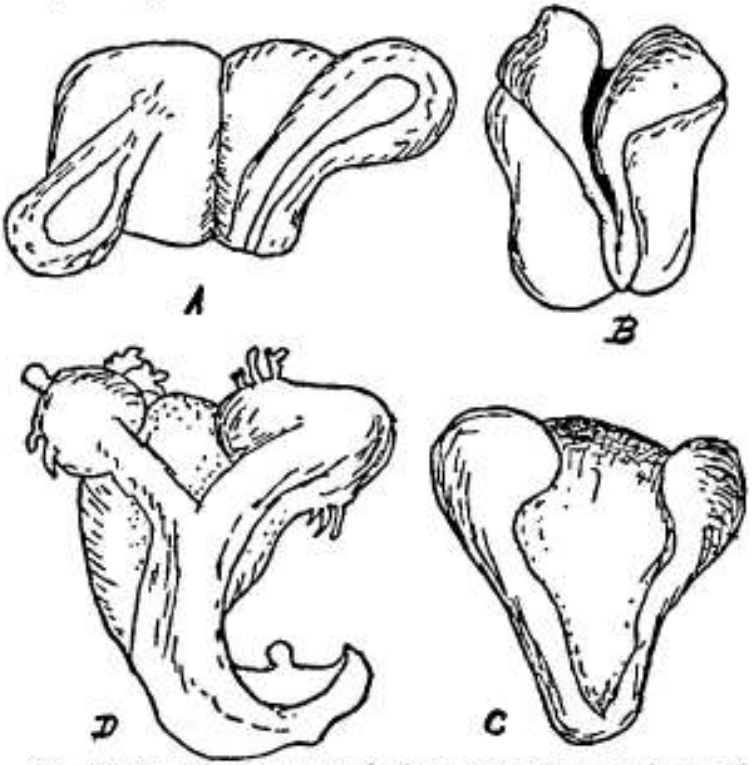


Fig. 28. Double embryos of the frog arising from eggs inverted at the two-cell stage and kept in the upside-down position. A, twins with heads in opposite directions; B, twins united back to back; C, twins united by their ventral surfaces; D, double-headed tadpoles. (O. Schultze from Wilson.)

Again it was shown by Enders, and later by Spemann, not only that double specimens resulted from the separation of the first two blastomeres, but that by mechanical means

the later many-celled germinal mass could be caused to develop into double instead of single individuals. This was done by tying a hair around the salamander embryo at a time in development called the gastrula or infolding stage. The degree of duplicity depended somewhat upon the extent to which the eggs were constricted in the given plane, Fig. 29. This result was evidently due to the division or separation into two parts of the growing region of a single individual, thereby establishing two new centers of growth in place of the original one. The division of a single grow-

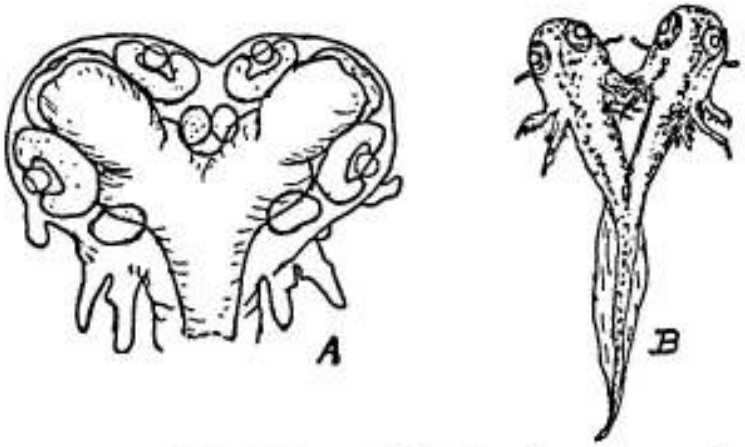


Fig. 29. Double-headed newts (Triton) produced by constricting the early developing egg with a loop of hair. (After Spemann.)

ing bud into two may be illustrated on plant buds, embryonic animal limb buds, et cetera. To interpret the two separated regions as being the exact derivatives of the two original blastomeres, as some have tried to suggest, is entirely implausible in many cases.

In all of these experiments the methods employed were unlike anything we would imagine to be operative in the natural production of twins. It is conceivable, however, that at times in nature the first division of the egg into two cells might go too far, almost or completely separating the blastomeres, and hence cause two independent developments.

Budding in the Armadillo Egg and Twin Formation

After much of this experimental work had been done, a very instructive natural case was fully studied by Newman and Patterson. The nine-banded armadillo in Texas is known to produce four young at a birth; these young are always of one sex and are closely alike. Newman and Patterson recognized the four offspring as being identical quadruplets; that is, they are four derivatives from a single fertilized ovum. In the light of the earlier experimental work, Newman and Patterson at first explained the origin of these quadruplets as the result of a separation and independent development of the first four cleavage cells of the egg.

Later, however, Patterson found with a much more complete series of the earliest developmental stages of the armadillo that the multiple embryo condition was due not to a separation of the first cells at either the two- or the four-cell stage, but to a subsequent process of budding. Patterson demonstrated this fact in most beautiful detail. The budding takes place in a very definite way during the infolding or gastrula stage. The embryonic mass first buds into two growing regions and each of these very soon again divides,

thus giving rise to four gastrula-like formations, each of which develops into a complete young armadillo.

The important discovery of this natural process of budding in a higher animal has suggested the probability that twinning in mammals may result in general from a somewhat similar budding process rather than from the early separation of single embryonic cells or blastomeres.

Twin Formations and Developmental Inhibitions

Not long after Patterson's studies on the armadillo, I found that fish eggs might be induced to form double monsters and twin embryos as a result of simply interrupting the early progress of development. The inhibition or interruption may be brought about very simply by placing normal eggs of the common minnow, *Fundulus heteroclitus*, in an unusually low temperature. This treatment serves either to interrupt completely or greatly to inhibit the rate of development. Other methods of slowing the developmental rate, such as reducing the supply of oxygen, also tend to produce occasional double specimens, particularly in the trout; Fig. 30 shows a series of these double fish. Certain species form twins much more readily than others, the quality of the egg itself being a factor in the process.

Dr. Marie Hinrichs has recently shown in a striking way, on the same fish, *Fundulus heteroclitus*, that similar double conditions may result from treatments with ultra-violet rays. Such treatments also inhibit and arrest the normal rate of development.

It may be correctly claimed, on the basis of much recent experimentation, that any environmental condition which

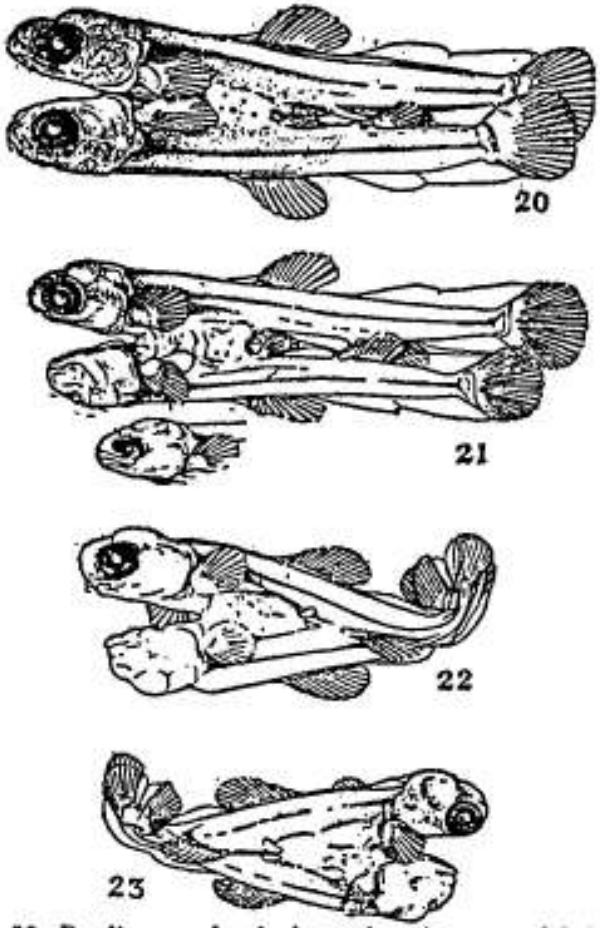


Fig. 30. Duplicate and twin formations in young fish induced by arresting early development through lack of oxygen. Similar conditions have been produced in minnows by lowering the temperature of the egg during early stages.

arrests the progress of development at a certain critical stage will tend to give rise to accessory budding and double embryo formation. The wide significance of arrests during development was appreciated by the French teratologist, Dareste, more than forty years ago, from his studies on structural deformities. But the experimental proof of the effects from arrests has only been obtained during recent years. Deductions are valuable, but experimental confirmations are invaluable, and no one need confuse the two.

What manner of budding process is this which results from an actual slowing of development, and why does it not occur more often? This is important for our point of view regarding personality since it actually involves the integrity of the individual as a whole. The process of budding to form twins and double embryos may well be considered in connection with more easily seen and better known budding phenomena, such as those commonly found among plants.

The Expression of the Budding Process

Jacques Loeb, the distinguished physiologist, devoted much of his interest during the latter part of his life to the budding reactions in the leaf of the tropical plant called Bryophyllum. The results of his studies seem to me applicable in an interpretation of embryonic budding.

The Bryophyllum leaf is beautifully suited for the study of budding, since it not only may live for a long time entirely separated from the mother plant, but every notch around the border of this isolated leaf possesses the potential power of budding into a new plant-shoot. When the Bryophyllum leaf is suspended for a time in a moist at-

mosphere one or more of the notches finally send out shoots, while all the other notches remain quiescent. It is difficult to predict exactly which notch on the leaf margin will first form the shoot. But if the leaf be placed over a shallow vessel of water so that one of the notches is covered by water and all the others are in the air, then the notch in water invariably sends out a shoot and the other notches do not. Thus the experimenter may determine at will which of the notches is to form the shoot by simply allowing this notch to dip into the water. We may say, in this case, that a certain advantage in position relative to the environment determines which notch is first to form the shoot; see Fig. 31, C.

What influences, then, prevent the remaining notches from later forming shoots? The growing shoot seems to exert an inhibiting force over the budding tendency of the other notches. Under usual conditions one notch, for reasons not entirely clear, has a slight advantage at a given time over all other notches and this advantage allows this notch to bud before the other notches. After the initial shoot has actually sprouted, it exerts a peculiar influence in the leaf which prevents other notches from budding. This may be due to an attraction or suction effect by the shoot on the direction of sap flow or some other invisible process. Be this as it may, it is readily demonstrable that if the shoot and its influence be removed or cut away from the leaf then very promptly another bud forms a shoot, and this shoot now again tends to suppress budding on the part of the other notches.

Finally, Loeb showed that every notch on the leaf could actually bud a shoot when freed from this inhibiting influence of the other buds and shoots. He demonstrated this by

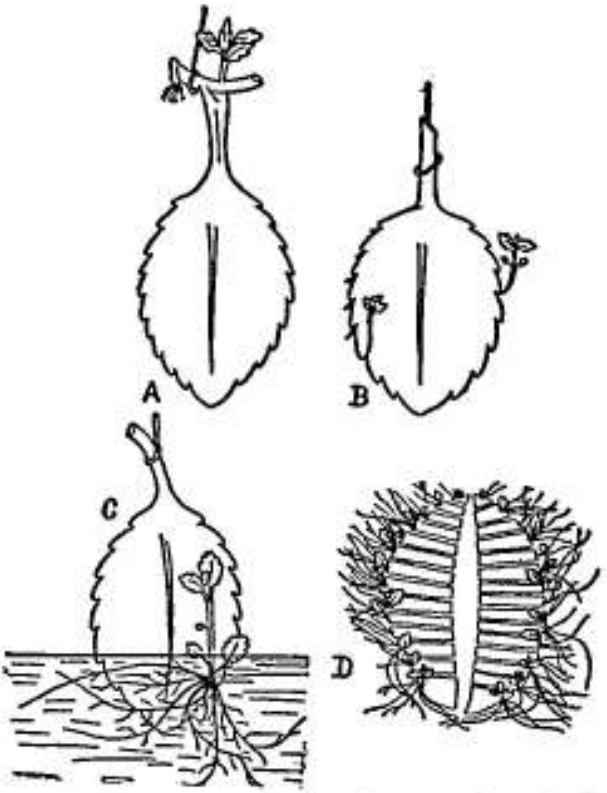


Fig. 31. Budding reactions in the leaves of Bryophyllum. A, the leaf attached to the stem forms no shoots, but a shoot and roots are seen arising from the stem, these inhibit shoot formation in the leaf; B, a leaf separated from the influence of the stem, forming shoots from two of its notches and roots from several others. It is not possible to predict which notch will bud the shoot although if, in C, a certain notch be placed below water and the other notches remain in air then the notch in water forms a shoot and roots and inhibits shoot formation from all other notches. D, if the leaf be cut into pieces so that every notch is separated from all other notches, then every notch expresses its budding ability and gives rise to a shoot. The inhibiting influence of the earliest shoot is thus isolated. (J. Loeb.)

placing the leaf on a moist surface, and cutting it in such a manner as to divide it into a number of small parts with each part containing at the leaf edge one of the notches. Figure 31, D, illustrates that under this condition of separation and isolation every one of the notches may give rise to a tiny shoot. It is probable, therefore, that this multiple budding would always occur but for some form of competition which exists among the potential buds. In the struggle for budding supremacy, one notch slightly dominates the situation and obtains an initial start which gives its shoot a lasting advantage over the other buds. This idea of competition for expression existing among the growing organs and parts of an individual, and of the alternate domination of certain parts in the developmental struggle, is a very old one in biology. It was first clearly expressed in considerable detail more than a century ago by the great French naturalist, Geoffroy St. Hilaire, in the consideration of his "*principe du balancement des organs.*" About two generations later Wilhelm Roux, in 1881, brilliantly developed a closely similar idea in his discussion of the "*Kampf der Teile,*" or the struggle among the parts in the organism.

Since these early times students of development have recognized that some such competitive relationships and influences do exist among the body parts in order to insure the normal balance and proportions among the functioning tissues in generating the successfully coördinated constitution. In spite of the antiquity of this conception of struggle and dominance among the parts, our understanding of the exact means through which the coördinated adjustments take place can only be expressed in the most

general terms, such as alternating periods of localized activity and rest during organ development, or the alternating accumulation and consumption of available stuff and energy for local growth and differentiation.

Returning to our particular point of discussion, it seems quite evident that only one bud usually forms the shoot because of some advantage it possesses over all the other buds, and after beginning its growth the dominance of this part over the potential buds becomes still more pronounced. It may, however, be shown, in the common privet bush as well as in many other plants, that when the budding shoot is injured or inhibited in its rate of growth, the suppressing effect over the other buds will be diminished and some of these will, therefore, be able to send out shoots and grow. From this it is plain that the dominating bud must maintain a vigorous growth in order to inhibit completely the growth of other buds. When the terminal bud of the privet plant is injured the lateral buds at the leaf attachments begin to grow and a multiple branching formation takes place as a result of the loss of dominating influence from the apical bud.

Twinning in the Egg and Bud Competition

Are the budding phenomena in plants in any way comparable to twinning in the animal egg? It is probable that they may be. In the early stage of the developing vertebrate egg there is a germinal disc-shaped formation, and the first indication of the axis of the embryonic body arises from some point near the margin of this disc. We may reasonably suppose the existence of more than one potential budding point from which the axis of an embryo may grow

forth. This supposition seems evident since we actually see in the case of twins two embryonic bodies growing from the single germinal region. Possibly there are a number of potential points along the periphery of the germ disc, many or all of which might bud into embryonic body formations. However, one of these points possesses an advantage not at all understood over all the others, and this one gives rise to the growing embryonic process. The growth of this embryonic bud, we may suppose, on the basis of facts from budding in general, dominates the entire germinal area and completely suppresses the potential power of any other point to form a primary body-bud.

Let us now assume that at times, as in the plants, the advantage of any one point may be unusually slight, and thus the embryonic bud arises at a reduced or slow rate of growth. Under this condition its inhibiting influence may not completely dominate the entire germinal region, and a second point may bud into a growing body axis. Twins would then arise because of the lowered developmental activity of the initial bud, or actually as the result of a reduction in developmental rate; see Fig. 32. This is exactly what seems to take place when the rate of development in the fish egg is artificially inhibited or slowed at an early developmental stage by cold and lack of oxygen, as in my experiments, or from the effects of ultra-violet rays as Dr. Hinrichs has found.

All unfavorable environmental conditions seem to affect the egg by slowing its developmental rate. The slow rate upsets the usual supremacy of what should be a rapidly growing part, and lessens its inhibiting influence over other parts; thus some of these parts are enabled to express

themselves ahead of their usual time. The doubling of parts is being more and more recognized as a common characteristic of many subnormal growth phenomena.

Therefore, what at first thought would seem paradoxical —the production of twins and double monsters, excessive conditions, as a result of developmental inhibitions or ar-

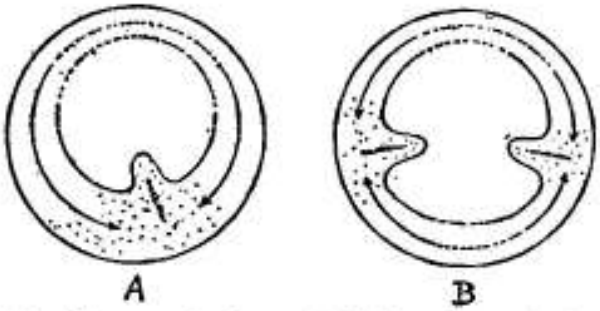


Fig. 32. Diagrams of the germinal disc of an animal egg. In A the single embryonic bud is beginning to grow towards the center; this growing bud exerts an influence, indicated by the two arrows, which suppresses the budding tendency from any other point on the disc. B produces an initial bud which is slow in arising and thus exerts a subnormal inhibiting influence, on this account a second embryonic bud is able to express itself and twin embryos are formed.

rests—is on careful examination a logically probable reaction. The fact that twins occur so much more frequently than triplets and higher multiple conditions is probably to be associated with the additional domination exerted by the second bud. The initial bud may not be sufficiently strong in its suppressing effect to prevent the growth of the second or twin bud, but once this has appeared, it supplies an additional dominating effect and the two buds, even

though they may be somewhat weak, are sufficient to dominate almost invariably the entire germinal area. The germinal area is normally mastered by a single embryonic formation, but when the supremacy of this is insufficient to prevent the origin of a second embryonic body, these two buds acting together rarely fail to dominate completely the potential budding area through their growth influences, and so the origin of a third embryonic bud becomes extremely rare. Out of thousands of eggs examined over a period of many years I have seen but two examples of triplet embryos and one example of quadruplet embryos in fish.

We may now conclude that doubleness in nature is probably due to a modification of a budding process, and that double monsters and actually identical twins, like most other embryonic anomalies, may result from an arrest or inhibition in development. To state that twins and double individuals are induced by a developmental arrest seems at first thought almost absurd; for how could an arrest serve to give a formation structurally exceeding the normal in extent? And yet in fact it does.

Polyembryony or twinning may be considered a typical form of asexual reproduction, that is, an increase in the number of individuals by a fission or budding process. The occurrence of this process of asexual reproduction in mammals and actually in man makes the phenomenon of so-called "alternation of generations" (a sexual generation alternating with an asexual generation) almost universal among animals.

Not only is the occurrence of twins and double embryos on the single egg of high significance from the standpoint

of developmental constitution, but the further development of these double specimens furnishes most instructive material for an understanding of the effects of developmental competition on the origin, growth and progressive differentiation of the various organs in the animal body.

The Two Components of the Double Individual

The two components of double individuals vary in their degrees of separateness in a series of such specimens: beginning with two partially separated heads on an otherwise single person through complete double-headedness: two heads and two upper body-regions on a single posterior region, Y-shaped embryos; two separate bodies with a single tail region, V-shaped embryos; and so on, to finally two completely separated twin bodies developing on the single yolk mass. (See Fig. 33 and explanation.)

Fig. 33. The distance apart of the two embryonic buds on the germ disc determines the degree of duplication in the animal bodies formed. The first figure indicates buds arising near one another and the dotted lines indicate a future double-headed specimen; the second figure shows the buds further apart and the future specimen further doubled, while the last case shows the buds 180° apart or opposite one another on the germ disc and two completely separate twin animals are developed.

The developmental competitions between the two components in the double individuals frequently seem equally balanced, where the two components are of equal size and are equally developed. Under these states of component equality, the development of each member is practically always normal, that is, as frequently normal as the development of single individuals. This double specimen with equal components is erroneously termed a double monster. Its development is not monstrous nor anomalous, it is simply a perfectly normal double individual which arises from an egg that did not bud in quite the manner to give two entirely separate twins. Twins are never considered monstrous, and yet they are clearly of the same class as these double individuals. We are using here the term twins in its strict sense. Twins, as a term, should only apply to two individuals derived from a single egg and not to two ordinary young simply born at one time. The latter is correctly termed a litter of two, and its members may be of different sex; while every pair of true twins is of one sex.

The two components in the double specimens are not necessarily either equal in size or equally well matched in their competitive reactions. And when they are not, the conditions of the two components are very different from that of the above-mentioned equal-component individuals in which both members were found to be structurally normal. Whenever the two members of a double specimen differ in size, the larger one is almost always normal in development and structure while the smaller is invariably retarded in development and defective in its structure.

The defects occurring in the smaller member are undoubtedly due to the unfavorable developmental competi-

tion with the larger confrère, since, as derivatives of the same egg, the genetic basis of both components is necessarily identical, and since their general external environment is practically the same limited sphere. One of the components gains an advantage over the other for reasons not entirely known, and seems to dominate its twin part in some such manner as the fast-growing shoot on the Bryophyllum leaf dominates the less potent buds. In all the double specimens examined among different animal forms, from fish to man, as well as the illustrations of duplicities in the literature of the subject, it is invariably seen that if the two components differ in size, the larger one is normally developed and the smaller more or less deformed. The degree of deformity varies directly with the discrepancies in size between the two components. For example, in a double-headed specimen in which one head is of normal size and the other only slightly smaller, the defects of the smaller head are slight, whereas in a specimen with one very small head and a normally large head, the smaller head is grossly defective and deformed. Figure 34 shows a series of double fish embryos with components of unequal size.

As the larger component reaches adult size the lesser member may have become so relatively small as to be represented only by a nodular mass on the larger body. Or the small component may be lost to sight entirely and become a so-called twin inclusion within the body of its brother. These conditions, which are not extremely rare even among human beings, make it seem probable that doubleness and twinning are actually a much more frequent phenomenon than records would indicate.

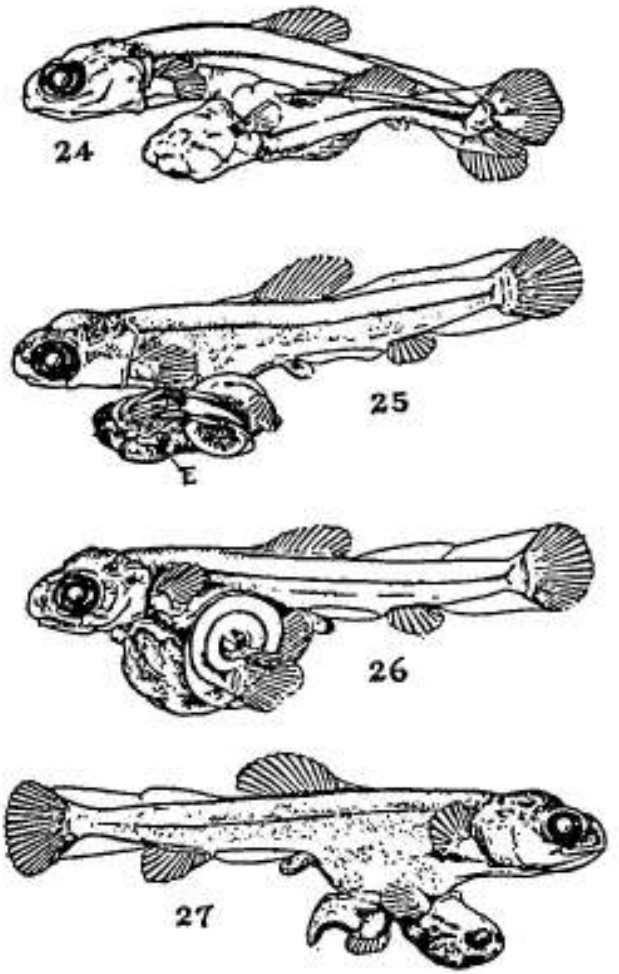


Fig. 34. A series of siamese-twin young fish with unequal components. The larger twin in all cases is a perfectly normal fish while the smaller twin is grossly deformed, and the greater the discrepancy in size between the two components the greater is the deformity of the smaller twin.

The cases of normally mature persons carrying the distorted tissues of the lesser twin included within their bodies are also of significance in connection with certain tumors or cancer-like conditions. If these tumors, or so-called *teratomatas,* in man ever do originate as a twin inclusion, we may expect the competitive growth reaction still to exist between the host and the tumor, just as we have found it between the two components. While the host is rapidly growing the teratoma will be suppressed, but when the growth of the host becomes slower or ceases, the teratoma, being somewhat embryonic, might be expected to begin growing more actively. Thus there might be a correlation between the postnatal growth rhythms of the individual and the time of enlargement or recognition of such tumor-like bodies. Dr. H. E. Himwich found from a wide survey of the literature on these tumors and the age of their occurrence, that some such correlation very probably does exist.

The Smaller Component and Defective Organs in Single Individuals

It has proved to be of great advantage in a study of developmental constitution to determine the nature of the defects and deformities in the lesser component of double individuals, since we may be quite sure that in these cases the defects have arisen solely as a result of the inhibited rate of development in the small component. The larger normal twin component has the same basic constitution and history as the smaller, differing only in that it has not been slowed in development. Therefore, the only modifying factor between normality in the larger and the abnormalities of

the smaller member is the difference in developmental rate of the two components. One member of the united pair has grown large and perfect in structure during the same time interval in which the other has become small and ill formed. There has been a contest in growth rate and the winner's prize is normality of structure.

The types of defects found in the lesser components of the double specimens are very much the same as those defects which may be induced experimentally in single individuals by slowing their rate of development with low temperature, lack of oxygen, or various chemical modifications of the environment as shown in Fig. 35. All the defects occur as results of developmental arrests.

The smaller component frequently exhibits eye deformities. It may have small and somewhat misplaced eyes, one normal eye with its mate either small and defective or completely absent, one median cyclopean eye which again may be of subnormal size, or, finally, only a minute central eye speck. All these conditions are to be found among the smaller components in a series of double embryos. A closely identical series of eye defects may occur among single embryos which have been arrested in their development at a critical stage of ophthalmic origin, Fig. 35. From a directly causal standpoint the two series of deformed eyes have arisen in the same way: in the first case, the small component was arrested in its rate of development by the dominating influence of the superior component; in the second case a similar arrest at a comparable developmental stage was induced in the single embryos by temporarily altering the environment in such a manner as to interrupt the rate of cellular activity. The inhibiting influ-

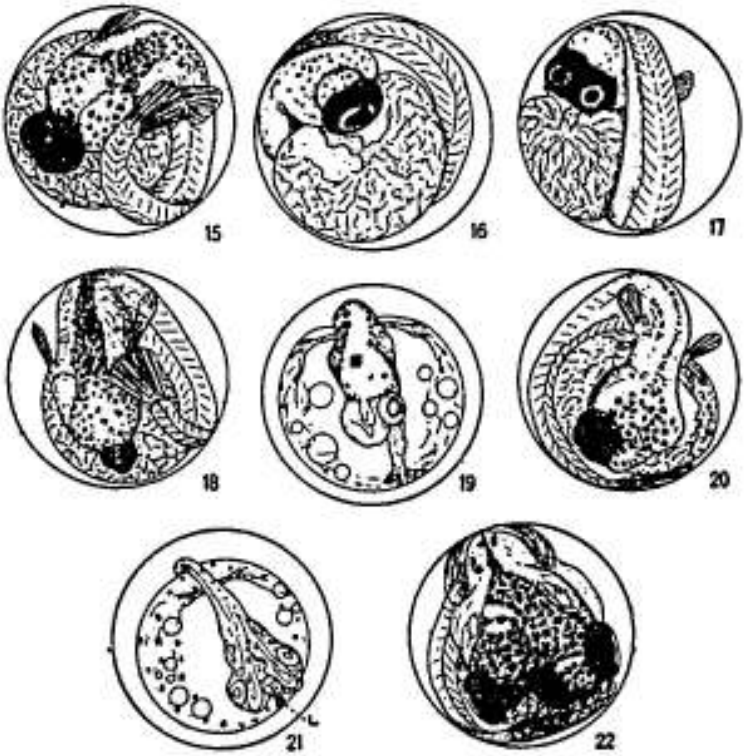


Fig. 35. A group of unhatched young fish showing abnormal development and eye deformities very similar in kind to the defects found in the smaller component of double specimens.

ences were acting on both the small component of the double embryos and the single series of embryos at similar developmental periods and, therefore, the responses were similar.

Developmental abnormalities resulting in excessive formations—that is, the production of more than normal structures, as for example, the two-headed specimens—

have been termed *monstra in excessu*. The contrasted abnormalities, in which less than the normal structural formation is present—as in eyeless conditions—are known as *monstra in defectu*. These two groups of deviations from the normal structural proportions have frequently been treated as distinctly contrasted classes of conditions. But we now understand them to be, as a matter of fact, very closely similar. Both classes of anomalies are due to a common cause and may exist in the same specimen. For example, an arrest in development during very early stages may cause the germ disc to form two embryonic processes which may develop into a double-headed individual—a typical *monstrum in excessu*. At a very definite stage one of these two embryonic processes may become inhibited, so that it forms a cyclopean eye instead of the usual two lateral eyes—a typical case of *monstrum in defectu*. The fact that the normal individual stands between these two arbitrary classes of abnormalities has no significance other than that the abnormal deviations are simply modifications of the normal condition resulting from unusual reductions in the rate of development during certain critical stages.

The significant importance of modifications in the developmental rate on influencing the type and quality of structure is not confined solely to embryonic development. Postnatal development and the differentiation of later structures are similarly influenced by the rate at which their formations are accomplished. A proper rate of growth and normal sequence of development in infants and children are highly essential for perfection of structure and capacity in the coming adult.

VII

THE CRITICAL MOMENTS DURING EARLY INDIVIDUAL DEVELOPMENT

THE same inhibiting influence, if allowed to act on the embryo during different developmental stages, will induce entirely different responses. This is due to the fact that the several embryonic organs reach their most critical stages of origin at different times. A given organ must be interrupted during the early stage of its development in order to be completely suppressed or grossly modified. The same interruption introduced at a much earlier or a much later time will fail to influence it seriously although at these other times some other organ, then in its critical stage of origin, will be grossly affected.

The Structural Modification and the Stage of Development during which the Inducing Agent Acts

The type of constitutional disturbance induced depends upon the developmental stage or moment during which the inhibiting agent or condition is effective. It is, therefore, clear that one and the same inhibiting agent, if acting at different developmental stages, may be experimentally employed to induce a great number of different develop-

mental modifications. The structural response of the embryo is not specific for a given chemical or physical arresting agent, but it is specific for the embryonic stage during which the agent acts.

The author showed, in 1909, that a definitely typical anomaly could be experimentally produced by several different anaesthetic agents. It was then pointed out that the defect was the result of the general arresting effects of these several agents on a certain developing organ. The same group of eye anomalies such as the formation of only a single median eye, small eyes, or the absence of one eye, were induced in fish embryos by the use of magnesium salts, ether, chloretone, and alcohol. The response in the embryo was not different for any one of the treatments and there was, therefore, no specific action of a given chemical stuff on the processes of embryonic development.

The primary response of the developing embryo to all effective stuffs was simply a slowing down in its rate of development. The effects of this slowing down in developmental rate was most severe on those organs or parts which were most rapidly developing at the time of the interruption. The series of eye conditions shown in Fig. 36 may be induced by any arresting agent acting during the critical moment of early eye formation.

Of course, all organs of the embryo are not formed at the same time: some, such as the neural-tube, the optic vesicle, the heart, et cetera, arise during very early stages; others, such as the liver, kidneys, and skeletal parts, during intermediate stages; and still other structures, such as pigmentation and hair, appear very late in development. The moment of origin for an organ seems, judging from

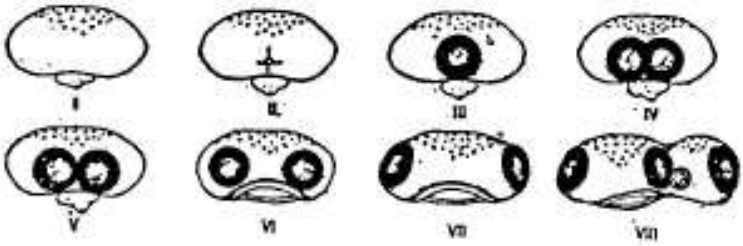


Fig. 36. Outlines of anterior views of the heads of fish showing a graded series of eye anomalies. These may be induced by treating eggs with many different—both chemical and physical—arresting agents.

experimental results, to be a most critically susceptible time in its development. At this stage we may imagine the organ to be in the same condition as a bud when immediately producing a shoot. The fundament of the organ, its so-called *Anlage* or potential basis, consists of only a limited number of cells which are initially in a rapid state of multiplication in order to build up the mass of the organ as it grows forth to express itself. An interruption in this budding reaction is more severely detrimental to the future organ than an injury at any later moment would be. After an organ has arisen successfully from the *Anlage* it may be lamed or runted, but its nature and actual existence can no longer be destroyed by interrupting the growth.

We are fairly certain that at any one time the various organs and parts of the embryo are developing at quite different rates. And these differences in rate may be represented by some such arbitrary series of numbers as 80, 65, 50, 35, and 10. If the total rate of development in this embryo be inhibited by low temperature the development of all parts may be reduced in rate to below 20, for example.

Under this new condition the organ that formerly developed at a rate of 80 is the most severely arrested since its rate of development has been reduced by at least 60 points. The next most rapidly growing organ which had had a rate of 65 is now also considerably arrested. The organ formerly at 50 is comparatively less arrested and the organ that was developing slowly at 35 is scarcely affected. The part which was progressing at the slow rate of 10 may be not at all changed. The competitive interaction which formerly existed among these organs is now completely altered. That organ which had dominated the situation through its most rapid growth is inhibited and no longer asserts an advantage over its competitors. Under the new conditions the part originally at 35, for example, may begin more vigorously to express itself. A new organ now gains supremacy and actually under the modified conditions it asserts an inhibiting influence over the previously dominant organ. Not only does the arrest of a rapidly budding part, therefore, tend to suppress its development temporarily; but the premature loss of supremacy to some other organ renders it impossible for the suppressed part to come again into dominance, so that it is permanently modified.

The general effect of arresting the rate of development is a disturbance of the normal coördination existing among the developing parts and this modifies their growth balance. The result of normal development is proper relationship of size and function among the body organs: the liver adjusted in size to the stomach and intestine, the heart and lungs properly balanced, and the capacity of the vascular system accurately proportioned to the body as a whole. Through developmental arrest one or more organs may become

disproportionately small; this upsets functional harmony and produces a defective person.

Time and Locus in Organ Origin

It becomes evident from the foregoing that the time of origin for an organ in the embryo is quite as important as its place of origin. The eye, for example, must not only arise from a limited locus in the embryo but must also appear at a definite developmental stage. If it does not arise at this moment it will never be able to express itself fully, since the moment for the rapid outgrowth of some other part will have arrived, and this will tend to dominate the less active region and suppress the belated tendency for eye expression.

During early stages of development these relationships among the parts are quite clear since only a few organs are actually budding forth. However, as development advances the situation becomes more complex and several parts in different regions may be developing with equal vigor of rate at one and the same time. At these later stages of development there may be in the embryo several different regional areas, within each of which local groups of organs and parts are competing with one another.

Whatever the relationships among the organs may be, the moment of origin for each organ in the vertebrate embryo is limited just as definitely as the fundaments or *Anlagen* from which the organ buds arise. The embryonic organ must appear at a definite time just as truly as from a certain place.

Competitive Reactions between Organs of a Bilateral Pair

Not only does the struggle among the parts during development and growth occur between organs of different kinds, but very probably a similar competition takes place between the two members of a bilateral pair of organs or even among the parts within an organ. The two optic vesicles or embryonic eyes may not be exactly equal in size during early stages. It is common knowledge that during later life certain organs on one side of the body are superior in strength and function to their mates of the opposite side. The two eyes of most adult individuals, for example, are not equally perfect in functional efficiency, the ears, particularly during later life, differ from one another, and the extremities of one side are often superior to those of the other. Everyone knows that individuals are right-handed or left-handed, and that one's own eyes are not both equally good.

There is in general a slight discrepancy in size and vigor between the bilateral halves of a vertebrate embryo. If one examines minutely in either an amphibian or a bird embryo the early neural plate stage, that is, the stage when the embryonic central nervous system is an unfolded flat region of cells—it will occasionally be noticeable that one side of the neural plate is somewhat ahead of the other in size and development.

Although these differences between the two sides and the members of organ pairs are usually so insignificant as to escape general notice, they are, nevertheless, sufficiently

important frequently to give rise to very puzzling conditions in our experimental studies of development. When subnormal development is induced in the embryos of fish, birds and mammals, it often occurs that the two eyes respond in a most exaggeratedly asymmetrical manner. In these specimens one eye may be typically normal in size and structure, while its fellow of the opposite side may exhibit all degrees of defect from slightly subnormal proportions through various conditions of micropthalmia, with tiny malformed eye-globe and lens, to complete absence of one of the eyes. Individuals of this kind, with one normal properly placed eye, and a complete absence of the opposite eye, *Monstrum Monophthalmicum asymetricum*, occur in the same experiments with cyclopean embryos possessing a single median eye and with anophthalmic or entirely eyeless specimens. A series of diagrams are given in Fig. 37 outlining the various degrees of the two types of single eye condition.

It is difficult to understand how the two members of a bilateral organ arrangement, such as the eyes represent, can respond so differently to a treatment which is in all probability acting equally on both. The two eyes arise from the floor of the neural trough or tube, the embryonic brain, both from the same segmental level. The two eye buds then grow laterally and very probably at a slightly different rate and, more important still, one eye bud may have begun to arise slightly ahead of the other. Granting these conditions, the explanation of the anomalies mentioned above need only involve the assumption that an inhibiting agent might act to exaggerate the slight advantage in moment of origin of one eye bud over the other. The earlier bud would

then chance to develop an unusual supremacy of growth which would depress the growth of the opposite eye to varying degrees. The greater susceptibility of one eye to the treatment could certainly not be due to a difference in

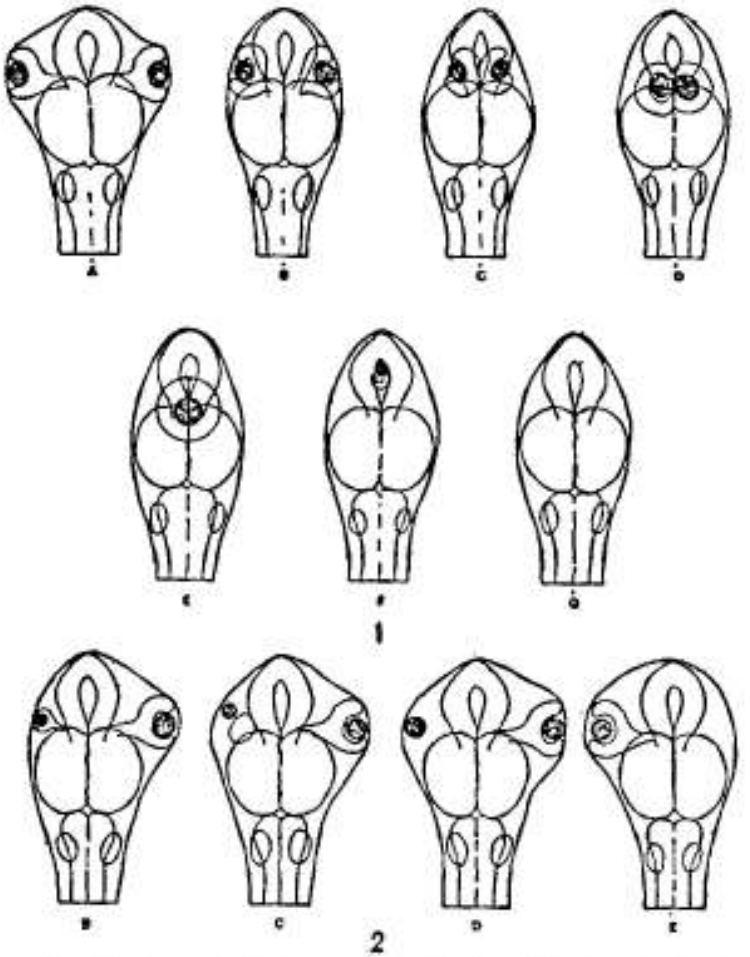


Fig. 37. A series of diagrams, 1, of the cyclopean defect and, 2, of asymmetrical ophthalmic defects.

position along the embryonic axis, since both eyes lie at exactly the same level. It must be due to a difference in rate of activity between the two eye buds, and the slight advantage in maturity of the one bud over the other seems to be the most probable explanation of these discrepancies between bilateral organs in embryonic expression. There are many comparable reactions in support of such a supposition which have been gathered from numerous studies on bud competition. In many of these cases the initial advantage of the dominating bud is extremely slight.

A somewhat similar situation is presented by the asymmetrical development of the reappearing small toe in the guinea-pig, by a sixth finger or toe on only one hand or one foot in human beings, and by other asymmetrical abnormalities; see again Fig. 21. If the development of the extra toe character in the guinea-pig is only due to genetic quality, then how is it possible that the toe may develop perfectly on one foot and yet be completely absent from the opposite foot on the same individual? This must be concerned with the physiological or developmental nature of the situation and not alone with the genetic composition. There may very probably be local competition among the toe buds for expression, and, in cases where the extra toe should be expressed on a purely genetic basis, a slight difference of time in the origin of buds might disturb the usual balance to an extent sufficient to suppress completely the postnatal presence of this character. The differences in development between the two lateral halves of the body, and the frequent variations normally found between the right and left extremities, are quite sufficient to account in general for the discrepancies in development shown by so

delicately expressed an affair as the extra toes and fingers on the two extremities of an animal. This explanation for these quite new experimental results goes back again to the early deductions of Geoffroy St. Hilaire, and the more recent, yet still old, conceptions of the German experimentalist, Wilhelm Roux, concerning the struggle of the parts as referred to before.

Thus the step-upon-step progression, or epigenetic changes, due to rhythmical cellular reproduction and cellular differentiation, constantly advance until the single-cell spherical egg finally gives rise to the complicated body of the completed young animal.

VIII

MUTATIONS AND CHARACTER CHANGES IN THE CELLS OF AN EMBRYONIC BODY

Do the embryonic body cells which are in the process of forming the organs and parts of the embryo ever undergo nuclear modifications or mutations such as we have occasionally found to occur in the germ cells? In other words, do body cell mutations ever take place in a developing organism? It is evident that they might have significant effect upon the individual constitution. These somatic mutations do occur.

Somatic mutations have been reported as arising in both plant and animal cells. Following such a mutation a localized area of the body will exhibit characters distinctly unlike the general characteristics of other comparable regions. This variant area is thought to be derived from the multiplication of probably one, possibly a few, cells which have spontaneously undergone a modification in their genetic balance. A recessive character completely unexpressed in other parts of the body, for example, may be expressed in a limited region. The occasional appearance of a blue segment in the brown iris of a person's eye, or blond and red areas in the head hair of a black-haired person, may possibly, in certain cases at least, be due to mutations in somatic cells resulting in a recessive expression in limited body areas.

Somatic Mutations from X-ray

J. T. Patterson of the University of Texas has recently reported what seems to be an important case of the experimental production of body cell mutations. These mutations have been brought about as a result of X-ray treatments on eggs and larvae of certain stocks of the common fruit-fly, Drosophila melanogaster.

Patterson found that if embryos from a cross between the normal red-eyed female fruit-fly and a white-eyed mutant male were irradiated with X-ray at different stages of development, a certain proportion of the flies arising from the treated embryos showed white ommatidial areas or patches on their eyes, see Fig. 38, A and D. (The ommatidia are the individual units which compose the large compound eyes in insects.) The variant area reveals the recessive character inherited from the white-eyed mutant father, and with but few exceptions it is made up of a definite number of white ommatidia. This expression of the recessive white ommatidial areas would only be possible as a result of the loss or suppression of the dominant red factor from the eye-forming cells.

It was found that the size of the white area on the eye was determined by the embryonic stage at which the treatment was given, and not by the strength of the dose of X-rays employed. If eggs are treated during the first few hours of their development, the white area produced will be large (Fig. 38, A and D.). If the treatment be given during the mid-larval period, the white area will be composed of from ten to twenty ommatidia, and if given during the late larval stages, it will be small, consisting in some

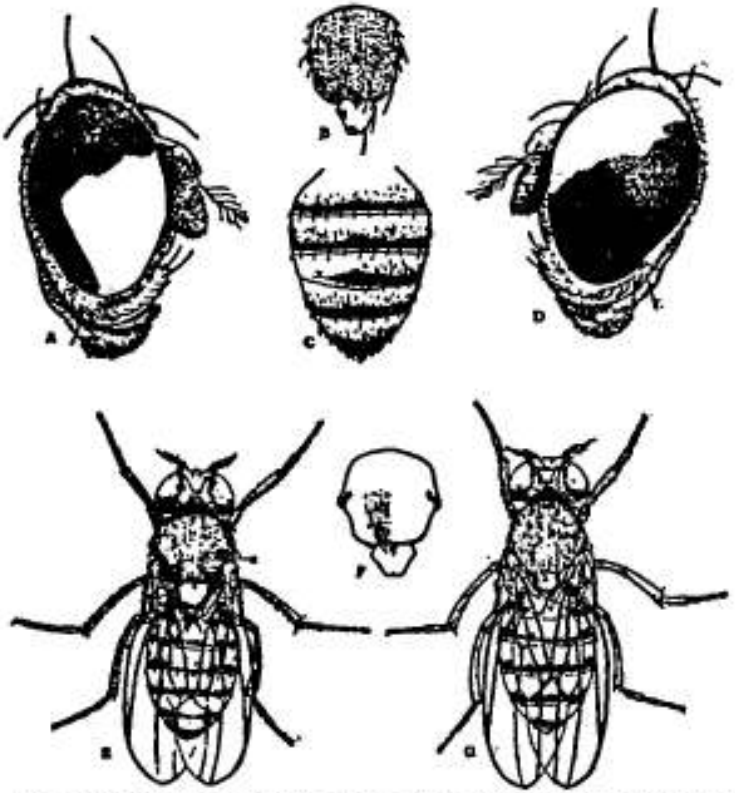


Fig. 38. Mutations in the body cells of fruit-flies induced by treatment with X-ray. Above, A and D, white spots arising in the red eye. The other figures show mutation in bristle shape, the bristle resembling singed hair. (After J. T. Patterson.)

cases of only a single white ommatidium. If pupal stages, which are later than the larval, are X-rayed, no change in eye color is produced.

From these results it is concluded that the change must be induced in a single cell of the eye rudiment, because otherwise it would be difficult to explain the variation in

size of the different variant areas. Obviously, if the mutation occurs in one of the first two cells of the eye rudiment, approximately one-half of the eye would be white, because the white area would be built up entirely by cells descended from this early affected cell. If the change is not induced until a later stage, then there would be fewer cell-descendants from the affected cell, and consequently a smaller white area will be produced.

Other crosses among fruit-flies involving several combinations of eye colors were treated by Patterson in the same ways with comparable results.

Among control flies of similar crosses white spots in the eye occur very rarely. The X-ray treatments undoubtedly increased this cellular reaction and the resulting somatic mutations many fold.

Additional gene changes which affected structures other than those belonging to the eye were induced by the X-ray. In Patterson's experiments practically any recessive character may be made to appear as a variant area, provided the proper combination of characters is used in the crosses which go to make up the fly stocks to be treated. Several different combinations were experimented with but for illustration we may refer to only one of these: the mutant hair shapes which are designated as "singed." Singed is a sex-linked character, the gene for which is, therefore, carried in the so-called sex-chromosome, or X-chromosome. This gene affects the shape not only of the large bristles, but also that of the small hairs found on various parts of the fly. The hairs and bristles have the appearance of hair that has been singed by fire, and this is readily detected even in a single bristle, see again Fig. 38.

The crosses were made up by mating yellow white-eyed females to eosin-eyed singed-bristle males. The yellow-white chromosome carried the gene for normal bristles which is dominant to singed, while the other X-chromosome from the male, in addition to the recessive gene for singed, carried gray color which is dominant to yellow, and eosin eye-color incompletely dominant to white eye. Normally the F_1, or first hybrid generation, females will, therefore, be gray, light-eosin-eyed, non-singed flies, while the F_1 males will be yellow, white-eyed, non-singed. From this it may be seen that if the X-rays will produce both gene mutations and chromosome breakages, three types of variant areas showing the recessive characters in question are to be expected. The F_1 females may show singed areas and yellow areas on the body, and white areas on the eyes; the F_1 males may show singed areas only. All three of these recessive areas were found among the F_1 flies developing from X-rayed eggs and larvae.

These experiments illustrate the possibility of chromosomal changes occurring in the body cells of the embryo and later giving rise to peculiarly aberrant areas in the adult. The cases are not altogether what one might classify as normally typical gene mutations; they partake rather of the nature of injuries or destruction of certain dominant factors or genes, followed by the appearance of characters resulting from the expression of the recessive antagonists or so-called allelomorphs of the dominant factors. Mutations, as mentioned in a previous chapter, are not necessarily thought of as actual losses of dominant genes with resulting expression of the recessive characters, but possibly as a disturbance in the balance of the gene complex

which gives modified characteristics to the resulting individual though the original genes may still be present. The case of the reappearance of lost toes in guinea-pigs emphasizes the fact that following a typical natural mutation there may actually be no loss of the old original genetic basis for certain characteristics. However, aside from the actual nature of the condition, the X-ray experiments of Patterson and the occasional appearance on the bodies of animals of areas showing recessive conditions indicate that gene disturbances do arise in somatic or body cells as well as in the germ cells.

It has been suggested that some such occurrence as somatic mutation might be the underlying cause for tumors and malignant tissue growths in localized body regions. This may be all the more probable if the chromosomal changes involve abnormal breakages, et cetera, rather than single gene or point mutations, since the tumor's growth and reactions are highly deranged and abnormal.

Epitome of Developmental Reactions

A review of the considerations presented in the last three chapters on development brings us to conclude that the actual constitution of the mature personality has truly depended upon the quality of the germ cells from which it originated, although this original genetic complex has constantly responded to the environmental conditions through which it has passed. Thus identical heredities under even slightly different developmental conditions are unable to produce identical individuals. This is clearly shown by the cases we have examined of doubled individ-

uals, necessarily possessing identical heredity, but in which one component attains an advantage over the other. Under these conditions one of the twins may be an entirely normal specimen while the sister, in extreme cases, may be only an amorphous mass of tissue. Twins derived from one egg, and of identical heredity, need not in any sense be strictly identical in their form, appearance, or character, unless they have actually continuously developed and grown under conditions of exactly equal advantage. The more nearly identical the developmental conditions have been, the more certain are the twins to approach complete resemblance.

Identical heredities may, therefore, under different conditions produce unlike individuals! On the other hand, very dissimilar heredities may under peculiarly similar conditions give rise to closely like individuals. The Negro, the Mongolian, and the Caucasian are genetically very different, yet with certain disturbances of development three children may arise from the three racial stocks and be as closely alike in general structure and behavior as three brothers might be, although differing in color. Following a probable disturbance of internal secretion, children from these stocks are born and develop with Mongolian idiocy, each one showing almost exactly the same facial structure and expression. Their bodily forms and sizes finally become closely the same, and the mental behavior and physiological functions of all three persons are surprisingly alike.

A condition of cretinism, or thyroid gland dwarfism, in the three races would give much the same results. Thus dissimilar heredities under peculiar developmental conditions

may produce closely similar constitutional make-ups and personalities.

In the following chapters we shall consider other ways in which this interplay of inheritance and development may act to determine finally the finished personality of the individual.

IX

QUALITATIVE DIFFERENCES AMONG CHILDREN OF THE SAME PARENTS

THE enthusiastic and generally well-meaning advocate of eugenics might lead one to believe that by marriage between the successful and influential members of the community a population of uniformly superior children would be obtained. The more thoughtful and less biased observer questions whether this is a fact. He knows that it is so unusual for an eminent parent to produce a child of like eminence that such cases are heralded and conspicuously advertised on all occasions. The observer further knows that unfortunately it is not at all uncommon for parents of outstanding ability and worth to produce children so mentally and physically inferior as to be unable to maintain themselves in the same community in which their parents prospered. A blacksmith may become the father of a president, and a president may be childless or produce a son whose performance is a miserable failure.

Differences in Abilities Within the Same Family

It is enlightening, although in some ways discouraging, to ask ourselves a series of questions regarding the parentage and offspring of eminent persons.

Who was the father of Sir Isaac Newton, the greatest mind in physical science of centuries, and who were his children? Who was the father, and who the son, of the greatest of English writers, Shakespeare? What of the same queries of Napoleon, of Pasteur, of Bismarck, and of Roentgen? What does history have to say of the fathers of George Washington, Thomas Jefferson, and Abraham Lincoln; and what does it have to say about their children!

A review of this sort might be long continued and applied to persons in all fields of human greatness. We might then arrange another list of families in which at least one prominent member might be cited for each of several generations—the Bacon and the Darwin families, or our Adams family, for example; yet actually there has been in these families rarely more than one conspicuously outstanding person, and it is he who has elevated the family for several generations.

These suggestions are not in any way intended as arguments against good stock, but they help us to recognize the problems to be understood in improvement of the stock. We must realize that eminence is necessarily rare, as Sir Francis Galton, a relative of the Darwin family, so emphatically pointed out; all families and stocks have a strong tendency to return to the mean of human ability, mediocrity. Finally, then, we come down to the very conservative and ordinary proposition that a better population may be obtained from normally capable parentage than from subnormal and incapable stock.

Speed in horses, milk production in cattle, and all desirable qualities in animal stocks are obtained frequently by inbreeding to a considerable extent. Inbreeding is prac-

tical, since by this method the breeder is more certain to unite germ cells both of which may carry the desirable quality, while with outbreeding such chance is poor. Actual genius, which occurs so rarely in the human population, has not been inbred but is always outbred and, therefore, practically always lost. Instincts and mental traits are as truly inherited as are physical characters, yet their determination is often more complex, and inbreeding will be even more necessary in obtaining the complete composition.

Inbreeding, as such, is neither beneficial nor harmful—it merely is more certain to bring about a uniformity of traits in a stock than is mixed breeding or outbreeding. If defective stocks are inbred the defects are accentuated, since each parent contributes the defective tendency to the progeny, and, on the other hand, when good stocks are inbred the perfection of the progeny is likewise insured. Therefore, the consequences of inbreeding depends upon the quality of the stock and inbreeding in itself contributes no additional quality. These considerations emphasize the importance of the study and understanding of quality differences among the germ cells and progeny in family stocks.

Good and Bad Eggs

Among almost all living things, for one reason or another, poor and defective specimens are to be found. All peas in a pod are not alike—the end ones are often small and defective; all the peanuts in a bag, or all of the grapes on a stem, are not of equally fine flavor. This generalization fully applies to the germ cells of higher animals. When

large numbers of eggs are spawned from the bodies of the "ripe" female amphibian or the female fish, a number of small and defective specimens are among them, some already opaque and dead. And, furthermore, among the eggs of normal size, shape, and appearance, there are still some which will fail to begin development or will barely start and then die.

When the experimenter places one hundred fish eggs in a bowl, fertilizes them with sperm from a "ripe" male, and then adds pure sea-water, the one hundred eggs do not all respond alike. A few of the eggs almost invariably fail to begin development, another small percentage develops for a short time and then dies. Most of the eggs, if from good parentage, continue to develop in a normally vigorous manner, but if they require several weeks before hatching it will be found that almost every day one or two more fall by the way and die. Only a certain lot of the one hundred eggs go through successfully to hatching and become free-swimming young fish. When the poultryman places one hundred hen's eggs in an incubator he usually obtains a very similar result; only a certain number of the eggs finally hatch into viable chicks. These were the originally good eggs, while those that have fallen by the way were the originally bad ones, not genetically equipped to perform the functions of development under the same conditions of environment in which the good eggs thrived.

With man and other mammals a comparable prenatal loss of bad eggs also occurs. Here, however, it is more difficult to demonstrate that this is simply a case of the bad egg and not some unfortunate environmental effect, since the mammalian egg requires so complex an environ-

mental arrangement for its care. There are, nevertheless, a few cases known among mammals in which embryonic death seems unquestionably an affair of bad eggs and nothing more. In such mammals as the pig, where large litters of young are produced at a birth, some observational data have been accumulated. Corner found, on examining the pregnant uteri taken from a number of sows during various stages of gestation, that considerable prenatal death occurred. MacDowell has found the same to be true for the mouse. These investigators suppose such deaths to be the result of originally defective eggs, since perfectly normal embryos are also present, and are developing immediately above and below the abnormal specimens in the same horn of the uterus. Papanicolaou and I (1918) had previously reported a number of such cases of uterine absorption and prenatal death among members of the embryonic litters in guinea-pigs; see Fig. 39.

The supposition that these embryos die on account of their inferior quality is in line with the old idea that all deformities and deaths of embryos are due to originally bad eggs. On the other hand, the experimental studies of "developmental mechanics" of the last fifty years have led many persons into overlooking or ignoring the genetic or innate causes of prenatal death. Thus for a period all defects are thought to result from bad eggs, at another time all defects are thought to result from environmental interference; yet fortunately all the while many investigators have been cognizant of the facts and have appreciated the probability that the same defects and deaths might occur as the result of either of the two causal conditions, or, in cases, from a combination of both.

Experimental Accentuation of the Differences between Good and Bad Eggs

During a number of years an extensive series of experiments with guinea-pigs has been conducted in the author's

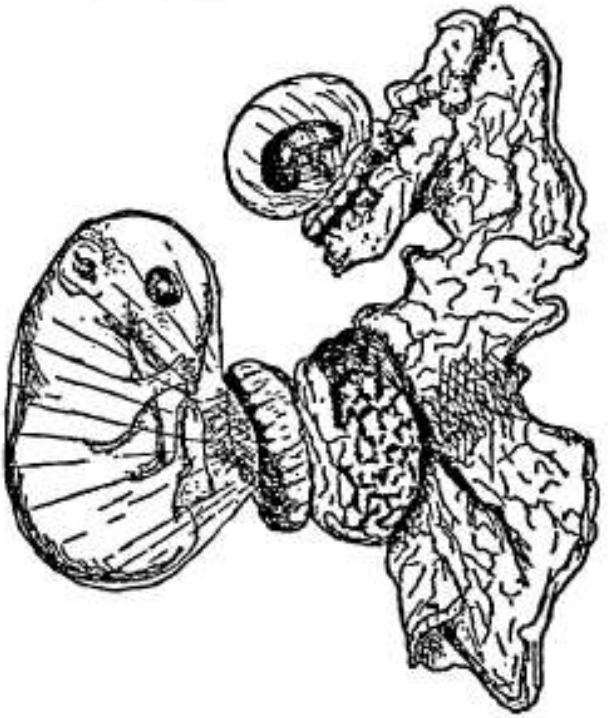


Fig. 39. Two guinea-pig foetuses of the same age still attached to the uterine wall, one large and normally formed and the other undergoing a process of uterine absorption; it is small and structureless and would have been finally destroyed.

laboratory, which chanced to supply very favorable circumstances for the detection of bad eggs in these mammals. These experiments also supply evidence of the rôle played

by a modified environment in determining the fate of such eggs. In them one may observe the effects of both classes of causes of deformity and prenatal death taking place at the same time on the same individual.

The study of a control stock of normal guinea-pigs over a period of fifteen years has seemed to show that there is a continuous loss of developing individuals at all ages prior to puberty, which for the guinea-pig occurs at about three months of postnatal age. Deaths occur among the young both before and after birth, and mortality records were obtained by uniformly examining all pregnant females each week during gestation. The embryos and foetuses may be quite accurately counted within the mother by careful palpation. Through these examinations the deaths *in utero*, or what may be termed the prenatal mortalities, were established. These prenatal records were then compared with the number of deaths which occurred between the birth of the guinea-pigs and the time of puberty. It was found as a surprising fact that the deaths during the prenatal period in the normal guinea-pig were just about equal to the mortality between birth and puberty, as is seen by comparing the last two sections of the first column in Table I. In other words, prenatal mortality and postnatal mortality under puberty are for these normal mammals closely the same. The prenatal records are probably less accurate than the postnatal, since the death of early eggs and embryos may at times escape detection by palpation. The results are, in spite of possible errors, of interest as emphasizing a high prenatal loss among normal stock, and any error in the calculations is on the conservative rather than the exaggerated side. Doubtless the prenatal death was somewhat

higher than we have recorded. An elimination of the unfit, or the survival of the fittest, in the Spencerian sense, is playing its rôle for the maintenance of vigor in this normal stock.

The records of premature death both before and after birth in the control guinea-pig stock are most instructive when compared with similar mortality records from stocks which had been heavily treated with the fumes of 95 per cent ethyl alcohol. The methods employed for detecting prenatal death by the loss of embryos were exactly the same on all stocks. Thus any error which may exist is not of serious consequence for the comparisons, since we probably miss as many early losses in the one group as in the other.

Animals that were directly subjected to the alcohol fume treatment showed a total mortality among their offspring almost twice as high as among the control offspring, being at the rate of 195 against 100, as is shown in the second column of the accompanying table. If this total mortality among offspring from the treated parents be separated into the prenatal deaths and the postnatal deaths under puberty, as arranged in the last two sections of the second column, the prenatal deaths are found to be two and one-third times greater than the postnatal death, 70.3 per cent against 29.7 per cent. This two and one-third to one is in contrast with the approximate one to one ratio shown by the control stock.

The prenatal mortality in the control stock is doubtless due to poor and defective eggs. The postnatal mortality of the control may also be largely due to innate defectiveness, since there is no *a priori* reason for assuming that the environment has at any time been different for the specimens

TABLE I

THE RECORDS OF ANIMALS OCCURRING IN THE DIFFERENT GENERATIONS OF THE ALCOHOLIC STOCK

	Normal Stock Control					Alcoholic Animals with Treated Parents, F1				
Total Number and Litter Sizes	1 19	2 114 Av. lit. 2.72 Av. lit. wt. 168.85 Total, 506	3 216	4 182	5 25	1 17	2 126 Av. lit. 2.56 Av. lit. wt. 165.89 Total, 450	3 240	4 52	5 15
Lived Over Three Months	1 18 %94.73	2 94 82.45 77.27%	3 172 79.62	4 88 66.66	5 19 76	1 15 %88.23	2 90 71.42 57.11%	3 136 56.66	4 14 26.92	5 2 13.33
Total Mort. Under Three Months	1 1 % 5.26	2 20 17.54 22.72% = 100	3 44 20.37	4 44 33.33	5 6 24	1 2 %11.76 42.88% = N	2 36 28.57 21.95% = 196	3 104 43.33	4 38 73.07	5 13 86.66
Prenatal Mortality	1 1	2 15 53.91%	3 20	4 26	5 0	1 1	2 26 70.81%	3 74	4 32	5 11
Postnatal Mort. Under Three Mos.	1 0	2 5 46.66%	3 24	4 18	5 6	1 1	2 10 29.68%	3 30	4 15	5 2

that died and those that lived. An environmental modification due to the alcohol treatment was introduced in the experimental stock of animals, but this also was as truly present for one egg or embryo as for another. We find as an effect of this experimental environment an increase, almost a doubling, in total mortality. This result one logically might expect. It simply means that certain individuals, although somewhat weak and below par, were sufficiently strong to survive the usual environment but could not withstand unfavorable conditions. However, the point of particular interest now comes with the fact that this total increase in mortality record is almost entirely due to an excessively high prenatal death. The postnatal mortality of the offspring from alcoholics, on the basis of the limited numbers concerned, is actually slightly better than the

TABLE I

THE RECORDS OF ANIMALS OCCURRING IN THE DIFFERENT GENERATIONS OF THE ALCOHOLIC STOCK

Alcoholic Animals with Treated Grandparents, Great-Grandparents, etc. F_{2-3-4}					Alcoholic Animals with Treated Great-Grandparents and Great-Great-Grandparents. F_{3-4}					Alcoholic Animals with Treated Great-Great-Grandparents. F_4				
1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
41	190	339	152	25	19	70	120	68	10	4	16	27	12	0
	Av. lit. 2.56					Av. lit. 2.54					Av. lit. 2.46			
	Av. lit. wt. 178.73					Av. lit. wt. 175.88					Av. lit. wt. 183.43			
	Total, 747					Total, 287					Total, 59			
1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
30	151	228	64	9	16	50	88	32	7	3	15	21	12	0
%73.17	79.47	67.25	42.10	36	%84.21	80	73.33	47.05	70	%75	93.75	77.77	100	0
		69.52%					69.83%					86.45%		
1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
11	39	111	58	16	3	14	32	36	3	1	1	6	0	0
%26.82	20.52	32.74	57.89	64	%15.78	20	26.66	52.94	30	%25	6.25	22.22	0	0
35.47% = N		21.57% = 164			30.66% = N		21.87% = 140			13.54% = N		21.21% = 64		
1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
8	25	63	60	11	2	9	16	21	2	1	0	2	0	0
		63.01%					56.81%					37.50%		
1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
8	14	48	28	5	1	5	16	15	1	0	1	4	0	0
		36.98%					43.19%					62.50%		

control, as the table shows. Thus the combination of bad eggs with a bad environment moves the moment of death back to an earlier stage in existence. The weaker specimens under the more severe environmental conditions are largely eliminated before birth and those that do survive to be born are only the more nearly normal and vigorous individuals.

Of course it must be recognized that the environment could be so modified as finally to affect even the strongest specimens; but before reaching this point all of the less hardy and more susceptible individuals would probably be eliminated.

The second filial generation, following the alcohol treatment in these experiments, still showed a high prenatal, as compared with the prepubertal postnatal, mortality. This

relation in mortality time is probably due to the fact that the alcoholic treatments were quite mild in their effect on certain somewhat susceptible individuals. Such specimens were not actually eliminated but lived to be adult, yet when put to the severe biological test of normality, the production of the next generation, their weakness exhibited itself in poor environment for the germ cells and subnormal uterine accommodation for the developing young. The more defective of their offspring under these conditions were again eliminated earlier than usual as prenatal losses.

In the still later generations from this alcoholic stock the normal equality between prenatal and postnatal mortality is reëstablished and those conditions no longer remain which tended to accentuate the difference between the good and the bad eggs in their ability to survive.

In view of the present state of agitation and misinformation over the virtues and vices of alcohol, let me hasten to add that the above effects are not at all due to any specific action on the part of this substance. In fact many other chemical substances in daily use, such as sugar or common table salt, if excessively administered to animals will induce results closely the same as those above described. This statement is fully justified by many experiments on the effects of various common substances on the eggs and embryos of many animal forms. No one is at present able to designate a given abnormality in an animal specimen as the specific reaction to the experimental administration of one chemical substance. It may be added further, as Pearl has called attention to from our experiments, and has clearly pointed out from experiments which he conducted with the

fowl, that in all these experiments the alcohol is highly beneficial as a selective agent tending to eliminate weak and defective individuals from the stock. It also may be noted that this elimination of defective individuals is performed in the gentlest manner by pushing the death moment back into the prenatal life-time, which in popular opinion is before the individual's existence has begun.

Variations in Susceptibility among Eggs

The differences among eggs and embryos which we have discussed in the foregoing consideration, may in many cases be simply recognized as normal variations. These variations may very often result from differences in the chance distributions and combinations of chromosomes in the maturating germ cells and fertilized egg. The different chromosomal combinations are the early germinal background for differences in susceptibility. Our present knowledge of chromosomal behavior makes it evident that disturbances in the pairing of the chromosomes during the reduction division, technically termed the synaptic reactions, and other anomalies in their sorting and distribution, may frequently produce non-viable eggs and embryos or give milder degrees of defective reaction. These unfortunate arrangements may arise just as frequently during the formation of the male germ cells as during the maturation of the egg. Such defects in germinal constitution of the individual may, therefore, be derived as truly from the father as from the mother. Among mammals in general we frequently know of sires with bad records for normal offspring even when paired with dams of excellent reproductive

capacity. Such unfavorable records are interpreted fairly as being due to the bad quality of the male germ cells, since the eggs and uterine reaction of the dam have been proved to be good in combination with other sires. Figure 40 illustrates visible defects in male germ cells.

It was experimentally demonstrated by Bardeen almost twenty-five years ago that amphibian spermatozoa could be so modified by treatment with X-ray that when normal eggs were fertilized by them, grossly deformed and non-viable embryos invariably resulted. These experiments have since been fully confirmed and extended by Oscar Hertwig and others, on several amphibian species. It was recognized by all of these workers that the chromosomes in the spermatozoön were the bodies or elements chiefly affected by the X-ray treatment.

On this supposition Oscar Hertwig subjected the sperm of frogs to severe X-ray treatments which he suspected might completely destroy the life of the chromosomes without eliminating the fertilizing power of the sperm. Such X-rayed spermatozoa of the frog were then used to fertilize the eggs of a salamander, a widely different animal, and rather normal development ensued. Now practically no normal development occurs in the salamander egg after fertilization with an untreated frog sperm because of the incompatibility of the salamander's chromosomal complex with that of the frog. Hertwig, therefore, interpreted the development, after fertilization with X-rayed frog sperm, to be parthenogenetic—that is, the embryo was produced solely by the egg without the spermatozoön having taken any part in the production other than serving as a stimulus to initiate development.

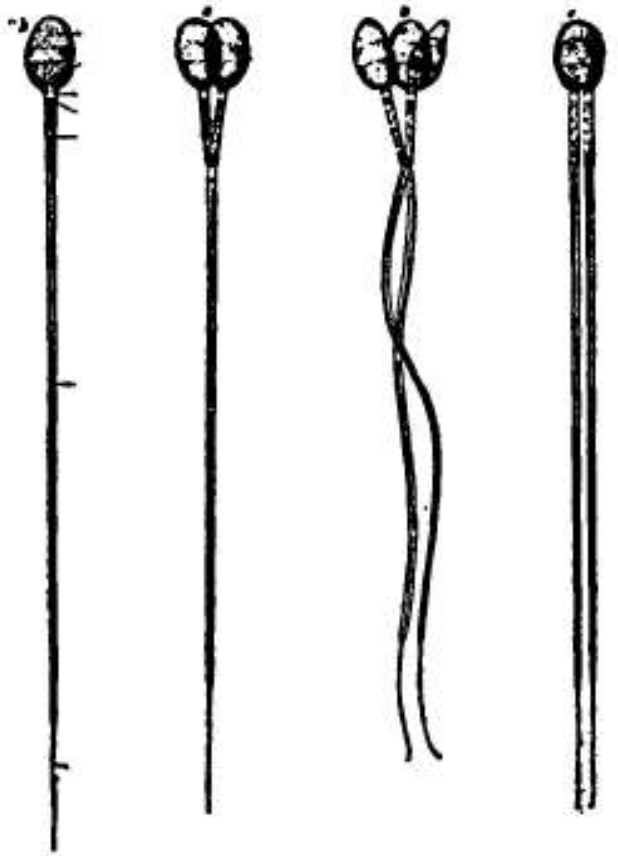


Fig. 40. A normal human spermatozoön on the left and three abnormal forms to the right. The rounded upper part is the head, which contains the chromatin or heredity material; the long filament is the tail which propels the spermatozoön with an undulating movement. (After G. Retzius and J. Bromann.)

We might readily prolong the discussion of differences in quality among the germ cells and progeny of common parentage, but illustrations enough have been cited to con-

vince us of the existence of these differences. It is the universal presence of differences and not equalities that one encounters in the biological world, all political efforts to the contrary notwithstanding!

X

THE EFFECTS ON DEVELOPING PERSONALITIES OF UNITING ENTIRE INDIVIDUALS, AND OF TRANSPLANTING ORGANS AND PARTS

We have repeatedly found in the foregoing pages that, when the internal conditions of the egg or embryo are abnormal, a perfect environment is unable to induce normal development. When internal factors are normal, on the other hand, unfavorable changes in environment may distort development, producing anomalous or monstrous reactions which vary in type with the developmental stage during which the unfavorable condition prevails. These distorted reactions are not specific for the disturbing agents, since in all cases the primary action of these agents on the embryo is a modification in the rate of metabolic activity or of embryonic development. The modified rate disturbs developmental coördination and abnormalities result. The change in developmental rate is probably a response to some change in oxygen consumption, such as may readily be brought about by a simple lowering of temperature.

In the present chapter we shall leave this consideration of the crude external environment, and attempt to follow the interplay between the genetic nature of the organism and the more subtle encroachments of environment within the embryo itself. What directing or determining effects, if

any, do the products or juices of certain regions and organs of the embryonic body exert over the development and differentiation of other organs and of the body as a whole? As development progresses the organism itself is constantly creating new internal environments which may influence the directions of further development. One may say that this is the phenomenon of development; but it is the different phases of this phenomenon that we must attempt to analyze for an understanding of constitutional up-building.

In considering the interaction of the internal environment with the specific nature of the developing embryo we must review an entirely different line of analytical experiments from those which we have so far surveyed. These experiments are in some ways more difficult to control, and more complex in their results, than the foregoing; but they no doubt give an insight into certain problems of development and constitution which the discussion up to now has not touched upon. They may be grouped under the general subject of the effects of transplantation on developing tissues and organs.

Germ Cell Transplantation and the Effects of the Foster-mother on the Germ

For a long time investigators in several fields have sought to determine whether the eggs from a given animal would develop in their typical way if placed in the body of a different female individual. Many such attempts to induce character modifications in the developing embryo as an effect of the influence of the foster-mother environment have been made, but very few have been at all successful.

The earliest experiments of this kind which gave anything like successful results were those reported by W. Heape, in 1890 and 1897, as short notes in the *Proceedings of the British Royal Society*. Heape removed the fertilized egg of a long-haired albino rabbit from the oviduct of the mother before it had become attached to the uterine wall, immediately transferring it to the oviduct of a rabbit of a different variety, which was neither white nor long-haired. In several cases the transfer was successful: the egg became attached in its new position and passed through all the stages of normal development.

One wonders that such an experiment could have succeeded at that time since its success would seem to depend upon the more exact knowledge of ovarian conditions, corpora lutea reactions and the proper uterine state for the reception of the embryo which has been so recently acquired.

Heape reported that young rabbits developed in this way were both long-haired and albinos, like the mother of the eggs, and were not like the foster-mother rabbit which bore them. The foster-mother, as Castle has remarked, "seemed not to have influenced the inheritance of the offspring any more than ordinary food supplied to growing young will determine their breed characters."

Transplantation of Immature Ovaries in Guinea-pigs

Although one might grant the above results to be entirely correct, there would still remain the question whether the earlier or immature germ cells might not be affected by a foster-mother. The transferred egg in Heape's case was already mature and fertilized. If the transfer had been

made at an earlier stage while the eggs were still immature and growing in the ovary, might not effects from the strange body have manifested themselves? The immature egg may be susceptible to modification under conditions which the full-grown and fertilized egg is not.

In order to answer these problems a large number of experiments have been made with ovarian transplantations in several species of animals. Most of these efforts have been poorly undertaken, and many are confused because of the strong tendency in the foster-mother or host female to regenerate her own ovaries after their removal unless every trace of ovarian material has been taken away. The most successful and reliable of all such experiments have been performed with guinea-pigs by Professor W. E. Castle and Dr. J. C. Phillips at Harvard University almost twenty years ago.

Castle and Phillips grafted ovaries from other individuals into 141 female guinea-pigs. Of these about 100 were later mated with males long enough to give definite indications of their ability to produce young. Only three of these females with engrafted foreign ovaries actually produced young, but in seven others the engrafted ovarian tissue persisted for many months. In eleven cases ovarian tissue was regenerated at the original ovarian site and from three of these cases young were produced which had the same genetic characters as the mother, and not at all those of the graft. In eighty-seven cases no ovarian tissue whatever was found on post-mortem examination.

It is of interest to review the three successful cases that actually produced young from the transplanted ovaries. First—the ovaries of an immature black guinea-pig were

transplanted into the body of a white albino female, where they developed and liberated ova for a period of more than one year. Six young were produced from two matings by a white albino male. The six young guinea-pigs were all black-coated like the animal which furnished the ovary, and were not like the albino animal which bore the young nor their white albino father. Figure 41 shows in diagram the outcome of this experiment.

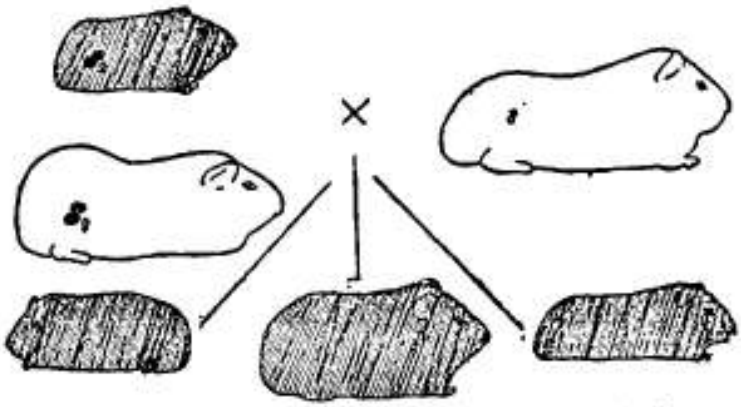


Fig. 41. Diagram to illustrate the transfer of ovaries from a black guinea-pig and their implantation into a white albino female after her ovaries had been removed; the result of later mating the albino female carrying the black ovaries to an albino male is the production of three black offspring, exactly what would have been expected had the albino male been mated to the original black female. (Modified from Castle and Phillips.)

The foster-mother, so far as known, differed from the female which furnished the ovarian graft by only a single genetic color factor. The ovarian tissue taken from the black animal evidently possessed the factor for black and retained it throughout the sojourn in the body of the albino,

inasmuch as black color transmission never occurs in pure albinos.

In the second case recorded by Castle and Phillips, the same color factor difference again existed between the animal which furnished the graft and the one which received it, the latter being an albino, the former being colored. However, in the first case the colored animal was black and the albino was a "*potential* black," lacking color, while in the second case the colored animal was a brown-eyed cream and the albino a "*potential* brown-eyed cream," lacking color. The two cases are, therefore, fully comparable though not exactly the same color is involved in both. The same negative result was observed in the two cases as regards the effects of grafting.

In case two, the grafted albino foster-mother bore a brown-eyed cream offspring by an albino mate. She also bore two albino young, but this is not to be regarded as evidence of somatic influence of the foster-mother, for it was known that animals of the stock of guinea-pigs which furnished the graft were heterozygous or impure and mixed for albinism. The engrafted ovarian tissue was expected to furnish equal numbers of ova carrying the brown-eyed cream character and the albinistic character, respectively. The character and numerical proportions of the young obtained from the foster-mother are exactly the same as the colored animal herself would have been expected to give had she retained her ovaries and been mated with the albino male.

The third case involved a wholly different factor, the agouti or wild hair pattern. Both animals, the donor and the foster-mother, were colored alike, so far as known,

in all genetic factors except the agouti. They were entirely brown pigmented, and in the families of both it was stated that albinism existed as a recessive character. At about six weeks of age the host animal was castrated, and then received the ovaries from a light cinnamon guinea-pig about one month old. On each side of the body an ovary was stitched to the horn of the uterus about a centimeter from the normal position of the ovary. The grafted animal and the planted ovary were both immature so that they grew and developed together.

This animal was repeatedly mated with an albino male and produced only one offspring at a birth—in all, five young were obtained. Six months after the transplant the first offspring, an albino male, was born; a year after the operation, a light cinnamon female; about three months later a light cinnamon yellow male; later a male albino; and, finally, a female albino was born. There were thus produced three albinos and two cinnamon offspring. Both of the colored young were cinnamon, like the female from which the graft was taken, rather than the dominant brown agouti color of the foster-mother. Thus Castle concludes that the sojourn and development, in the body of a brown agouti animal, of an ovary taken from a cinnamon animal does not seem to have altered in any respect the initial genetic potentialities of the germinal substance, at least so far as hair color is concerned.

Castle concluded that these three cases of ovarian transplantation give substantial evidence in favor of the view, originally proposed by Weismann, that in the higher animals the germinal substance and the body tissues or soma are physiologically separate and distinct, and also that the

genetic potentialities of the former are not subject to modification through somatic influence.

This experiment clearly showed that at least the genetic factor for pigment expression was not influenced by the condition of pigment in the body of the foster-mother. It is very probable that this lack of foster-mother effect would also hold true for all other characters thought of in a strictly genetic way. But it is easily conceivable that the uterine environment of the foster-mother might itself modify the type of development or growth in the offspring. For example, an egg from a large variety of parent might not attain its full body size if nurtured in the uterus of a smaller variety foster-mother. Such a reaction would not be considered a genetic modification but merely a response to an unusual developmental environment.

The Implantation of One Individual on Another and True Parabiosis

From the standpoint of the determination and modification of personality and constitutional conditions, one may ask what effects will the body, or parts of the body, of one developing individual exert if attached to, or introduced into, the body of another? Or stating the problem otherwise, what would result from uniting two different and already determined constitutions? Will one dominate and tend to transform the other, or will the two blend into a combination differing from either of the constituents, or will something of both effects take place? In any case the results are of interest to us since they may show what a new bodily condition may do in the way of modifying the existing con-

stitution. A mass of experimental data has been accumulated in an effort to bring about and analyze such combinations.

The subject may be approached by considering first the possible influences of an organic connection between two entire developing individuals, and next the transplantation of organs and smaller parts from one embryo or young individual into another.

The Case of the Free-martin in Cattle

Nature has arranged for us a most illuminating demonstration of the effects of fluids produced in the body of one developing embryo on the character of development in its sister twin. Cattle breeders have known for a long time that, when a cow gives birth to twin calves of different sex, the bull calf is a perfectly normal male whereas in almost all cases the female or heifer calf is abnormal, with somewhat deformed genitalia, and is sterile for breeding. This defective female is known in the breeder's terminology as a "free-martin." Among sheep and goats such defective females also occasionally occur. The cause of this peculiar free-martin condition remained a puzzle until 1911, when the Austrian workers, Tandler and Keller, reported a study of the fusions between the embryonic membranes or placentae of the two oppositely sexed twins, and discussed the morphology of the genitalia in the female twin. These investigators found the twins, one of which is a free-martin, to be derived from two eggs. The calves are thus brother-sister individuals, and are not technically true twins derived from a single egg. Tandler and Keller demonstrated the presence

of a vascular connection between the two embryos *in utero* which permitted the blood of each to circulate within the body of the other. They considered this circulatory communication to be the causal factor in the modification of the female twin. F. R. Lillie, in 1917, fully confirmed these findings in an entirely independent way, not having known of the work of Tandler and Keller. Lillie and his students have extended and expanded the study of the free-martin until the conclusion is fully certain that the ovaries of this female are arrested and modified in their development as a result of the early flow through her body of blood from the brother twin; see in Fig. 42 an outline of the vascular arrangement connecting the twin calves.

What the element is in the male blood that induces the

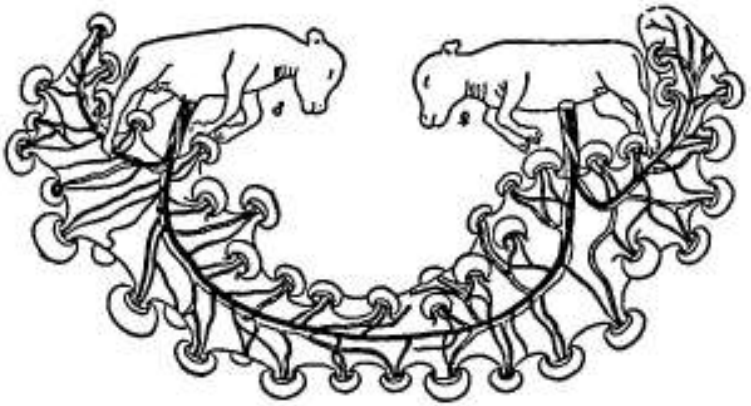


Fig. 42. Twin calves of opposite sex, the male on the left, showing a blood vascular connection between the two placentae illustrated by the heavy black vessel. This connection permits the blood to flow from one twin to the other. The substances derived from the blood of the male causes a depressed development of the reproductive organs in the female and a so-called free-martin sterile individual. (Modified after F. R. Lillie.)

free-martin condition is not yet entirely clear. Willier, from a careful study of early embryos, was led to agree with Lillie's suggestion that it might be a secretion from the male interstitial cells. He found these cells in the testes earlier than in the ovary; the modification in ovarian development begins to show itself only following their appearance. Although this modification takes place, the important fact must not be overlooked that true male germ cells are never produced in the free-martin. As Morgan has expressed it, the influence of the blood of the male co-twin does *not* bring about the transformation of the primordial egg cells into sperm-producing cells.

The Mixed Male-and-Female Individual

Many examples are known among mammals, including man, of individuals with mixed male and female sexual organs and actually having both ovaries and testes. The two different gonads or sex-glands must necessarily have developed in each of these individuals, and their embryonic origin must have occurred at very nearly the same time. It is evident in these cases that neither the testis nor the ovary was sufficiently dominant to prevent the differentiation of the other, and certainly there was an entire failure to transform either gonad from one sex into the other. These cases make it seem that the different genetic constitutions of the male and female sex-glands may often overbalance any hormonal or chemical influence from the opposite sex secretions. In such competitive reactions there is, however, the quantitative element; and possibly it may be that a sufficient quantity of the hormone from the male sex at a

proper developmental time might transform the potential ovary into an indifferent state if not into a testis.

Individuals of mixed sex, or sex intergrades, are so common in certain stocks of hogs as to be almost universal. So-called *gynandromorph* individuals, with a male sex-gland on one side and an ovary on the other side, have been reported among several species of mammals. All such conditions demonstrate the fact that the two different sex-glands—a well developed male testis and a female ovary —may exist normally, without either gland necessarily suppressing the other, in the one body of bisexual individuals. We have illustrated this condition in flies by Fig. 17, page 82, though in insects a sex hormone is unknown.

There are very probably some cases, like that of the free-martin, in which one of the sexes seems to dominate the development of its opposite, causing this to be defective and sterile.

Sex in United Pairs of Amphibian Embryos

To gain further light on the mixed sex conditions, the entire bodies of amphibian embryos have been united side-to-side. Young embryos were taken just following the closure of the embryonic brain and spinal cord, and a small skin area removed from one side of each, leaving an exposed surface; the exposed surfaces of the two embryos were then placed together and their union quickly followed. Burns has recently studied the sex of such united, so-called, *parabiotic* twins. They may be considered an artificial imitation of the communicating circulatory systems of the free-martin and its twin. Burns also hoped to learn whether one

sex in the salamander would tend to transform or suppress the development of the other sex, see Fig. 43.

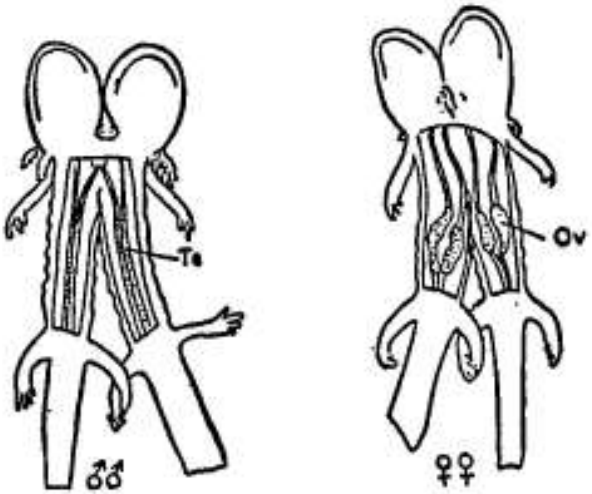


Fig. 43. Salamander larvæ artificially fused together in pairs so as to allow the body fluids to flow through both individuals. In these cases the members of a pair were always of the same sex. The two on the left are males and the right pair are females. Te, testis; ov, ovary. (Sketched after Burns.)

In uniting random pairs of salamander embryos before sex differentiation has occurred, the chance expectation of sex combinations will be one pair of potential males, to two pairs of male with female, to one pair of females, a 1: 2: 1 ratio. Should any decided deviation from this expectation occur, it would be thought to arise from some modification in sex condition due to the parabiotic arrangement. Burns found from his earlier studies that the two members of a pair were always of the same sex: forty-four pairs were both males and thirty-six pairs were both females. No male-female pairs existed, though on the basis of chance

half of all the pairs should have been of this kind; hence it follows either that such combinations always die or that the sex of one individual changes over to that of the other. And strangely enough, this changing over must be sometimes in one direction and sometimes in the other, since both male and female pairs were found to be about equally abundant.

In Burns' later experiments he has found mixed male-female pairs, but almost all of the members in these pairs show some degree of bisexuality. He also continues to find both changed-over males and changed-over females, and it becomes a most difficult problem to determine how these reciprocal effects are possible, even though actual transformation in sex differentiation may take place. If the action is so indeterminate as to play in one direction in one case and oppositely in the next, it is very difficult to imagine how it ever can be sufficiently strong to reverse the nature of the affected sex-glands in any case.

Burns' results differ from Lillie's observations on the free-martin and Witschi's experiments on the parabiotic frogs in that the male sex is not invariably dominant. Burns also finally states that there is positive evidence of sex-transforming influences prior to morphological or structural differentiation.

The Transplantation of Organs

During the past thirty years there have been a great number of experimental studies on the effects of transplanting an organ from one place to another in the same individual. This procedure is known as autoplastic transplantation,

Does the transplanted part lose anything of its normal characteristics in its changed position, and does it modify at all the parts newly coming into relationship with it? Eyes, embryonic ears or auditory vesicles, nasal placodes or early olfactory epithelium, limbs and parts of the neural plate or embryonic nervous system and many other tissues have been transferred from their normal sites of development to various positions.

In these cases the changes induced in the transplants have varied chiefly with the degree of structural differentiation which had already taken place before the removal of the part. If groups of cells are removed very early, before the specific rudiment or *Anlage* of a given organ has been established, the transplant develops in accordance with the usual nature of the new surroundings in which it is placed. For example, cells removed from a region which later would produce eyes will, when planted early enough on the side of the body, give rise to ordinary skin. When, however, the bud or beginning of an organ has definitely established itself, it will often continue to develop into this organ, no matter where in the body it may be placed. Between these two extremes of expression on the part of the transplant are to be found many modified and partial developments. The strange location may have a slightly unfavorable effect on a developing organ, though this will not be sufficient to change its nature provided the organ has reached the state of a fully determined bud before removal. In the other direction, the transplanted organ produces an effect on its new surroundings, particularly on the growth of the nerve fibers which it usually tends to call into itself from the near-by region of the spinal cord. These are not actual con-

stitutional changes but merely modified adjustments and accommodations to the misplaced part.

Another class of transplantations are those made from one individual to other individuals of the same species. These are known as *homoplastic* transplants. Finally, transplantations may be made in a still wider fashion by removing organs from an embryo of one species and implanting them into an embryo of a different species. These are *heteroplastic* transplants, and it may readily be understood that such transplants may have an immediate bearing on constitutional modifications, especially under strange developmental influences. Here again a large number of different tissues and organs have been employed in the transplants. Skin from the body of one species has been induced to develop into the crystalline lens for the eye in another species. The eye region of the neural plate from one species has developed into skin when planted upon another species, and so on.

Transplantation of Embryonic Limbs from One Species to Another

R. G. Harrison at Yale University, and his students, have devised ingenious methods for the early removal and transfer of embryonic parts; and have supplied a most important series of investigations bearing on the results of heteroplastic organ transplantations.

Harrison showed with a very striking experiment that when the arm bud from one species of salamander was transplanted onto another species it grew to a different size from the normal arm size of both itself and its host species.

This arm in the new animal, being a strange part in a strange environment, was stimulated by somewhat different food and different chemical surroundings, decidedly unlike those it would have experienced in its normal place. The

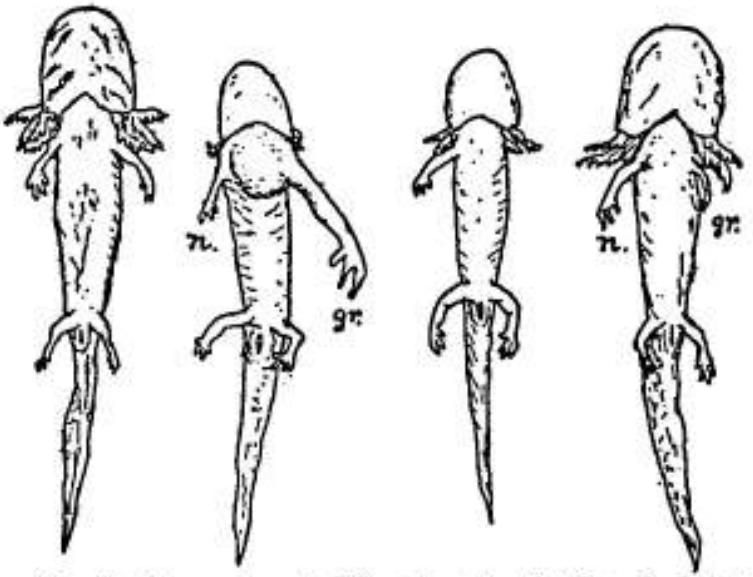


Fig. 44. Salamanders of different species that have had their right arms interchanged in transplantation. The left pair shows that the transplanted arm may in cases grow larger than normal for either the donor or the host. (After Harrison.)

transplanted arm was also constitutionally different from the arm of the host, and it responded differently from the host's arm to the host's internal environment. Giant-like arms were carried by some of the specimens, and this disproportionately large limb tended also to modify the functional behavior of the animal, see Fig. 44. A strange condition of growth regulation was met by the foreign ex-

tremity in its new position, and its growth-potential responded to this in a way differing somewhat from the mode of extremity growth in either of the species involved.

Grafting Eyes from One Species to Another

Stone, in 1929, found that larval eyes when grafted from one species to another follow closely the growth curves of their donor controls. That is, they grow after transplantation as they would have grown in their original site. Harrison had shown a similar growth constancy in the case of heteroplastic transplants of early optic vesicles between the same two species.

Under ordinary conditions of feeding, the eyes from one species of salamander, *Amblystoma tigrinum*, when transplanted to another species, *A. punctatum*, grew more rapidly than the normal eyes of the host, and, up to the time of metamorphosis of the larva into the adult *Amblystoma punctatum*, they exceeded in size the donor control eyes. The reciprocal transplantation from the species *punctatum* to *tigrinum* as the host, gave eyes that were smaller in size than their normal donor controls during the same period; the transplanted eyes are outlined in Fig. 45.

The transplanted optic vesicles, or earlier embryonic stages of the eyes, between the same two species, had previously been shown to exhibit similar relations. These different growth-reactions, when the transplant is made in opposite directions, show that the specific growth-potential of the grafted cells responds to a regulatory condition which differs in the two species. The genetically specific growth-potential, therefore, is modified through interaction with

the body stuffs in finally determining the structural proportions of the finished organ.

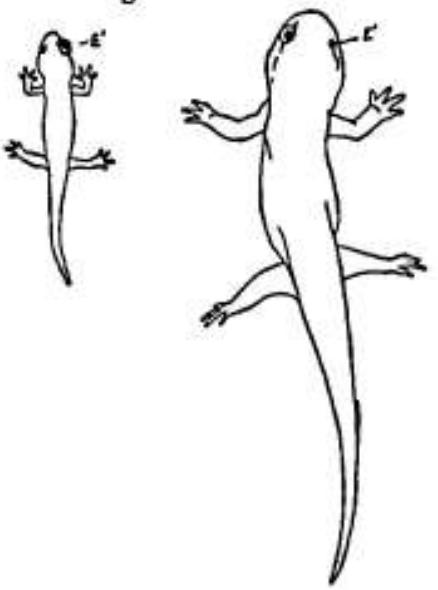


Fig. 45. Interchanged eyes between two species of salamanders. The smaller species has a large right eye derived from the larger species and the larger one has a small right eye taken from the small species. Each eye grows according to the size of its own species and not like the host species. (Outlined after Stone.)

Transplantation of Early Embryonic Areas

It has been learned both through general studies of development and by methods of following the lineage of single cells, that certain areas of the fertilized ovum will differentiate, under normal conditions, into definite parts of the invertebrate embryo and adult animal. This knowledge has been acquired in a most painstaking way by a host of able

investigators. Further, by methods of intra-vitam staining, several investigators have partially traced these processes in vertebrate embryos. And very recently the German embryologist Walther Vogt, of Munich, has shown by most careful and ingenious intra-vitam staining that small areas, or actually only a few cells, may be followed until they give rise to definite parts of the medullary plate or early nervous system, epidermis, and other structures in the amphibian embryo. Such early cell groups in the egg may be regarded as "presumptive" medullary plate or "presumptive" gill structures, et cetera, as Spemann has termed them.

The question now arises; what will develop if these "presumptive" areas be transplanted to strange places in different embryos? In other words, where are the causes for differentiations in development in these cell groups, or "presumptive" areas, to be found? Are they in the particular area itself, or are they in its peculiar surroundings?

During the past ten years Hans Spemann, the eminent German zoölogist at Freiburg, and his students, have made a most vigorous and telling effort to answer these questions. And they have carried their analysis through to a surprising degree. Starting with the gastrula or infolding embryonic stage a portion of "presumptive" medullary plate or nervous tissue was replaced by "presumptive" epidermal skin, and vice versa. Spemann made successful combinations of the double transplantations. Two embryos of different coloration were selected—one light and the other dark, thus making it possible to distinguish readily both transplants over a long period of time, with the further advantage that each transplant in this combined operation

indicates in the host embryo the exact place from which the other transplant has been taken. The experimenter thus knows definitely what the transplant would have developed into had it remained in its normal surroundings, see Fig. 46.

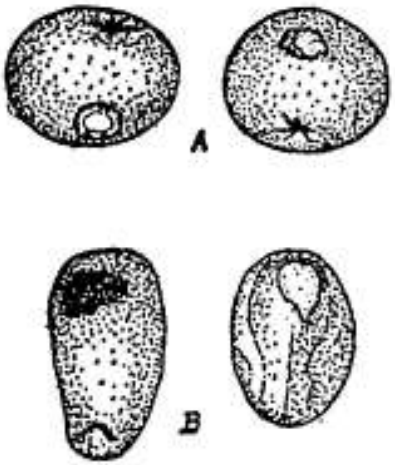


Fig. 46. The interchange of pieces of different colors from one species of salamander to another and the subsequent retention of the original color in spite of modifications in the future tissues of the transplants in the new host species. (After Spemann.)

The results of these experiments on this early gastrulation stage of the embryo are quite conclusive. The transplants developed in very exact accordance with their new environment and without indication of the regions from which they had come. The "presumptive" medullary plate, or "presumptive" nervous tissue planted within the epidermis or embryonic skin, became epidermal skin on the ventral body surface, while "presumptive" epidermis

planted within the medullary plate differentiated into embryonic brain. In simpler words, a piece of the future brain of one embryo developed into ordinary abdominal skin on another embryo, and a piece of embryonic skin planted on the dorsal surface of the first embryo formed true brain tissue. Thus one may change future brain into skin, or future skin into brain.

These experiments were equally successful when carried out not only between embryos of the same species (homoplastically) but also between different species (heteroplastically). A region of presumptive medullary plate such as the rudiment of an eye from *Triton taeniatus*, a species of the common European salamander, was exchanged with a presumptive epidermal or skin area from the gill region of *T. cristatus*, another species of this salamander. Both transplants differentiated according to their new environments, but a fact of high significance is that each transplant retained at the same time its species characteristics; thus the external gill-stumps on *T. cristatus* in this experiment, although perfectly formed, had the characters of a gill-stump of the species *taeniatus* from which the transplant had come, and not those of *cristatus* which furnished the internal environment and blood supply and actually brought about the differentiation into gill instead of eye, as it was "presumptive" to be.

This fact is of great importance as indicating that although complete differentiation and regulation of tissue may be induced through a definite environment or location in the embryo, yet such an environment is entirely unable to make over or alter the characteristics of the species from which the tissue was derived.

The Species of the Cellular Transplant

The character or species of the transplanted cells is inherent in their chromosomes or gene complex, and this remains uninfluenced by an environment which is fully able to mold their functional differentiation. This fact indicates in a most emphatic way the independence of the chromosomes from somatic influence, although these are actually chromosomes of body or soma cells. Facts such as this lead us to realize that activities and qualities acquired by the cell itself do not affect its genetic constitution. The persistence of the species characteristics of the transplanted cells most convincingly demonstrates the high improbability of the inheritance of acquired characters, and this is of special interest since the experiments involved were not at all designed to bear upon this problem.

Determination in the Transplant

Spemann's experiments on very early embryonic stages show for such animals as the European salamanders that presumptive medulla and epidermis are yet indifferent, or at least are capable of a re-orientation of differentiation. At a little later embryonic stage the situation alters entirely, and in an experiment similar to the one described above the transplant develops according to its place of origin, and not in accordance with its new transplanted position. Thus if a presumptive eye-fundament be removed at a stage when the medullary plate of the embryo is already formed, and transplanted into the epidermis of another embryo at a

comparable developmental stage, it develops in the same way and at the same time as the normal eye-anlage should develop, and it differentiates into a normal eye-vesicle. Therefore, during a short developmental interval, the eye-fundament has ceased to be indifferent and has become *determined* as regards its further development and differentiation, in spite of being placed in entirely strange surroundings.

One of Spemann's associates, O. Mangold, in 1923, carried out still wider reciprocal transplants on a large scale and with remarkable results. Mangold showed that presumptive ectoderm, which if left in its normal position would give rise to either medullary plate or epidermis, could on transplantation into a proper region be stimulated to differentiate into mesoblastic somites and later into muscle, pronephros or embryonic kidney, or into intestinal wall—and, therefore, change itself into organs which normally are derived from other germinal layers than the ectoderm. This fact is clearly proven by heteroplastic transplantations between the two species of the common salamander, *Triton cristatus* and *T. taeniatus*.

The indifference of the early embryonic tissue, as evidenced by its ability to develop into organs normally derived from another germinal layer, is of primary significance; yet this is not the only important conclusion to be drawn from such transplantation experiments; they further indicate that there must be factors at work in the new environment which have the power to alter and determine the direction of differentiation of the early transplants. How may we discover the source of these influences?

Transplantations and the Discovery of "Organizers"

Spemann and his associates have been more successful than any other workers in attempting to locate the source of origin of the influences which determine and direct structural differentiation during early embryonic development. One of the most instructive experiments in this direction was the transplantation of a small portion from the dorsal lip of the infolding region which goes to form the two primary germ layers in the salamander egg, that is a piece from the dorsal lip of the blastopore or embryonic mouth. If such a piece be removed from the embryo of one species of salamander at the beginning of gastrulation, and transplanted into the indifferent outer surface or ectoderm of an embryo of another species at the same stage of development, it does not behave indifferently as did the presumptive medullary plate or epidermis described in the foregoing section. On the contrary, it asserts itself in the new environment, makes use of the surrounding material for its own developmental purposes, and actually forms a new embryo on the body of the host, as is shown in Fig. 47. Anyone may see that this reaction is a considerable accomplishment. This experiment was first performed by H. Mangold in 1924 under Spemann's supervision.

In the most successful experiment the newly called forth embryo possessed a central nervous system, with adjacent auditory vesicles, a notochord, mesoblastic segments, and the Wolffian ducts of the embryonic kidney. It was thus complete but for the anterior cephalic portion. Its structure, however, was most peculiar, being composed of cells derived both from the transplanted portion from the species

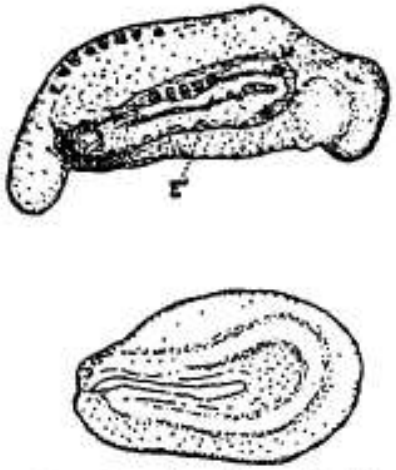


Fig. 47. Transplantation of an "organizer" from one embryo onto another of a different species and the calling forth of a complete twin individual through the action of the "organizer" on the body of the host. (After Spemann.)

T. cristatus, which had induced the appearance of the new embryo, and the cells taken over from the host species, *T. taeniatus*, which supplied the environment. The body of this embryo was thus made up of a mixture of cells from two species of salamander and each of the two classes of cells retained its species characteristics irrespective of the organs it contributed to form. The embryo was a cellular mosaic of the two species. This result shows that these particular transplanted early cells are not directed in their development and differentiation by a definite environment, but have the power within themselves of organizing the surrounding cells for new formations. They seem to carry within themselves the factors which determine the direction of differentiation.

Spemann has applied the term "organizers" to cells such as these which are capable of inducing the formation of new fundaments, and the designation "centers of organization" to the regions where these cells are situated at the onset of gastrulation. A portion from the lips of the infolding region capable of inducing a new entire embryonic formation is composed either completely or partially of two primary germ layers known as the endoderm and mesoderm or combined ento-mesoderm. Such cells, during the course of the infolding or invagination, normally form in the embryo the roof of the primitive intestine. Thus the roof of the embryonic gut, as Spemann had previously surmised, is an important organizer in the differentiation of the central nervous system.

A further proof of this power of the organizer material has been shown in experiments by Geinitz. He found that pieces of embryonic tissue may easily be brought to lie under the ectoderm, or covering layer, by transferring the piece into the cleavage cavity which exists in the blastula or in the early gastrula stage of the embryo. At this stage many embryos are simply a hollow sphere of cells, then a region on the surface begins to dimple or invaginate, which finally obliterates the central cavity by forming a two-layered sac. This two-layered stage is the gastrula. A small piece of tissue introduced into the cleavage cavity does not interfere with the infolding process, and during the invagination the piece becomes caught between the two germinal layers, as indicated in the diagrams, Fig. 48. Geinitz succeeded in bringing a piece of the dorsal lip of the infolding region of one embryo under the outer layer of another embryo, and this called forth the formation of medullary plate

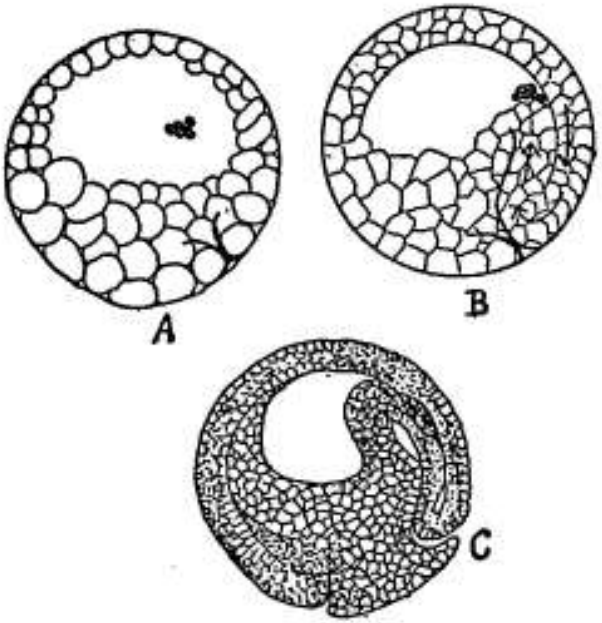


Fig. 48. Illustrating the position of a piece of tissue planted into the cleavage cavity of an early embryo, a, and being later caught between the two embryonic layers, in b and c, during the infolding growth of gastrulation.

or embryonic brain. A piece from the roof of the infolded region of a complete gastrula induced a new entire embryonic body in the host. A piece of ectoderm or embryonic skin from another region when implanted in the same manner in control embryos did not have this effect.

Since the inner and middle embryonic layers, entomesoderm, are capable of thus influencing the outer or ectodermal layer, it seems probable that it is this element in transplants from the dorsal lip of the infolding region that calls forth an entire embryonic body formation.

What now determines the orientation of the differentiation in the body induced by the implanted organizer? There have been no fully conclusive results bearing on this question, but from experiments available it may be anticipated that the host embryo plays some part at least in determining the orientation of the developing transplant.

The Nature of the Organizer Influence

Spemann suggests that the implantations into the cleavage cavity of the early hollow sphere stage of the embryo may yet make it possible to determine whether only the living cells of the organizers are capable of inducing new formations, or whether the same effects may follow the use of disintegrated cell material or even extracts from such cells. The fact that effective interaction between organizers and host tissues exists not only between different species of salamanders, but, as shown by Geinitz, also between distantly related animals such as salamanders and frogs, suggests to us an activating stuff, possibly of the nature of the hormones in internal secretions. It is a well-known fact that a given hormone from one vertebrate animal will induce a characteristic reaction in almost all vertebrates with only minor modifications. The way in which an "organizer" from one species excites developmental activity in other species would in this respect at least put the organizer in the hormone class.

Interactions very much like those described in the previous section have long been known to exist between certain structures in embryonic development. The classical case is the effect of the embryonic optic vesicle in calling forth the

formation of the crystalline lens of the eye from the overlying skin-ectoderm. Although a crystalline lens may in some embryos arise independently of the optic vesicle stimulus, yet it always seems quite certain that the vesicle may call forth a lens from any portion of undifferentiated skin-ectoderm with which it may come in contact during the proper developmental time. From Spemann's point of view such an organ as the optic vesicle may be classed as an organizer of the second grade.

Successive Transformations through Organizers

Finally, it has been shown that these organizing effects may be induced in a given embryonic part, and that this part may then be further transferred through secondary transplantation to still other embryos. For example, Geinitz removed a piece of presumptive epidermis at the beginning of gastrulation from an embryo heavily colored with intravitam stain, and implanted it into the dorsal lip of the infolding region of an unstained embryo at the same stage of development. The piece was placed in such a position that it folded in and formed a portion of the embryonic intestine. He then removed it, and this time transplanted it into the cleavage cavity of a third embryo at the onset of gastrulation. In this third embryo the piece came to lie under the ectodermic layer and induced in this layer the formation of a secondary embryonic brain. It must now be recalled with careful attention that this transplant, if it had remained in its original environment, would have differentiated into skin-epidermis. In the second embryo it was transformed into embryonic intestine or endodermal tissue, thus becoming itself an organizer which, when implanted

in the third embryo, induced the formation of a part of a secondary nervous system. Thus the principle of progressive determination through the action of "organizers" of ascending grades seems to hold good, at least for the earlier stages of development in amphibian embryos. At the present time this is as far as these highly suggestive studies have progressed.

The exact range of their application is as yet impossible to suggest. Yet they have a wide significance in any consideration of the interplay of inheritance and environment during the development and differentiation of animal constitutions and physical personality.

Deductions Regarding Differential Developments

We have now, in our consideration of the rôle of inheritance and environment in the formation of personal constitution, briefly related the importance of variations in quality of the germ cells, of good and bad eggs. We have pointed out the accentuation of these quality differences in the germ cells through reactions to modified environments along with examples of variation in resistance and susceptibility among eggs. In analyzing the effects of complex and peculiar biological environments we have seen that the transplantation of germ cells and developing eggs into a foreign or foster-mother is apparently non-effective in modifying constitutional characteristics.

We have considered the results of the implantation of one embryonic individual on another, of transplanting embryonic organs from place to place within the same individual, of similar transplantations from one embryo to another embryo of the same species, and from one species to an-

other species. And finally we have examined the reaction of smaller and earlier embryonic transplants made in a variety of ways. Through these transplantations we have learned of a peculiar power on the part of certain cells to act as organizers. The organizers may completely direct the course of differentiation in other neighboring cells. Yet through all these modifications and influences we always find that the specific characteristics of the embryonic cells and tissues remain true to their chromosomal composition and species kind.

The results would seem to mean, in the first place, that no organic environment yet employed has the power to alter the specific characteristics of the somatic cells. In the second place, it appears that cells which come to lie in a definite embryonic area elaborate within themselves hormones, or some such stuffs, which initiate and regulate the direction of embryonic differentiation. The actual nature of this reaction is completely unknown, yet there is the possibility that the organizers are embryologically the earliest hormone-secreting cells.

The quality of the chromosomes in all probability fully determines the cell species, and the organizing substance regulates the direction of differential development. Combinations of different embryonic persons or parts of embryos may completely modify the developing personality and actually change future eyes into skin, but such combinations are entirely without influence upon the species characteristics of the cells involved. The species type is maintained through the genetic complex within the cell chromosomes, regardless of exposure to the bodily environments of other species of embryos.

XI

POSTNATAL DEVELOPMENT AND PERIODIC CHANGES IN PERSONALITY

IN the foregoing chapters we have carried our survey of the developing personality from the germ cells and the fertilized egg, through the various changes and processes of embryonic life, and up to the state of equipment sufficient for a free-living postnatal existence. Thus we arrive at the day of birth, which, as pointed out in an early chapter, is taken by most people as the starting point for individual existence. However, for those of us interested in the problem of personality and constitution, this can never be the beginning: we have seen that the fundamental basis for all that the individual may possibly attain is already contributed at the moment when the egg is fertilized by the male germ cell. We have also learned that this fundamental endowment is an uncertain quantity, in so far as its ability to express itself along a particular line of development is concerned. The developmental tendencies are constantly bent in one way and then another in response to environmental influences. We finally have been led to the conclusion that the child at birth is the resultant of the interaction of a genetic foundation with the internal and external conditions under which it has existed and developed.

We now arrive at the question: Do these internal and ex-

ternal environmental changes continue to induce growth and developmental responses and modifications in personalities after birth? It is well known to most of us that they do. But the environmental influences acting on the individual during the more mature stages give rise to postnatal modifications of less severity to the gross structure and nature of the person than do comparable prenatal irritations. Nevertheless, from a standpoint of individual personality, the postnatal development and differentiation are modified by progressive experiences to an extent of serious importance.

The Internal Environment and Postnatal Epigenetic Changes

What are the varying conditions of the internal environment which still influence the nature of the individual after birth? Some of them are the results of the same general epigenetic changes which were observed before birth. As the function of each organ and part is initiated, the products of its activities are added as stuff new in either quantity or quality to the chemical coördination of this organism. The body responds through the reactions of all its parts, and normally balances itself to these new internal compositions. Certain organs or glands begin to elaborate peculiarly effective products. These substances have been termed hormones by the late English physiologist, Starling, who contributed so fundamentally to our understanding of the function of such stuffs. Hormones from the glands of internal secretion circulate in the fluids of the body, and are highly effective in regulating and controlling growth and differentiation.

Development after birth, like embryonic development, is, therefore, not merely a growth or increase in size but still an epigenetic process, each stage to come depending upon the perfection and quality of the preceding stage. No step can be omitted or misplaced without producing an effect on all subsequent processes of maturation. This progression is largely accomplished through a continuous elaboration of new internal products which tend to direct and insure the nature of the final individual.

The Radical Change in External Environment at Birth

The most commonly striking feature of birth is the adoption of a new external environment: the young animal is born from the mother or the egg into the outside world. This external environment of postnatal life now begins to influence, as did the surroundings of the womb or egg in the prenatal time, the success of the internally directing forces in the young individual.

The new environment is freer and more extensive in its possibilities than the prenatal surroundings, and the young animal must react to it in far more complex ways. The external environment supplies all the needs of the growing young, and the quality of these supplies is most significant for constitutional perfection. The quantity and quality of ordinary foods, the supply of necessary mineral salts and the availability of those peculiar substances, the vitamines, can never be disregarded in a consideration of the influences of external environments on the internal chemistry and the final personality of the developing animal. But to

attempt a detailed consideration—which would, of necessity, be voluminous—of the various effects which might result from modifications in the supply of any of these stuffs, is unnecessary for our immediate topic.

The environment supplies everything material and the organism develops only the desire, which itself arises from imbalance in stuffs, to use these materials.

We have frequently been surprised during recent years to learn that the merest traces of some almost unrecognized stuff are of profound significance in the economy of the animal constitution. The absence of only a single vitamine, usually derived from a certain vegetable food, may cause the most alarming nervous symptoms with distortions of the body-chemistry and growth in the young animal. Again, the absence of a single trace of some chemical element may derange the function of an important organ. The absence of iodine from the environment, for example, may modify the growth and alter the health of man and other mammals on account of its apparent necessity for the thyroid gland function. Thus after birth, as before, the life and activities of the organism are so interwoven with the environment that no biologist may think of the one without the other. The animal and its environment are really a single compound curiously knitted together: either would be different if the other should change.

The postnatal environment differs from the prenatal in one other important regard. It is the outside world in which a multitude of other organisms exist which may come in various degrees of contact with the newborn individual. Such contact comprises a complex part of our postnatal existence, and includes all forms of association with others of our

own kind, commensalisms with domestic animals of other kinds, parasitisms in which we usually play the rôle of host, symbioses or mutually beneficial associations which we may enjoy with certain friendly bacteria, the consumption of living things as food, and the harboring of both harmless and disease-causing organisms. A discussion of any one of these forms of contact is not within our present province, but it may be readily realized that all or any one of them may be most intimately related to the constitutional nature of the personality concerned.

The constant presence of a chronic bacterial infection, for instance, may modify the secretions and chemistry of the body in such a way as considerably to influence the nervous system, causing a formerly kind and agreeable person to become nervously distorted and unbearable. Physical changes, such as modifications in the bony frame and alteration of personality, may be similarly brought about by infection.

The same disease-causing organism does not induce the same effect on all personalities. It may produce in one person a fatal effect, in another a severe illness, in another only mild consequences, and in another no ill effects whatever. These different effects are not due in all cases to differences in the attacking organism, not to differences in virulence, but rather to differences in the constitutional quality of the individual persons attacked.

Another phase of these biological associations in which we are interested is the actual change in constitution which they themselves may induce. The best-known examples of these changes are the constitutional states called immunity in which the individual animal has become so altered that

the given disease germ can no longer produce inconvenience to its body. Immunities in themselves may very probably induce constitutional states which modify to some extent the further growth and developmental qualities of the individual.

Racial resistances to certain organisms are peculiar to definite constitutions, and these reactions may be inherited through generations as actual constitutional qualities.

Periodic Changes in Constitutional Personality

The definite changes in form and disposition which occur at clearly accented periods of life are of peculiar interest in the process of postnatal human development. These changes bear an important relation to subsequent normality of structure in the individual, and particularly to his mode of response to various constitutional and infectious diseases. The most obvious periodic occurrences are those associated with sexual development and maturity. These are made particularly conspicuous because of the contrasted features and dimorphic responses of the two sexes. Each sex not only shows different primary sex characters, but exhibits a list of so-called secondary sex characters which are strongly contrasted between males and females.

The periodic changes in structure associated with the reproductive apparatus and the final attainment of sexual maturity are thought to be brought about through growth-stimulating substances which arise in the germ-glands, the testis and ovary. These, technically called gonads, are not alone germ-glands in which the male and female germ cells

are produced but in addition highly important glands of internal secretion. It is the influences of the internal secretions from these gonads which bring about the normal development and the periodic changes in structures and functions associated with the processes of reproduction in mammals.

The Early Influence of the Gonadal Hormone in Development

The gonads in both sexes seem to exert definite effects on important structural developments during three different periods of life. Modifications and failures in the formation of the genital structures are readily demonstrated to follow either alteration or removal of the gonads. We have already, in connection with the free-martin calf and experimental grafts, considered in a general way the effects of gonadal secretions on the development of the reproductive tracts during embryonic and foetal life. It may be recalled that when "twins" of opposite sex are produced in cattle it frequently happens that their two placentae become fused so that the blood from one embryo circulates through the body of the other, and the female twin becomes modified into a free-martin. The free-martin twin calf has been shown to possess abnormal external genitalia, the ovary is modified in structure and sterile for egg production, and the female genital tracts are arrested and undeveloped, probably on account of the circulation in her body of a hormone from the male gonad. We have also called attention to experiments which seemed to show that when embryos are grafted together in parabiotic pairs, the gonadal development of one member

of the pair may possibly modify the opposite sexual structures of the attached mate.

Natural cases are known in which animals are born with degenerate and abnormally developed gonads that may possibly lack the proper secreting or interstitial tissues. In such specimens as these the internal genital tracts of either the male or female sex may be deformed, defective or almost completely absent. The external genitalia of the same specimens are undeveloped and imperfectly formed. From evidence presented by various workers, after examinations of a large number of such defective individuals, it seems highly probable that the abnormal development of the gonad is the primary defect; and the direct consequences of this are the deformities and arrests in the internal and external genital organs. This interpretation is also largely strengthened by the results of early castration in immature and newborn mammals. The reproductive tracts in such castrates remain infantile or else become greatly reduced and degenerate, and the growth and development of the external genitalia are much arrested.

From these reactions we assume that the earliest effects of the gonads on structural development are the stimulations which call forth the normal, fully-expressed condition of the reproductive tracts and the external genitalia in the male and the female infant. The rôle of the gonadal secretions during prenatal development is to bring about the progressive development of these structures, and these developmental reactions furnish the best example of the early influence of a typical secretory hormone on structural expression.

Reactions to the Sex Hormones at Puberty

After birth there seems to be a cessation of secretory activity on the part of the gonads; or, at any rate, little structural response to such secretions takes place until just prior to the stage of puberty. During the time of puberty gonadal activity increases, and the resulting secretions exert important influences in bringing about the second great series of structural reactions in sexual expression. In a very short while the animal attains a fully completed development of the secondary sex characters, as illustrated by the gaudy plumage in birds, the horns and hair growths in the male of mammals, and the mammary gland development in the female. It is readily demonstrated that the development of these secondary sex characters, differing so greatly between the two sexes, is highly dependent upon secretions from the sex-glands. If the gonads be removed sometime before puberty, there follows either a more or less complete failure or a greatly altered expression in the development of secondary sex characters. This modification is clearly shown by failure in growth of the mammary glands, of the beard, of the distribution of the coarse hair on the body, general modification in body form, et cetera. Figure 49 illustrates the sudden and marked alterations in body form and plumage following castration in the Sebright bantam cock.

After puberty, the male and female constitutions are still more widely different from one another than they had been before.

The two sexes are of course constitutionally different

Fig. 49. Sebright bantam cocks: the upper specimen is the normal hen-feathered male with the head furnishings of the rooster; the lower figure shows a similar bird after being castrated. The plumage becomes gaudy and more rooster-like but the head of the capon now resembles that of the hen. (After Morgan.)

from the time of fertilization of the egg and, as we learn more about the details of growth and development, we are more and more impressed with the presence of these differences even during early childhood, when the secondary sexual dimorphism is not so universally evident. For example, the calcium metabolism and the important reactions depending upon it seem far better provided for in the female child than in the male; this is shown by the higher frequency of infantile tetany in boys as Bakwin and Bakwin have found and the probable high tendency towards rickets in the young male which Nonidez has found among fowls and I have found among dogs.

It seems quite definite that the probable interaction between the ovary and the parathyroid and pituitary glands gives a somewhat different balance of body stuffs and, therefore, a different growth matrix than that resulting from the interaction of the testis in a similar situation. When ovarian secretions are exchanged for testicular secretions, the entire animal body reacts to the changed endocrine complex. These differences are so accentuated after puberty that it becomes apparent that the male and the female of a species are constitutionally quite different animals—possibly in some cases their internal chemistry may be as far apart as that of two males or two females of different species.

The Third Period of Sex Hormone Influence on Structural Growth

Following the heightened activity of the gonadal secretions at puberty which has called forth the secondary sex

characters, we find the gonads entering their third period of influence over the structural reactions of the body. They now exert an important rôle in molding the general type of growth and development of the youthful individual striving for the adult state. This influence on body form again is evidenced by the abnormal youthful growth shown in eunuchoid individuals from whom the gonadal secretions are absent.

There are reasons which would lead us to think that the gonadal secretions actually influence the development of head form and body build. The sisters in a family, for example, have a higher cephalic index or rounder heads than the brothers. The general form and height of the individual is clearly different for the two sexes. And these differences are due to the different gonadal secretions in the sexes, the testicular hormone in balance with the other bodily juices forming a different chemical complex from that given by the ovarian hormone acting with the same juices. It is clear that, since the gonadal hormones do influence the development of form, the eunuch cannot present the typical shape and stature of a normal man; the ox differs in form from the bull; the castrated horse differs in several ways from the stallion; the capon is atypical for the rooster form; and there are pronounced differences between the spayed and the normal female body forms. The altered form of the cow after removal of the ovaries is shown in outline by Fig. 50.

Still other well-recognized structural changes—such as those that occur after menopause in the woman and during senility in the man, the more or less pronounced beard in

some women, and the general change in body form of both sexes—may be either primarily or secondarily associated with the modification and disappearance of gonadal secretions.

It must not be assumed, however, that the gonadal secretions independently and alone accomplish these changes.

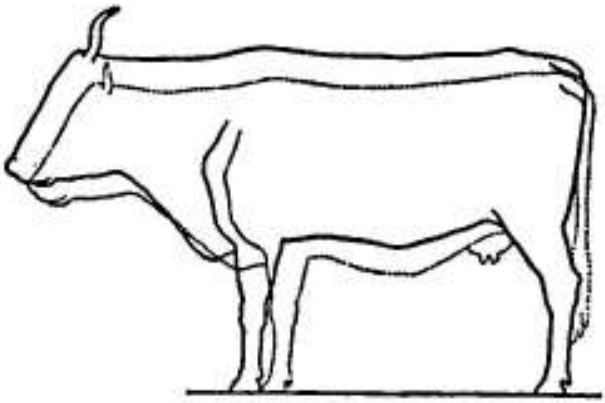


Fig. 50. The dotted line shows the average proportions of 100 normal cows from herd book records, and the solid line indicates the average of body form in eleven cows after removal of the ovaries. Castration produces modification in both body size and form. (After J. Tandler and Karl Keller.)

It is the presence of such secretions in the normal body chemistry as a whole which brings about normal growth. When the gonadal secretion is removed the entire chemical nature of the body is altered, and growth consequently takes place in a different way. When, therefore, the secretion is present, we should not say that it as such induces

a definite growth, but rather that its presence influences all other things in such a way as to give rise to this definite growth and typical form; without this one secretory constituent all other things are unable to bring about the same definite growth pattern; as is shown in Fig. 51 with the outlines of a normal man and the eunuch.

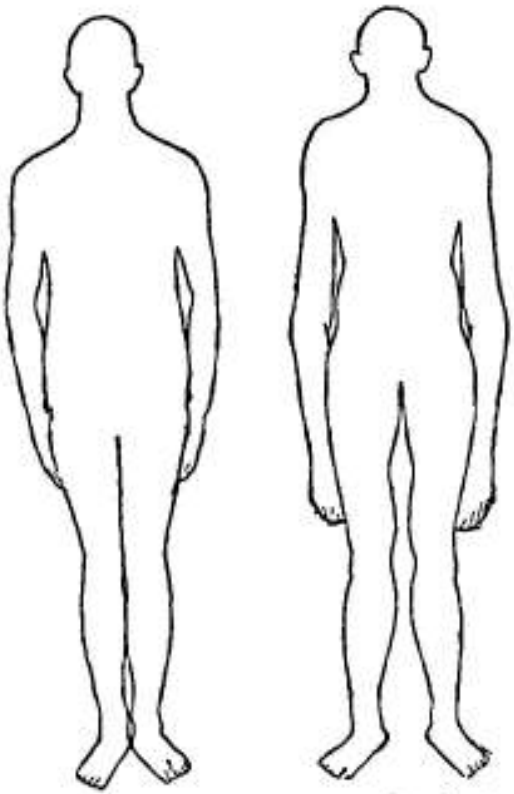


Fig. 51. Outline at the left of normal man showing the usual proportions. On the right the outline from a photograph of the modified proportions of the Skopec eunuch, Iwan Gregor. (Modified after J. Tandler and S. Grosz.)

Variations in General Growth and Functional Responses

The recognition of the personality changes resulting from modifications in the gonadal secretions serves to impress us with the fact that more or less marked responses to other chemical changes and varying hormonal relations are constantly arising within the body during the growth and development of the postnatal animal. Great variations in the size and functional activity of the glands of internal secretion are well known even among closely related individuals. Partly on account of these variations in the growth-affecting centers, which are largely expressions of the genetic backgrounds, it is a rare sight indeed to find every member of a family growing exactly alike. It is in general also true that the more mixed the race and the more artificial the environment, the more pronounced are the variations in the endocrine glands and the more varied the population becomes.

It is well known that certain races among men and other mammals tend to be short and small, while others are tall and large; some are stocky and fat, while others are thin and lean. We have the race-horse type and the draft-horse type, the beef cattle and the milk cattle, the dwarf-like African pigmy and the tall coastline Negro, the short statured Japanese and the tall races of China. These racial states are probably related in most cases to genetic tendencies for the determination of a given constitutional balance or, as Sir Arthur Keith has suggested, to a given endocrine complex. We also find in great abundance individual variations in personalities. The thin Jack Spratt who

could eat no fat and his buxom wife who could eat no lean are old acquaintances of ours.

All of these different personalities are normal variations in so far as they constitute the community population. Persons are accepted by the community and graded by their friends as lazy or industrious, stupid or intelligent, ugly or beautiful, melancholy or happy, serious or frivolous, good or bad, honest or rascally; and, to the casual mind, there the matter begins and there it ends. But we know from all that has gone before that these attributes do not begin in the adult and, furthermore, that they need not in all cases remain there. There must be a cause for each of the contrasted states. Genetic backgrounds tend toward certain of them, and in all the developmental expression and the growth balance of the individual play a determining rôle.

We might boldly state that almost any one of us could from time to time embrace all of the contrasted characters mentioned in the previous paragraph. We usually make too little use of ourselves as a specimen in analyzing the reactions of others. I may be lazy and unable to drive myself even to a pleasant task; I wonder at the cause and find that I may have a disturbed digestion, or have had too little sleep and am slightly out of industrious condition. A perpetually lazy man is an unbalanced man and we might discover his handicap, even though it be impossible to remove. Wild animals are not lazy unless actually unwell or constitutionally distorted, and in the latter case we term the condition the "nature of the brute." When a commonly industrious man becomes lazy he has a constitutional disturbance. Stupidity and intelligence may often be alternating states of the same mind.

When a person has been without sleep for several days, or is ill and exhausted, his mental reaction may be decidedly stupid. He may be unable to reason logically or fairly. Yet on restoring a wholesome condition this same mind may function with high intelligence. Doubtless many men are stupid on account of some chronic nervous irritation which if removed might decidedly elevate their mental level. Bad food frequently induces awkward thinking.

Ugliness and beauty are frequently observed in the same individual under different physiological states. Any chronic disease may mar the beauty of the fair. As the Germans express it, *Schönheit bedeutet Gesundheit*, beauty indicates health. The melancholy man may become happy and the happy man may become melancholy, the serious may become frivolous or the frivolous serious, as the results of changes in their relation to their environments which tend to alter the physiological states of their constitutions. If we understand what makes a happy person temporarily melancholy, we may surmise something of the state which induces permanent melancholia in another individual. Goodness and badness, honesty and dishonesty, in common parlance, may, in certain cases at least, result from differences in functional state.

Although the above point of view might be admitted as correct in some cases, it must be remembered that it is not at all applicable in many others. There are of course definite defects and distortions in certain individuals which cannot be altered. Stupidity and ugly appearance may be of genetic origin and permanent; or similar conditions may have resulted from developmental arrests and are, therefore, congenital and cannot be removed. It becomes a duty

of the student of personality to be able to differentiate the types of causes for abnormal conditions, and on this basis to prognosticate the possibilities of establishing the normal state.

XII

EXAGGERATED DEVIATIONS FROM RACIAL TYPE

WHEN the clever prestidigitator performs his trick with accurate precision we marvel at the result. But when, through some slip or accident, the trick fails we laugh at its absurd simplicity. And so when nature produces the normal individual, with only slight deviations from the standard type, we get little inkling of the parts played by the many different factors concerned; but, when the process slips on account of an upset in the balance of parts, and the resulting individual is far from the standard type, then we may find it a simpler problem to unravel the skein of controlling threads.

If this supposition be correct, we may well afford to give attention to peculiar types and the so-called freak individuals which occasionally occur among men and other mammals. It has long been known that certain freak individuals may arise with surprising frequency in a given family or in a particular community. Among certain breeds of animals, peculiar types may appear as the common run of things. These facts suggest a probable genetic or hereditary origin for the unusual forms.

Hereditary Gland Defects Causing Modified Form

When we examine the structures and shapes of modified animal types, we often observe many conditions closely

similar to the peculiar growth reactions known to result from disturbances and deficiencies in endocrine gland secretions. We might, on this account, attribute some of the freak types to deviations or disease in the glands of internal secretion. On further study, we may find that the strange type is actually of genetic origin, a mutant or sport; nevertheless the primary effect of this mutation is the production of a peculiar deviation in glandular development. And these glandular deviations are the directly responsible elements in bringing about the peculiar freak type of development which is the noticeable end result of the primary gland mutation. Thus, for example, one might think that the bulldog inherits his grotesque form and appearance as such, while, as we interpret it, he directly inherits definite abnormality of internally secreting glands and these defective glands act as the secondary cause for the bulldog pattern.

If such an interpretation be permitted, it becomes of prime importance to determine, in the first place, whether the apparently comparable freak types found among different kinds of mammals are truly similar conditions and, secondly, whether the strange glandular complexes which must underlie these types are also similar in their deviations. And, finally, if such conditions are found to be of genetic origin, the mode of inheritance of these distortions should be accurately studied and analyzed.

The types to be kept in mind are the frequently seen dwarfs, giants, and otherwise unusually formed but *definitely typical* individuals. The small, gracefully formed dwarfs, usually termed midgets or ateliotic dwarfs, constitute one of these types. Other persons are seen to be

dwarf-like but stocky individuals with large heads and flat, often sunken-in, faces and a protruding or undershot lower jaw. The body or trunk of such dwarfs is large and long, almost or quite of the common size, but their arms and legs are short and peculiarly bent. These are the so-termed achondroplasic dwarfs or stocky bulldog dwarfs. The point of particular significance is that all of the individuals oc-

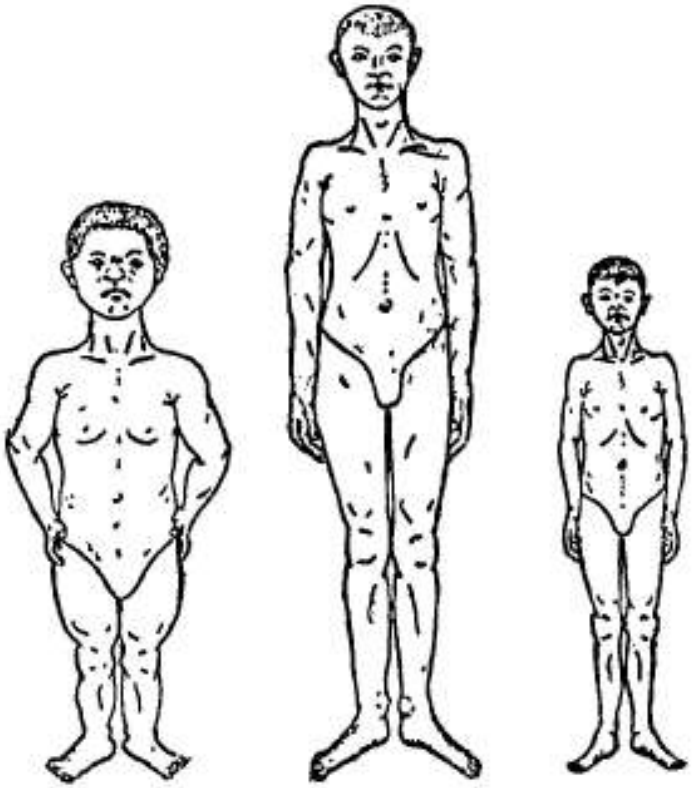


Fig. 52. The body form of a normal full-sized man between the outlines of a stocky achondroplasic dwarf on the left and the gracefully tiny form of a true midget on the right.

curring under any one of these types are closely similar in form, structure and functional reactions. Their general behavior and the tone and pitch of their voices are on a singularly uniform pattern. The group constitutes a new race, as it were. Fig. 52 shows the two dwarf types contrasted with the outline of a normal person.

In contrast to these diminutive types, there are other equally definite gigantic deviations from the common size and form. Human individuals occasionally grow to be seven or eight feet tall and may weigh as much as four hundred pounds. Some of these giant persons are well-proportioned, with pleasing features, particularly during youth. They are simply giant individuals. Most giants, however, show a strong tendency to develop heavily exaggerated facial features and disproportionately large and heavy hands and feet, characters which are generally associated with glandular disease and usually termed acromegalic overgrowths. These giants with exaggerated heaviness of features are classed as acromegalic giants in contrast to the normally proportioned giant. Large animals are particularly liable to develop acromegaly or thickening of the features as a complication, just as dwarf individuals are so apt to show some degree of peculiar cartilage growth which produces the short-bent legs and "dish-faced" condition technically termed achondroplasia.

Various degrees of insufficient cartilage growth, achondroplasia, may be present only as a localized expression while in other cases it may be a general skeletal condition, or it may exist simply as a mild expression in normal full-sized animals, apparently unassociated with dwarfism. There is a strong probability, however, that some degree of

dwarfism may occur in the families of persons stamped with this inclination. In the same way excessive growth of facial features and heavy hands and feet, acromegaly, may appear in individuals of normal size among human beings as well as lower animals, although again we find this to be associated with the secondary tendency to produce large and giant-like descendants.

The Remarkable Diversity in Structural Types among Dogs

The deviations in structural types are more clearly pronounced and more widely differentiated among the numerous breeds of dogs than among any other species of mammals. Dog fanciers, for reasons of their own, have shown a peculiar taste for these strange and often grotesque individuals.

Practically all of the peculiar dog breeds have been derived through hybridization, and it may have been due to the crossings that so many germinal mutations and sport-like forms have appeared. When odd types began to occur, the breeders carefully isolated and preserved them in order to bring about the artificial races. Many of these breeds exhibit some form of structural distortion, which may be associated with strange and widely modified complexes of the endocrine glands. The breeders, of course, have been entirely ignorant of the basis for their selection. They have chosen specimens solely on account of their strange forms, which could be readily observed. But in many cases the form was only the symptomatic expression of the distorted growth-controlling complex of internal secretions which lay

behind the situation. And behind all this were the genetic mutations which gradually became purified through selective breeding.

Other mammals, and birds also, frequently show structural peculiarities closely similar to those exhibited by the various dog breeds. There are giant and dwarf horses of comparatively simple type. There are giant and bantam breeds among fowls. There are large and dwarf cattle and, among the smallest, the Dexter breed originally from Ireland shows a marked degree of achondroplasia, which is, as remarked above, so frequently associated with dwarfism. Professor F. A. E. Crew, at Edinburgh, has quite recently studied cases of the extreme achondroplasic condition in the monstrous "bulldog" calf which is produced only by Dexter-with-Dexter cattle matings. The Dexter cattle are quite certainly of hybrid origin, and Crew regards them as a Mendelian di-hybrid, the parental stocks having differed from one another at least in respect to two pairs of contrasted characters—coat color and bodily conformation.

Crew supposed a malfunctioning of the pituitary gland to be the responsible causal agent in the production of the "bulldog" abnormality. This peculiarity of the gland he believes to be inherited in a definite manner.

Only a short time before these reports on cattle, we had pointed out, from an investigation of the glands in various dog breeds, that the bodily forms and unusual conditions in these animals were closely comparable to similar human types and were probably associated in similar ways with glandular peculiarities; see Fig. 53 showing closely comparable skull forms in men and dogs.

Many records from the literature had seemed to indicate

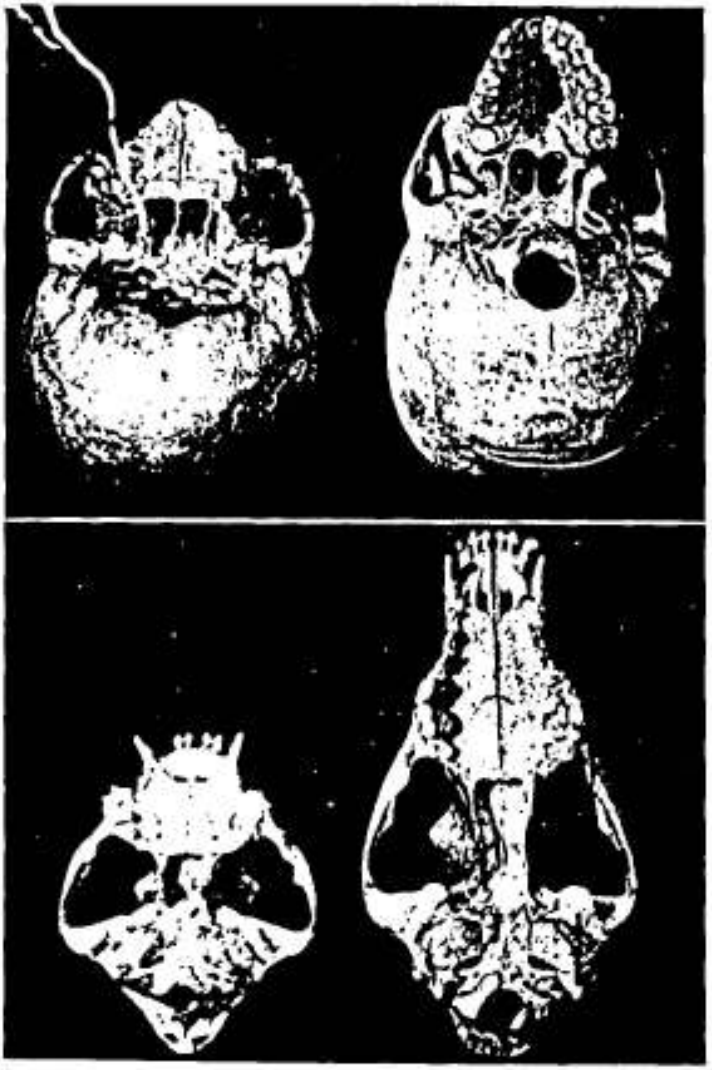


Fig. 53. The lower surface of the skull of a normal man, upper right, beside a similar view of the achondroplasic skull from a stocky dwarf. Below is the lower surface view of the normal dog skull, German shepherd, and the shortened, abnormal and achondroplasic skull of the English bulldog. The similar contrasts between the two human and the two dog skulls is very marked even in detail.

Fig. 54. (Right) *The enormous difference in size and strength between the skeletal frames of a giant St. Bernard dog and a dwarf toy poodle; showing contrast in form between domestic breeds of the same animal species comparable to the contrast between human giants and dwarfs.*

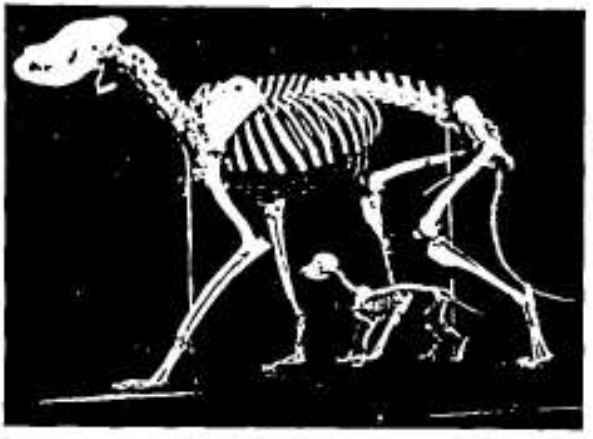
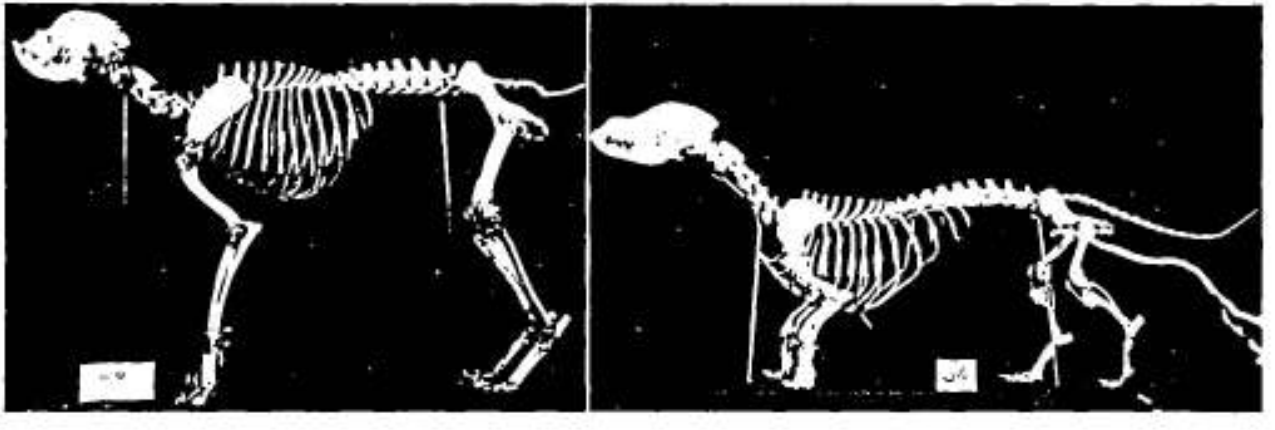


Fig. 55. (Below) *The completely contrasted skeletons of the bulldog and the dachshund. The head and vertebral column is deformed in the bull and normal in the dachshund, while the extremities are shortened and deformed in the dachshund and normal in the bulldog.*



that these conditions are clearly genetic in origin, since they were found to be definitely transmitted through the male. Ries. hbieth and Barrington, in 1912, brought together in a splendid monograph various studies of dwarf conditions in man. They showed the short and peculiarly formed bones in achondroplasia, for example, to be already present far back in the early foetus. This typically peculiar growth continues throughout development until the adult dwarf condition is attained. Such a state is in no sense the result of peculiar secretions in the mother, since a dwarf child may be born from a normal mother who at other times has given normal offspring. The achondroplasia is due to certain definite complexes within the developing individual itself. And pedigree records show cases of achondroplasic dwarf men siring both male and female achondroplasic dwarf children even though married to normal women.

In these highly modified types the coordination of the normal growth-regulating mechanisms have slipped, as it were, and nature thus furnishes us with exaggerated expressions on the basis of which it may be possible to analyze the milder normal variations in constitution. For such an analysis the modern dog breeds provide a splendid amount of material, carefully selected through a long number of generations and in respect to a few breeds for at least centuries of time. Strangely enough, dog fanciers have been unconsciously selecting and preparing a splendid array of material, most ideally suited for a scientific investigation both of the inheritance of endocrine gland disturbance and of the effects of such disturbances on the growth and form of the mammalian body.

The Breeds of Dogs and Their Type Classification

Among dogs there are typical giants without acromegaly like the great Dane and the Irish stag-hound. Again there are giants with strong acromegalic symptoms, like the St. Bernard and the mastiff. And again there are bloodhounds with apparent acromegaly in the absence of pronounced gigantism. There are hounds, pointers, shepherds, and huskies, representing the normal growth type for the dog. Ateliotic dwarfs, or typical midgets, are found among the toy dogs with only slight if any symptoms of achondroplasia. Figure 54 illustrates the enormous difference in size between the skeletons of a giant and dwarf dog. Other dwarf dogs exhibit decided achondroplasia, as the Pekingese and the French bull. There is sharply localized achondroplasia in the axial skeleton of the Boston terrier, particularly in the basicranium, the sacrum, and the coccygeal region; and an equally distinct but differently localized achondroplasia in the legs of the dachshund and the basset hound, while the head and vertebral skeleton in these dogs are perfectly normal. (See Fig. 55.) The British bulldog has highly marked achondroplasia without much dwarfism.

There are nervous hyperthyroid types of dogs among the terriers, such as the Brussels griffon and the small black-and-tan, with marked exophthalmia. There are microcephalic races in which the brain is disproportionately small, like the wolfhounds, and other breeds with very frequent internal hydrocephalus in which the brain appears large but is structurally thin and distended with fluid; this occurs in the German boxer dogs and the bulldogs.

All of these types are commercially valuable to the dog

fanciers and, consequently, they have been carefully selected and purely bred. It has been found, in our experience, that the pedigrees of valuable dog stocks are surprisingly reliable and this is constantly demonstrated by crucial breeding tests.

Animals that exhibit such a variety of conditions, closely resembling many structural reactions of serious importance in human personality, appeal to one as exceptional material for an analysis of the inheritance and development of these widely modified characteristics.

XIII

INHERITANCE OF FORM AS RELATED TO PERSONALITY AMONG DOGS

EVERY one acquainted with dogs is aware of the fact that the breeds differ not only in shape and size but just as truly in manners of behavior. With closer observation and study it will be found that the characteristic behavior of each breed fits in a very definite way the form and appearance of the animal and follows what we know about the modified behaviors of peculiar types of human beings. The bearing, the stride in walking, and the heavy sweeping gesticulations of the human giant are strikingly simulated in the actions of the St. Bernard dog, and the deep hoarseness of the voice is the same in the two. The quick nervous vivacity and squeaky yapping voice of the black-and-tan toy dog or the Pomeranian poodle resembles in a most suggestive way the manner, reactions, and voice of the tiny human midget. Few companionships attract so much attention as that of the midget man and the tiny dog on promenade together. The quiet, determined, and rather severe attitude of the stocky achondroplasic human dwarf is very closely paralleled by the demeanor and voice of the bulldog.

Certain breeds of dogs are known for their friendliness and others for their shyness, some for a dignity of bearing and others for their frivolous foolishness. And the playful

irresponsibility of puppies is contrasted with the reliability of the adult dog in much the same general way as the natural behavior of childhood is with that of the average man.

An analysis of the behaviors in the different dog breeds as associated with their physical types and forms is by no means a casual or simple undertaking. Yet this variety of behavior and diversity of form supplies material extremely useful for most careful experimental study—a study, however, which at this time is but in its beginning. So that our present discussion is more profitably confined to the question of inheritance and development of the modified structures and shapes which have appealed so directly to the fanciers of dogs, and which are so exactly comparable to important conditions in man.

The Genetics of Short-bent Legs in Crosses between Basset Hounds and Shepherd Dogs

The manner of inheritance for short-bent, achondroplasic legs in dogs otherwise normally formed serves very well to demonstrate the actual genetic basis for many peculiar structural reactions. As we have seen, achondroplasia appears sporadically among almost all classes of mammals, including man, and its origin and expression are very probably due to similar causes wherever it occurs.

The basset hound originating among the dogs in western Europe and the dachshund in central Europe are the two simplest cases in dogs of localized shortening and deformity of the extremities. In these animals the front legs may show a most extreme degree of achondroplasia in all the long bones, resembling in every detail of structure the well-

known condition found in man. The hind legs are somewhat less affected, as is usually the case with achondroplasia, and the proximal segment of all extremities is the most abnormal; the feet are disproportionately large with toes tending to spread apart. In these two breeds of dogs no other region of the body shows any noticeable trace of achondroplasia; the condition is strictly confined to the feet and the long bones of the extremities. The probable reason for this localization we shall discuss later.

The human achondroplasic dwarf, modified in the axial as well as the limb skeleton, has a quite easily recognized behavior and disposition. It is suggestive to find that dogs only show a comparable behavior and disposition when the skull and, therefore, the brain is affected by the dwarfing and shortening. The basset hound and dachshund with only their legs affected show no such dwarf behavior at all.

When the short-bent-legged basset hound is crossed with the normal, wild-type, long-legged German shepherd, often in error called police dog, the hybrid offspring are all very closely alike in form, coat texture, color, and behavior; and this is true, no matter which breed is used as sire or dam. The progeny are all short-legged like the basset parent and none have the long legs of the shepherd. The shortness, however, may vary somewhat and is rarely so pronounced as in the pure basset hound. Even among pure breeds the achondroplasic shortening shows some variation in its degrees of growth expression, but shortness in the pure state is more extreme than in the hybrid or mixed condition. The short-legged, F_1, hybrids all have the long drooping ears of the hound and never the erect ears of the shepherd, and the voice or bark is also more hound-like

than shepherd-like. When these hybrid pups are reared by a shepherd mother and have never seen a basset hound, they will, when put on the field for the first time, scent with their noses down and bark as they run, behaving as their hound father would do, acting in a manner entirely unlike the reactions of their shepherd mother with whom they have always associated. Thus their hunting instincts are as truly inherited as leg-lengths or hair color, being probably associated with acuteness of smell, and are not, in this case at least, developed as a conditioned reflex.

The quality of hair and the coat in general is shepherd-like in the hybrids, as is also the color except for a more frequent white foot or small white spot on the chest. The shepherd coat and color is dominant over the hound hair and pattern, but not completely so; the hybrid is slightly intermediate in these respects. The hybrids are large and quite alike in size, and anyone seeing a pack of them for the first time will be struck by their remarkably uniform type.

When the short-legged first generation hybrids are mated *inter se*, their offspring, the second generation, show a clear-cut redistribution of a number of the contrasted grandparental characters; see Fig. 56 showing the conditions involved in this cross. Both the short-bent legs of the basset and the long straight shepherd legs reappear in the second hybrid generation in the expected Mendelian ratio of 3 to 1. The shortness of legs differs among the members of the short group; about one in three is as short as the pure basset, while the two others are not so short, resembling more closely in length the legs of the F_1 hybrids. The long-legged animals of the F_2 generation are truly long, like the shep-

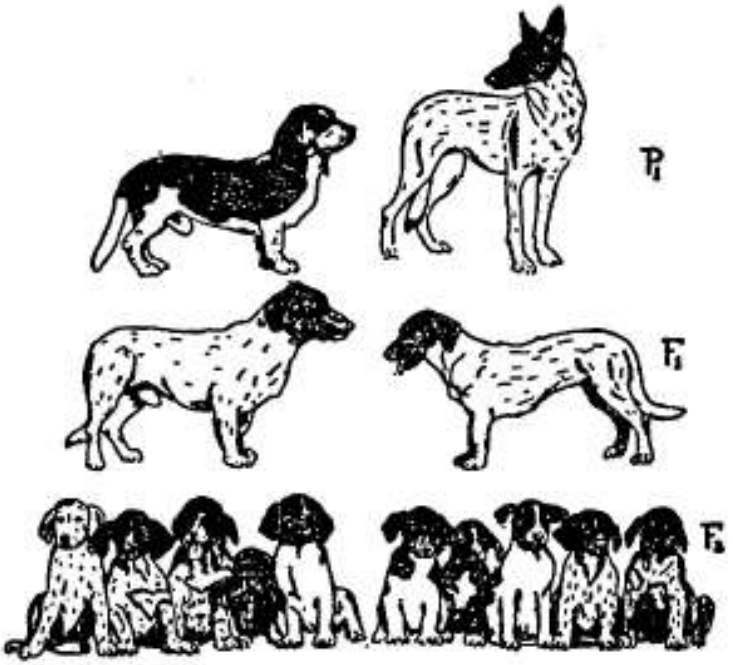


Fig. 56. Inheritance of leg length in the basset hound German shepherd cross. The F_1 generation are all short-legged but somewhat longer than the basset. The F_2 generation has individuals with very short basset legs, intermediate legs as in F_1 and the recessive long leg of the shepherd. Short legs are dominant but only fully expressed in the pure homozygous condition.

herd grandparent, and are thus a typically extracted recessive for leg length. The typical behavior of such a recessive character is clearly shown in the diagram, Fig. 57.

The strange achondroplasic modification of the legs would thus seem to be inherited as a single-factor Mendelian dominant, in spite of the apparently complex nature of its growth and development. It may also be that in the

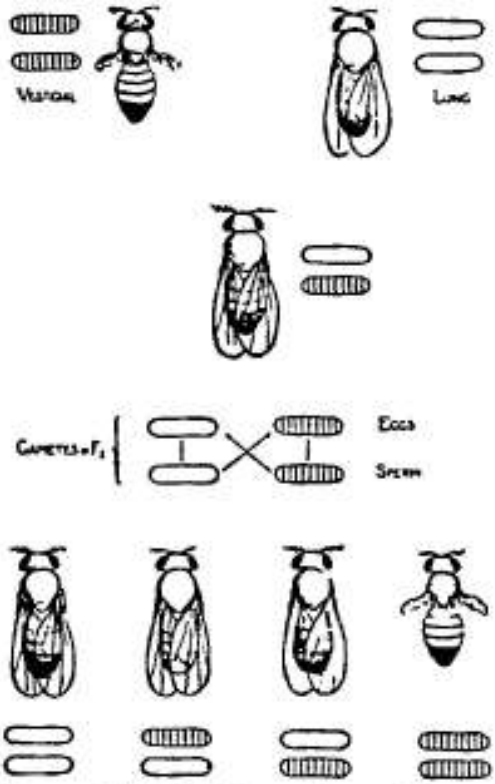


Fig. 57. Diagram of the inheritance of a purely recessive character, vestigial wings, and a purely dominant, long wings. The basis of the two characters is carried in corresponding chromosomes; the one for vestigial is cross-barred and the one for long wing is white. The first generation hybrids are all long wing though carrying the vestigial chromosome. In forming the second generation there is only one in four chances of two white or two cross-barred chromosomes meeting; therefore, there results one pure long wing with two white chromosomes, one pure vestigial wing with two cross-barred chromosomes and two impure long wing with both a white and a cross-barred chromosome. ***(After Morgan.)***

mixed hybrid, or heterozygous, condition shown in the F_1s and in some F_2s the reaction is not so heavily expressed as in the pure, homozygous, basset parent stock and the very short, probably pure F_2s. The very short-legged F_2s may be homozygous dominants, and they occur in about the expected 1 to 3 ratio. Thus the entire F_2 group for leg length may be divided into the classical Mendelian ratio of 1: 2: 1 —one very short-legged, two short-legged, and one long-legged. The certainty of the mixed partial and pure complete conditions are now being tested by breeding. Figure 58 shows the contrasted leg lengths in adult F_2 animals.

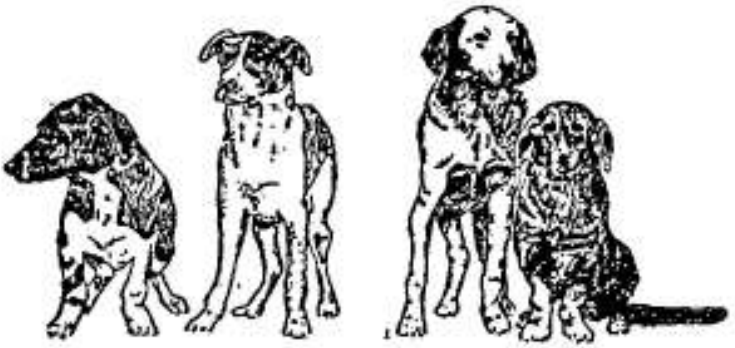


Fig. 58. Adult F_2 basset-shepherd hybrids showing contrasted long and short leg lengths.

The manner of inheritance for achondroplasia in the extremities has been further tested in these breeds by back-crossing the first generation hybrids on both parent stocks. Back-crossing is a prompt and effective way of testing the inheritance of a single character, since the expected numerical proportions are not so complex. When an incompletely expressed dominant character in the first hybrid is tested by breeding back on the parent from which it came,

all the young will be expected to show this character; but only half of the offspring by chance will have received a factor for this character from the hybrid parent and, therefore, only these will be pure and show full expression of the dominant trait. The other half of the offspring will have received the factor only from the pure parent and not from the hybrid, and these will thus again show an incomplete expression of the character, just as the first hybrid generation did. The expectation in our present case is, therefore, for equal numbers of pups with very short and with incompletely short legs.

When a member of the short-legged, first hybrid generation is bred to the pure basset hound parent, all of the offspring are short-legged, but about half of them have much shorter legs than the others. This fact again would indicate that the dominant achondroplasic character of the legs is more fully expressed when homozygous or pure than when mixed or heterozygous, see Fig. 59 illustrating this back-cross.

This incomplete expression in the hybrid condition is found for a number of well-known dominant characters, as was first clearly shown in the blossoms of the cross between white and red "four o'clocks" by the eminent German botanist, Correns, one of the three rediscoverers of the Mendelian laws. Figure 60 illustrates the result of crossing white and red "four o'clocks," giving in the first hybrid generation pink blossoms as an incomplete dominant expression, and in the second generation one white blossom pure recessive plant, one red pure dominant, and two pink blossom hybrids.

The back-cross in the other direction between the hybrid,

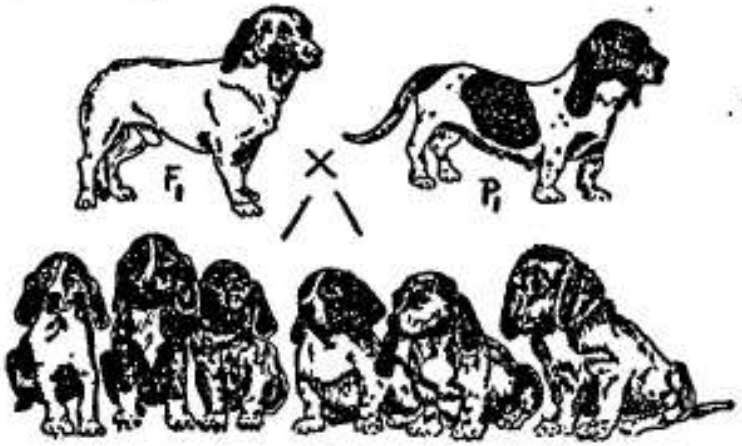


Fig. 59. Back-cross of F_1 basset-shepherd hybrid on pure basset stock giving equal numbers of full short and intermediate short-legged pups.

F_1, shepherd-basset and the shepherd parent gives both pure recessive long-legged shepherd-like pups and mixed or heterozygous short-legged shepherd-coated pups. At present the number of these recessive back-cross young is small, and the expected ratio of one long to one short-legged animal has not exactly obtained, there being ten long to seven short-legged pups; see Fig. 61.

In these crosses it is also interesting to note that the hound coat pattern of white, black and brown spotting acts as a single-factor recessive and is not linked with the leg condition. Some of the long-legged F_2 pups may be hound-spotted, as the illustrations show. The erect ears of the shepherd dog is a character more complex in its genetic background, probably a multiple factor recessive but not definitely linked with the dominant shepherd coat, nor with

the long legs, as one of the specimens in Fig. 61 will show. We have obtained one erect-eared, short-legged shepherd-coated dog, a very odd specimen in general appearance.

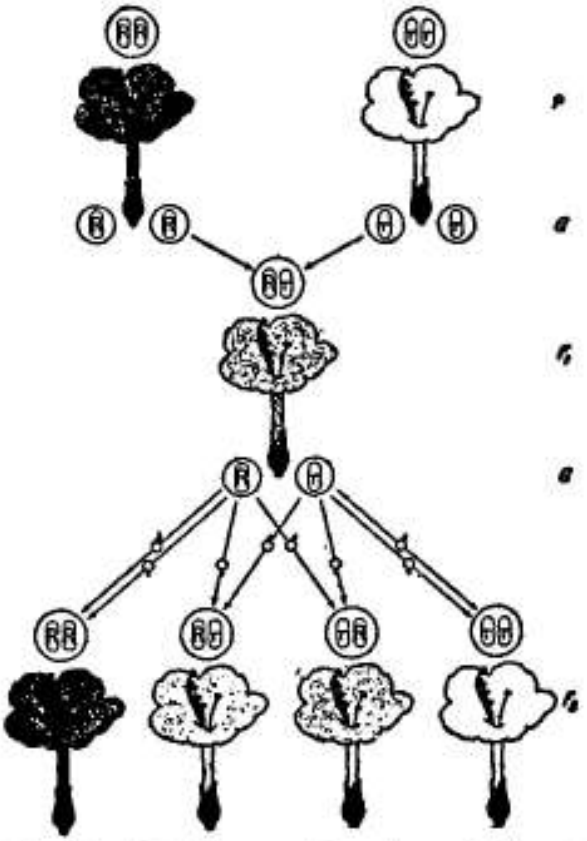


Fig. 60. The classical case of an incompletely expressed dominant character in the blossoms of the "four-o'clock," Mirabilis jalapa. When red- and white-blossom plants are crossed, the first hybrids are pink in color and when these are bred together the second generation shows one red-blossom plant to two pink and one white. (After Correns.)

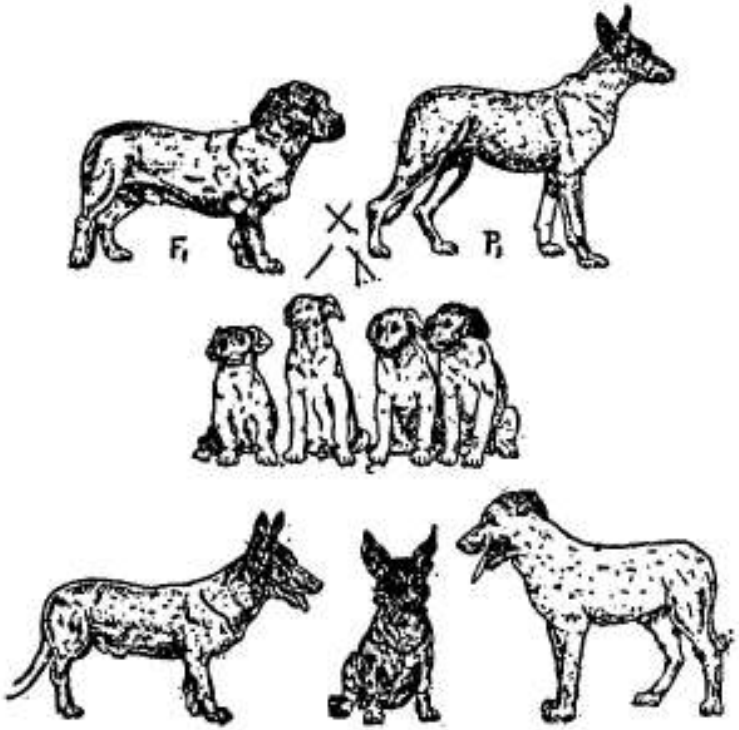


Fig. 61. Back-cross of F_1 basset-shepherd hybrid on the pure shepherd stock. This produces intermediate length legs and long legs on shepherd-like dogs. The lower figures show the contrast between short and long legs and also the typical shepherd body and head with erect ears and short legs, a very queer combination.

Finally, from the basset-shepherd experiments, when an extracted recessive, F_2, long-legged animal is mated with the pure shepherd stock it would be expected that all the offspring should show a truly long-legged condition, and no contamination whatever should appear from the former association with the achondroplasia. At present we have no results from exactly such a mating. In Fig. 62, however, is

illustrated a somewhat parallel case: a short-legged hybrid basset hound male was mated with a pure shepherd female, and the exact expectation of two long and two short-legged pups was produced. One of the long-legged females was mated with a pure shepherd male and nine young were born and lived to be adults. All of the nine dogs were long-legged, with no symptom whatever of the achondroplasic shortening. These results strongly indicate that if the factor for achondroplasia is present within the germ cells, it will assert itself as a dominant character in the offspring.

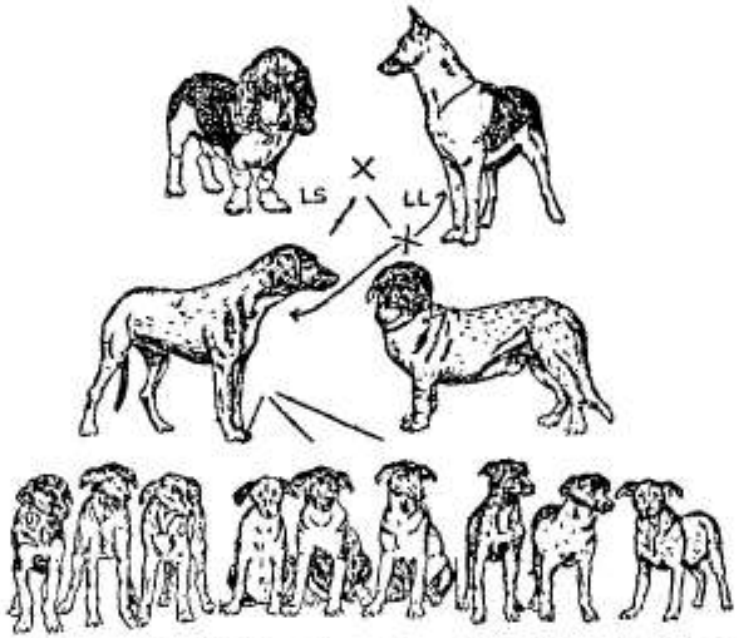


Fig. 62. A hybrid short-legged hound by a German shepherd gives half long and half short-legged offspring. The long-legged mated back to the shepherd gives all pure recessive long-legged dogs.

Crosses Between Animals Having Differently Localized Dwarfed and Shortened Body Parts

The German dachshund has a normal head, body, and tail; and it is a well-balanced normal animal in its behavior, although retiring and shy. On the other hand, it shows pronounced achondroplasia in the much shortened extremities, as the illustrations indicate.

The Boston terrier is an almost perfect contrast to the dachshund. It is a partial bulldog type, with straight long and well-developed legs but with a very much shortened base of the skull and face and a short broad palate. The cranium in the Boston terrier is rounded and wide, with a marked depression below the forehead at the nasion; the upper jaw or muzzle is short and reduced, while the lower jaw is almost normally long and, therefore, somewhat undershot and protruding. These are, in other words, the gross characteristics of achondroplasia in the head as recognized for that condition in man. The Boston terrier also presents other symptoms of achondroplasia and deformity located in the vertebral column, particularly in the short and twisted tail and the sacral regions. In the female Boston terrier, as in the human achondroplasic female, the pelvic outlet is thus reduced and normal delivery of the young is frequently impossible. Operations must at times be resorted to in order to deliver the young and save the life of the mother. The contrasted skeletons of these two dogs are shown in Fig. 55 facing page 223.

Both the dachshund and the Boston terrier are considerably dwarfed in size. When these breeds are crossed,

either dog being used as sire or dam, the F_1 hybrids are uniformly alike. The legs of the hybrids are achondroplasic and short from the dachshund parent and their heads are somewhat modified, the muzzle being shorter than in the dachshund and the cranium wider, yet not completely reaching the Boston type of head. The tail is long and well-developed, the pelvis normal, and these hybrids whelp their pups without trouble.

In color, the F_1 hybrids are a striped brindle with small white spots or flashes on the chest, the basic Boston pattern. They are all uniform in size and closely alike. Their cranial shape more nearly approaches the Boston and, in behavior, they show rather the nervous, jumping, noisy disposition of the Boston terrier than the quiet and shy demeanor of the dachshund.

On mating these hybrids *inter se*, the resulting second generation gives animals which show most curious combinations of the grandparental characters. The short-legged condition is here again expressed as a single-factor dominant in conformity with its record in the basset-shepherd cross. The Boston head and tail are multiple-factor expressions and are quite independent of the leg condition. There are dachshund-legged dogs with Boston head and long bent-tail or short screw-tail. There are tall long-legged F_2 animals with dachshund heads and tails as well as coat color (refer to Fig. 63).

The Boston head is not altogether recessive nor dominant: its full expression would seem to concern both dominant and recessive factors, and some resemblance to this head type exists in almost all members of the F_2 generation.

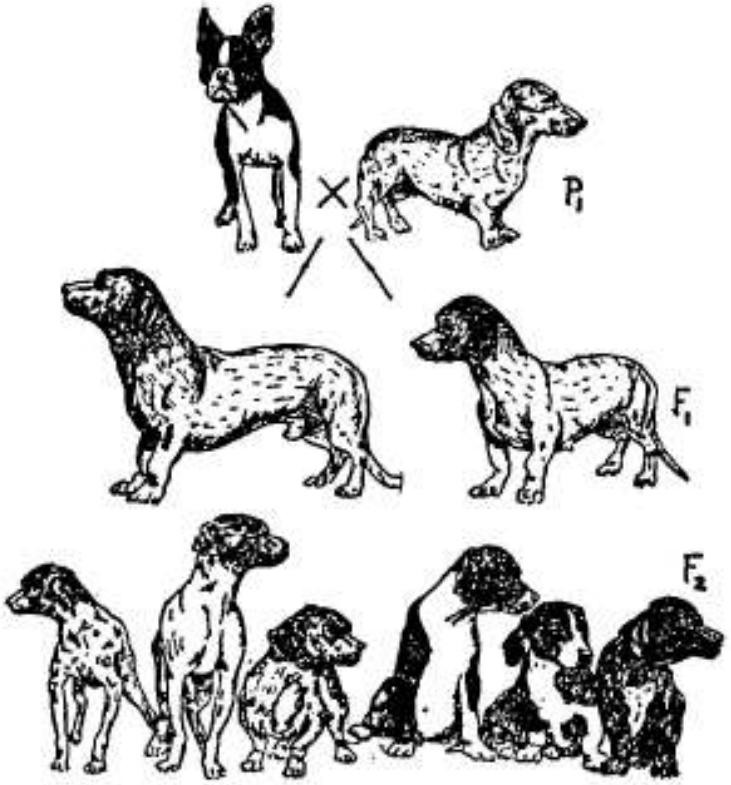


Fig. 63. The Boston terrier, with short round head and deformed tail end of vertebral column, crossed with long-headed long-tailed dachshund with short bent legs. The first generation hybrids have long heads, long bodies and tails, and short bent legs. The second generation hybrids exhibit various combinations of short heads and legs and long heads and long legs.

The bent-tail of the Boston seems to be inherited somewhat independently of tail length; it is a definite vertebral deformity, though not apparently linked with the short condition. From the numbers at present available, the bent-tail

seems dependent in expression upon a single recessive factor and, therefore, appears in about one in four pups of the second generation, while the typical short screw-tail from the Boston appears only once in about sixteen F_2 pups, thus approaching the Mendelian expectation for a character dependent upon two recessive factors. Some extreme conditions in the F_2 hybrids are shown in Fig. 64.

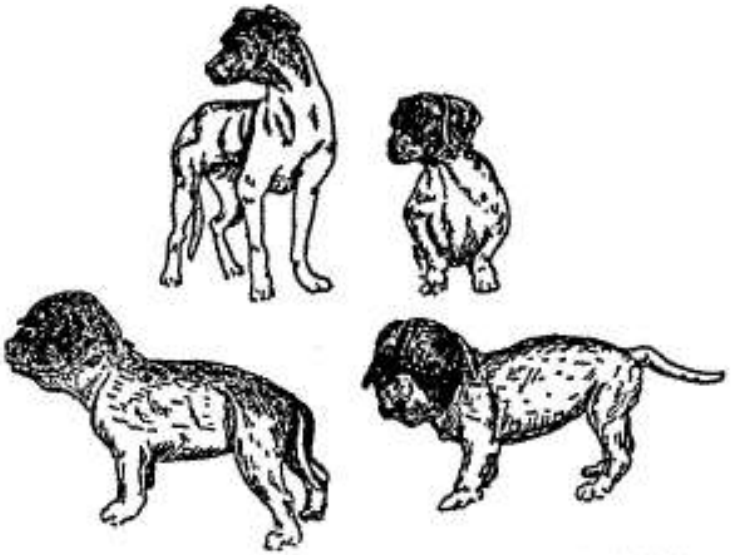


Fig. 64. Extreme types in the second generation hybrids from Boston terrier by dachshund, as shown in Fig. 63. The bent-tail appears as a single-factor recessive about one in four and the short "screw" tail, not shown here, seems to be inherited as a double-factor recessive. Many of these hybrids are very exophthalmic with abnormal brain and they die within a few days.

If the dachshund-Boston F_1 hybrids be back-crossed on the dachshund parent the offspring are all short-legged; see Fig. 65. But, here again, half are full short and half are

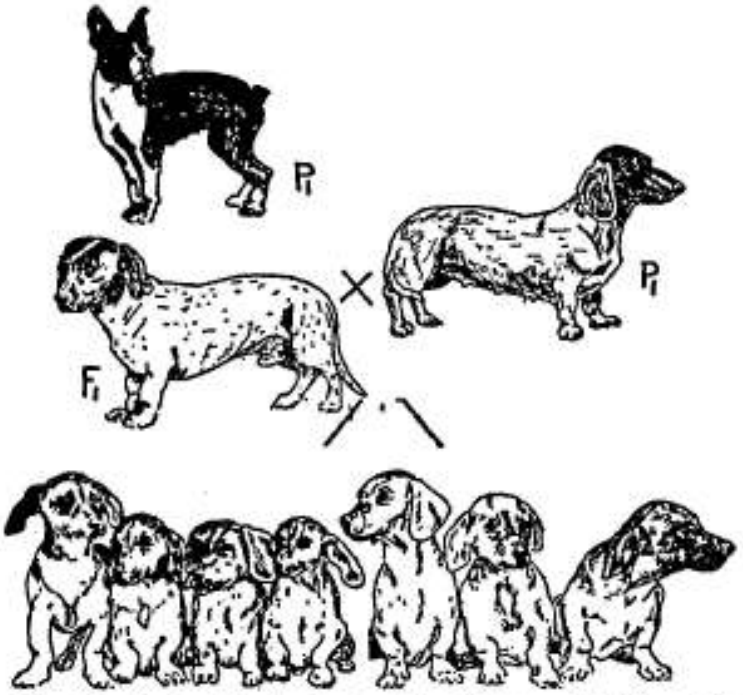


Fig. 65. Back-cross of the dachshund-Boston hybrid on the dachshund giving all short-legged dogs but half of them are full short and half are incompletely short.

intermediate in leg length as was the case for the basset-shepherd back-cross.

When the French bulldog, having more pronounced achondroplasia of the head than the Boston terrier, is crossed with the dachshund, the results in the first and second hybrid generations are closely parallel to those of the dachshund-Boston cross. In both combinations the extreme head conditions found in the second generation show exaggerated exophthalmia, or bulging eyes; there is also

a tendency for the accumulation of fluid in the ventricles of the brain, the condition of internal hydrocephalus; a number of these pups are lost at birth or die within a short time afterwards. Figure 66 illustrates the abnormal appearance of the defective second generation pups.

On back-crossing the F_1 hybrids on the dachshund parent, all offspring have short legs, half of them being very short and fully dachshund in type, and half being definitely short but less pronounced than the dachshund legs. These intermediate length legs are the same mixed or heterozygous condition as was shown in the F_1 generation, and are also the same incomplete dominant expression of short-leg as was found in the basset-shepherd hybrid. The dachshund coat pattern, black and tan or brown color, which behaves as a recessive character in this cross with the bulldog, appears in half the back-cross pups, as is expected, while half of them show the brindle bulldog coloring. The head shape is typically dachshund in some, while in others it is slightly heavier but less rounded than in the first generation hybrid parent. The tail is, as anticipated, strong, straight, and of full length. Only a few specimens from back-crosses of the first generation hybrids on the French bull and Boston terrier parents are yet available for record; these are quite bull-type with bent but long tails, short-bent or screw-tails appearing in only a few cases.

These experiments seem to indicate definitely that localized skeletal parts may inherit an achondroplasic growth reaction, while other skeletal regions are developed normally; and also that localized achondroplasia in two separate skeletal regions may be inherited in completely independent fashion. This would seem to mean that some-

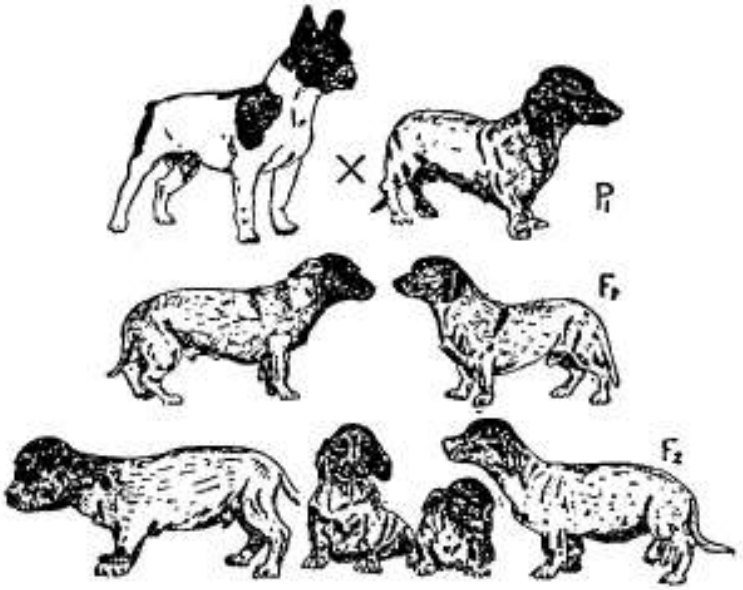


Fig. 66. The French bull with abnormal head and tail crossed with the short-legged dachshund. The first hybrid generation is much the same as the Boston cross and the second generation again showing peculiar combinations and very defective.

thing within the particular bone itself is essential in this growth reaction rather than, or in addition to, the influence of a peculiar internal environment. The breeding experiments also indicate that a double dose or a pure unmixed factorial condition induces a more pronounced expression of the dominant short-leg than does the hybrid or mixed factor state. Varying degrees of expression would seem to indicate that different degrees of disturbance in the glands of internal secretion, if they be the modifying factors, are inherited in a definite way. Many family resemblances also suggest this as a probable fact. Or it is equally proper to

surmise that factors within the bone are affected to different and definite degrees. It seems probable that in some way the modified bone growth in the legs is a reaction to an hereditary modification of the secretory growth-regulating complex, on the one hand, and to something within the local part, on the other.

That an organ or a gland might inherit a capacity to act or function to a definitely limited degree, and that the pure or homozygous genetic state might induce a slightly more modified expression than does the weaker mixed heterozygous basis, is by no means impossible. Indeed, in the case of many structural features, which are undoubtedly symptomatic of certain endocrine gland influences, we frequently find clearly limited reactions occurring in entire families and groups of human beings. This is also true among lower animals. Almost everyone may recall acquaintances with mild symptoms of dwarfism or certain conditions of overgrowth. Many ordinary family resemblances in facial features, bodily form, and size are probably due to growth reactions of this nature and result from the inheritance of a definite glandular complex, the components of which are typically limited in their degrees of activity. There are facts which seem to indicate for many of the organs that differences in degree of function may be inherited as well as differences in quality. Milk production in certain breeds of cattle and egg laying in certain fowls are cases in point.

Further Experiment on the Inheritance of Localized Dwarf Conditions

Achondroplasia, or failure in bone length, in the extremities, is pathologically a sclerosis of the growth cartilages.

This condition in dogs depends upon a single dominant factor in its heredity, while achondroplasia, or shortness, of the head and vertebral column, is determined by a multiple-factor condition and is probably partly recessive in its hereditary reaction.

We have further tested the inheritance of these conditions with one other hybrid combination which, however, has not yet been carried very far. In this case the dachshund is crossed with the Brussels griffon. The griffon is a midget with the most extreme achondroplasia of the head. The face is almost completely flat and resembles much more nearly that of a small monkey than that of a dog. This animal is also very exophthalmic, with prominently bulging eyes, and is highly nervous in disposition. The legs are long, slender and straight, and the vertebral column is quite normal; the tail is usually amputated in order to enhance the queer appearance. The short achondroplasic growth inhibition is here as completely localized in the skull as it is in the appendages of the dachshund.

The hybrid derived from the cross between these two breeds is again short-legged like the dachshund and unlike the griffon. The skull of the hybrid is only slightly modified by shortening, and the eyes do not bulge but the coat and color are much like the griffon, as is shown in Fig. 67. All of the first generation hybrid pups, both males and females, are uniformly of the same appearance and are mistaken for a rough-haired dachshund breed.

A second generation from matings among these hybrids is not yet available, but the hybrids have been bred back with the dachshund. The offspring from such matings are almost indistinguishable from pure bred dachshunds, ex-

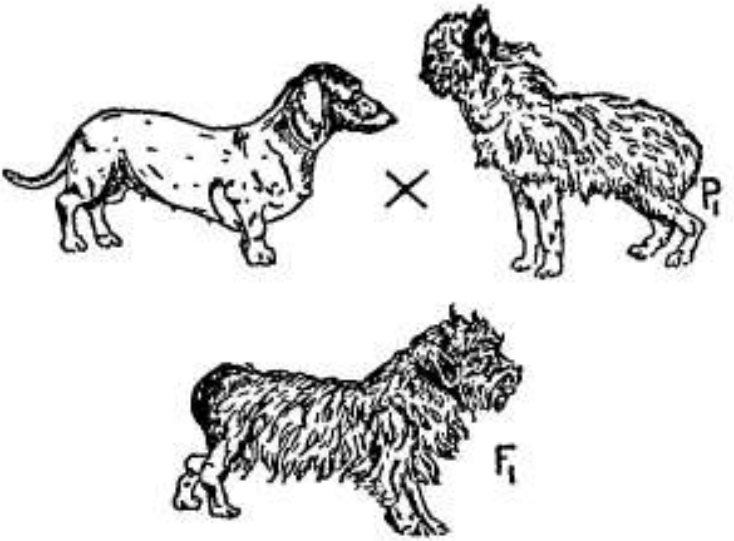


Fig. 67. The dachshund crossed with a still more pronounced short-headed type, the Brussels toy griffon. The hybrid is again long muzzled, long bodied and short-legged.

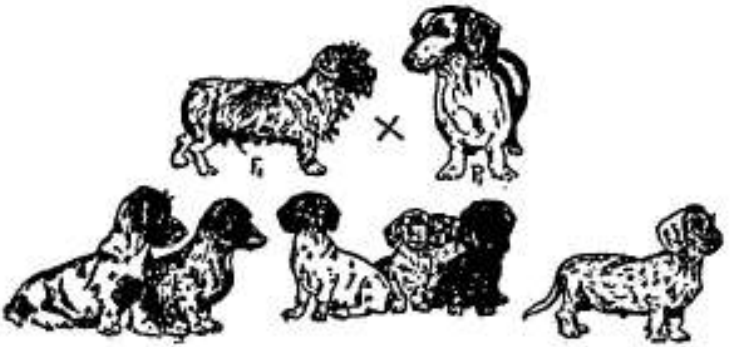


Fig. 68. The hybrid dachshund-griffon back-crossed on the dachshund, giving again all short legs, but half very short and half intermediate.

cept for the fact that half of them have long hair which may be either rough or silky. The illustrations in Fig. 68 show how decidedly dachshund-like these back-crossed animals are.

How May a Dwarfed Condition Develop in Only Localized Parts of the Body?

We return now to the question of a possible explanation for the modified, shortened or achondroplasic condition which may arise within one region of the body without being present in other regions. If it be true that the developmental expression of this dwarfing results from an hereditary modification in the internal secretions, then why may one part be affected and not another? How is it possible that the dachshund and basset hound come to have modified short-bent legs while their heads and bodies are normally developed? And why do the Boston terrier and French bulldog suffer marked abnormality in the head and vertebral column and not in the extremities? The present answer to these questions is largely theoretical, and must take us back to a consideration of certain responses that we have found in the embryo.

It may be recalled from the previous pages that when a modified or unfavorable situation temporarily arises for the embryo, those organs which should be in their most active state of development at the unfavorable period are most affected, while those parts less active at this time may escape the unfavorable influence entirely. After the very early growth of an organ becomes modified, it is often unable to recover from this handicap—even though the modi-

fying cause acts for only a short time and the later surroundings become entirely normal. Also, as we have seen in our review of such cases, the same agent acting at one moment will have an effect upon one organ, and acting at another time will affect an entirely different part.

The explanation of the localized expression of dwarfed structure, or achondroplasic conditions, may be based upon these facts. Let us make what seems at present the probable assumption that the dwarfing reaction is due to some hereditary disturbance of pituitary gland secretions causing abnormal pituitary-thyroid-parathyroid gland coördinations. These are the glands of internal secretion which so decidedly modify the structure and growth proportions in the developing bones. The disturbance in the dachshund and basset hound I assume to be of short duration, acting only during a critical moment in the origin or development of the embryonic limb skeletons. A normal or proper glandular balance is thereafter very soon established, and thus the laying down of other skeletal parts is not affected.

It is well known that the different parts of the skeleton originate at quite different developmental times, extending through a long embryonic and foetal period. The modified condition in the achondroplasic extremity is known to be present in the earliest foetal stages as a number of investigators have shown. The appendicular or limb skeletons arise very early, and possibly are permanently modified from their beginning even though the secretory balance later becomes normally established.

The skeletal formations for the base of the skull and the centra of the vertebral column originate later in the developing individual than the cartilage and bone basis in the

extremities. The growth disturbance in achondroplàsia of the skull and vertebral column is chiefly within the basicranium, or bones at the skull base, and the centra of the vertebrae; many of the other bony modifications in the face, et cetera, are the secondary results of the primary shortenings in these basal parts.

Achondroplasia in the axial skeleton, the skull and vertebral column, may be, therefore, a somewhat later modification than in the legs, and due to a later glandular disharmony which arose after the appendicular skeleton had already attained a normal start and was no longer acutely susceptible. An important fact in support of this interpretation is that the basset hound and dachshund are entirely free of postnatal abnormality and later signs of secretory disturbance. While on the other hand, the later disharmony—which probably brings about the achondroplasic expression in the head and vertebrae of the Boston and French bull—is more persistent in nature, and remains as a permanent disharmony which modifies the behavior and functional reactions of these animals throughout their postnatal life. Both the Boston terrier and French bulldog have marked symptoms of abnormal thyroid activity with pronounced exophthalmia and nervous disturbance.

Temporary disturbances in the functions of the glands of internal secretion followed by complete readjustment are common occurrences during childhood and later life. A well-known example is the enlargement of the thyroid gland with the development of a mild colloidal goitre, chiefly in girls, during puberty, in certain regions rather unfavorable to thyroid activity. This condition usually disappears completely within a few years. It may be logically

supposed that comparable temporary disharmonies might arise during prenatal periods. Certain it is that the cause which brings about the modified growth or achondroplasia in the legs of the basset hound entirely disappears, leaving the animal normally perfect during the remainder of its life. It is also certain that the probably similar complex which arises during a later period and affects the development of the skull and vertebral column in the Boston terrier remains permanently to handicap this dog's future existence. Finally, it is certain that by crossing two such modified breeds, one may obtain animals in the second generation which inherit both the early disturbance producing the leg-alterations and a failure to readjust which results in the later modifications in head and tail. It is also found that the histological conditions of the endocrine glands, thyroid, pituitary, parathyroids, and gonads in the Boston terrier, the French bull and the distorted F_2 pups, may be pathological in various ways. The endocrine glands from the basset hound and the dachshund, on the other hand, are much more nearly normal in character; and in these dogs the life functions, resistance to parasites and disease, and particularly their reproductive capacities, are far superior to the Boston terrier and its kind.

Giants and the Types of Overgrowth

Among dog breeds there are several giant types and supernormal size reactions. The well-proportioned simple giant is illustrated by the Irish wolf hound and the great Dane. These animals are large or gigantic with no other modifications. In the bloodhound there is a pronounced

overgrowth of the skin, giving excessively long hanging ears, a heavy wrinkling of the forehead and muzzle, and a dew-lap formation; the bones of the extremities are heavy. and the entire body has an exaggerated stocky appearance. All of these symptoms are commonly associated with the condition of overgrowth in man known as acromegaly. A combination of this acromegalic overgrowth, thickening of skin, and skeletal structures with gigantic size is a condition frequently seen among human beings. In fact, almost all human giants show a decided tendency towards the complex for acromegaly, a condition quite certainly associated with modifications due to disease and tumor growths in the pituitary gland at the base of the brain. The cause of gigantism itself has a very probable relation with modification in the pituitary gland. The two alterations in growth, gigantism and acromegaly, are naturally, therefore, often associated in the one individual. Professor Harvey Cushing has contributed much to our knowledge of these conditions. Among dogs, the St. Bernard and the mastiff are splendid examples of the combination of gigantic size with acromegalic overgrowth. The male St. Bernard may weigh more than two hundred pounds, and is covered by excessively loose skin that may sag on the head to such an extent as to completely overhang the eyes, making it impossible for the dog to see unless the head is much raised or the skin lifted from above the eyes.

The dogs are thus found to exhibit the three conditions well known among men of excessive growth; namely, simple gigantism, simple acromegaly, and a combination of the two.

In human pathology these three conditions are supposed in some way, as mentioned above, to be associated with ab-

normal or peculiar reactions of the pituitary gland. Diseased and abnormal pituitary glands have frequently been recovered from post-mortem examination of such individuals. We have some, though not yet complete, evidence in this direction from dogs. There are further indications that the parathyroid glands, which are in a way involved with calcium metabolism and bone growth, may be modified in several of these large types of dogs.

In order to understand better the conditions of overgrowth, and to attempt a determination of their genetic background, it has seemed desirable to cross-breed the several different giant reactions. We may use for present illustration only one of these crosses, since several of them are not yet fully followed out.

Crosses Between Simple Giants and the Giant with Excessive Overgrowth

When the simple giant, great Dane, is crossed with the acromegalic giant, St. Bernard dog, large litters of hybrid pups are obtained, and all the individuals are very uniformly alike. They are far above the normal dog in size, inheriting the giant stature from both parents.

When less than three months old, the head and body-form of these puppies is in general similar to that of the great Dane of the same age. They are not so heavy in type as the young of the St. Bernard.

Between the third and the fifth months after birth two very striking reactions occur among these St. Bernard-Dane hybrids. The frontal region of the head becomes pronounced and rounded, taking on much of the appearance of the St,

Bernard, although it never becomes typically St. Bernard in complete shape. Accompanying this head growth there is an excessive skin growth varying in extent among the individuals, but producing the typical looseness and wrinkling of the St. Bernard, though not to so pronounced an extent. The brain may also in many cases become distended with fluid, giving a condition of hydrocephalus which is not uncommon in the big-headed breeds of dogs. All of these changes develop only after the third month of age; see Fig. 69.

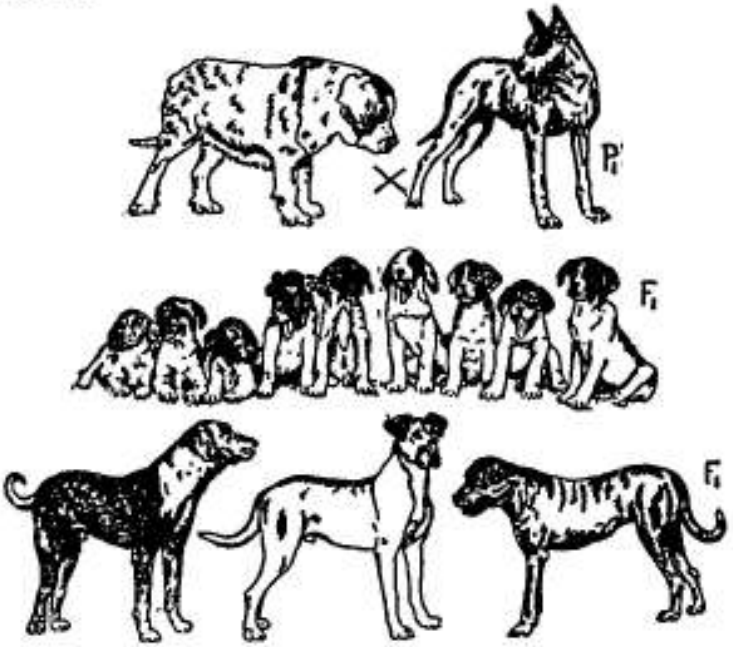


Fig. 69. The giant St. Bernard with heavy overgrowth crossed with the giant Dane. The hybrid offspring are vigorous until three months old and later all become paralyzed in the hind legs; after five months they develop varying degrees of the St. Bernard overgrowth as shown in the lower figures.

Hereditary Paralysis of the Hind Legs

Another even more peculiar reaction, arriving in these hybrid puppies shortly after three months of age, is the appearance of a strange paralysis of the hind extremities. These pups may all be vigorous, active, and well, when suddenly one or two in a group are unable to support their bodies on their hind legs and are completely unable to stand or walk. Closely following the first cases every individual of the litter is similarly attacked. This condition of inability to stand or walk may last for only a day or so, or for as long as several weeks. After a time, the animal learns in most ingenious ways to compensate for the partially paralyzed condition by twisting the legs into various positions, and is again able to stand and walk with, as a rule, a more or less abnormal seal-like gait. In two cases the dogs actually learned to raise their bodies from the ground and to walk on their front legs exactly as a man does when walking on his hands. The dogs did this for a number of days whenever they walked and then became able to use their hind legs again.

There is a certain amount of pain accompanying any movement or manipulation of the affected limb during the first day or so of the condition. Later, however, there seems to be no pain associated with the lameness. After the animal readjusts, and again learns to walk in a limping fashion, the involved muscle groups never recover their function; and wilted, atrophied regions in the thigh may be strongly marked in many of the animals. The attack of paralysis may involve only one leg at a time, although usually both hind legs are simultaneously affected.

There have been produced in all seventy-eight of these F_1 hybrid St. Bernard-Danes, and more than fifty of them have lived to reach the stage of life when the above-described symptoms appear. Practically every one of the fifty has been paralyzed in an almost identical fashion. We have attempted the use of every reasonable precaution in order to make certain that no infectious disease and no food deficiency could be involved. These animals have been born during all seasons of the year, and puppies of a number of other breeds have in all cases been kenneled on both sides of them, and all were similarly fed. In spite of this, no puppy of another breed—out of more than five hundred bred in the kennel—has shown this definite type of paralytic condition. The first several litters of the St. Bernard-Dane hybrids were somewhat neglected; their food was probably not properly balanced and they were poorly looked after. On this account it was decided to breed and rear further litters, with carefully balanced food conditions, while the kennel was in practically perfect health. Under this present careful and efficient management, the paralysis occurs in one after another of these pups as previously, with almost scheduled regularity.

The nature of this crippled condition has not yet been fully analyzed; and it is quite uncertain whether the condition arises in the nerve trunks or in the spinal cord. The muscles once lost or paralyzed are never regenerated or restored. It seems clear from the sudden onset of the paralysis, however, that the condition is not a type of hereditary primary muscular atrophy, but is probably of nervous origin. In any case it is perfectly clear that these St. Bernard-

Dane hybrids inherit a constitution which exhibits this condition in practically 100 per cent of the individuals.

A very similar paralysis of the hind extremities is occasionally met with in certain stocks of the St. Bernard breed, and it occurs, though very rarely, in the great Dane. The combination of the two breeds seems to bring about an accentuation of this defective condition in the hind legs. The lower illustrations in Fig. 69 show the adult hybrids with badly wilted thighs, though these dogs are otherwise large and often handsome specimens. The fore quarters, neck and head are particularly strong and heavily developed.

Further Generations from Giant Dog Crosses

There appears to be a certain amount of sterility among the St. Bernard-Dane hybrids, as there occasionally is among the St. Bernards. Yet we have now succeeded in obtaining back-crosses with the hybrids on both parent stocks, as well as a second, F_2, generation from *inter se* matings among the hybrids themselves; see Fig. 70. The numbers of animals at present available from these back-crosses and the second generations are not yet altogether satisfactory for a definite analysis of the characters involved in the crosses, yet they are instructive for brief consideration.

When a male hybrid St. Bernard-Dane was bred back to a pure St. Bernard female a large litter of thirteen pups was produced by this excellent dam. Four of the puppies died very soon after birth, as frequently happens in litters of this size.

A few of the pups in large litters are smaller than their

mates; they have probably not been so favorably located during development in the overcrowded uterus. These less vigorous specimens usually succumb during the first few days since they are not successful in the struggle for food from the mother and hence remain weak and hungry. All of the members of small litters, up to as many as eight, may frequently survive as uniformly vigorous animals.

Nine out of the thirteen puppies from the back-cross on the St. Bernard female lived to be more than three months old. Up to this age they were all strong, attractive-looking, lion-like young animals, vigorous feeders and most rapidly growing. After three months of age, here again, one after another of these young dogs became paralyzed in their hind extremities to different extents. The mildest expression was a dragging or limping of the hind legs, while others were completely unable to raise their bodies throughout periods of more than a week. All of these dogs finally show more or less shrunken and degenerate thigh areas. The most severely affected ones walk with the typically modified seal-like eversion of the hind extremities which, as previously stated, is common among the first hybrid generation. Figure 71 illustrates a back-cross litter.

Although the numbers are not sufficiently large for definite conclusions, it does seem probable at present that this defective condition is hereditary in nature and quite like a dominant character in its mode of expression. A back-cross of the Dane-St. Bernard hybrid on a pure Dane mother has given but one successful result, and this a small litter of only six. Four of these died, from no fault in handling, within a few days after birth and only two survived to maturity. Both of these were typically paralyzed

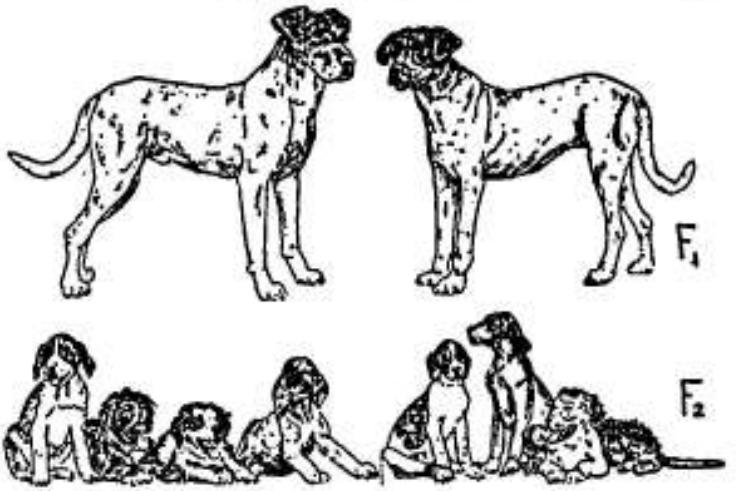


Fig. 70. First generation St. Bernard-Dane hybrids and their second generation offspring.

soon after three months of age. With so few cases the result can only mean that this peculiar paralysis may still occur in the back-cross on the Dane parent, but it gives no idea whatever of the proportions or frequency which might be found in a large series of such offspring.

Several matings between F_1 hybrids have resulted in pregnancies, but all of them with two exceptions have been resorbed, aborted or in some way lost before reaching full-term births.

From one litter of eight second generation, or F_2, Dane-St. Bernard progeny seven animals have lived to maturity. The grandparental characters are segregated or redistributed in these second generation animals in several suggestive ways, although the numbers, of course, permit of no analysis at present. There are long-haired St. Bernard

patterns and short-haired Dane coats, various spotting combinations, and body forms resembling both ancestral stocks as is seen in Fig. 70.

The point of particular interest is that a number of these second generation puppies after three months of age have suffered the same paralysis of the hind extremity as was shown in the first hybrid generation. It also seems probable

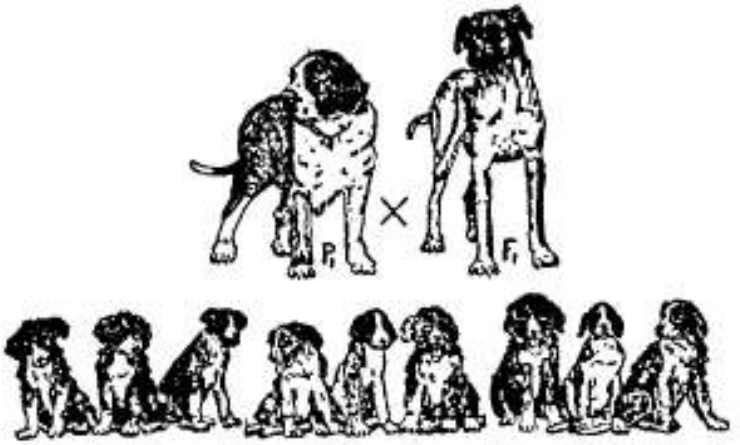


Fig. 71. The weak-legged St. Bernard-Dane hybrid back-crossed on the St. Bernard giving again paralysis and degeneration in the posterior region.

that several of these have entirely escaped this unfortunate condition or else it has been expressed in an unrecognizably mild degree. It seems probable that there may be segregation and definite transmission of factors determining the paralysis. Only greater numbers can make the frequency in occurrence of the paralysis in this generation satisfactorily clear.

Finally, we may conclude that this particular combina-

tion between a simple giant type dog and a giant with symptoms of acromegaly does seem to produce a peculiar complex in the progeny which causes all members of the first hybrid generation to suffer a definite paralysis with subsequent loss of certain muscle groups in the hind extremities. The data at present available seem to indicate that this paralysis results from definitely inherited conditions, although it has not yet been possible to analyze the exact genetics concerned in the expression of the character.

We have made only one cross between the giant Dane and the normally-sized but acromegalic bloodhound. This combination gives a pronounced overgrowth and wrinkling of the skin on a giant animal in the first generation of hybrids, but here there has been no paralysis.

Among human families there is known a condition of primary muscular atrophy which frequently affects definite muscle groups and results in crippling and inability to walk. This disease occurs in families in such a way as to make it seem probable that it may be hereditary in origin. The lameness in the dogs arises more suddenly than a muscular atrophy would appear and at the beginning of the paralysis the muscles are large and strong. Nervous degenerations and paralyses are known in human beings which in some respects resemble the peculiar paralysis occurring in the dogs. It is hoped that within the near future an exact understanding of the nature of this defective state may become clear, and that such an understanding may aid in an analysis of the human conditions.

In the meanwhile we may venture to suggest that the appearance of paralysis in these races of dogs, in which unstable and modified function of the glands of internal

secretion quite probably exists, leads one to suspect that an unfavorable glandular complex is either primarily or secondarily responsible for the paralytic condition.

The internal chemical constitution and the general modifications in human beings suffering with nervous symptoms are now being quite widely recognized as intricate subjects which nevertheless are open to investigation and serious study from the constitutional standpoint. Any experimental analysis of the inheritance of such conditions must necessarily depend upon investigations on lower animal forms.

XIV

ORGAN-VARIATIONS AND ORGAN-EQUILIBRIUM IN NORMAL INDIVIDUALS

After considering the foregoing modified and peculiar individuals and briefly surveying parts of an experimental study of the genetics and development of their exaggerated structures, an examination of the "normal" person will be found to show mild degrees of exactly the same expressions. Normal animals incline, in one direction or another, towards the marked reactions exhibited by the unusual types. From this point of view, all the modified conditions we have considered are really derivatives from the normal which have escaped the usually balanced or coördinated growth-regulating influences. It might be claimed that every normal individual is potentially a complex of possible distortions, this potentiality being either lightly or strongly expressed by different personalities. This assumption is of great value in considering certain features of the normal adult constitution, for while in general one prefers to think of the normal individual as simply the natural perfection of coördinated developments, such an indefinite attitude does not carry us very far.

Organic Variations among "Normal" Individuals

Dr. Wade Brown and his associates at the Rockefeller Institute have recently contributed highly important records

of organ variations in perfectly normal mammals. These studies add more to a comprehensive appreciation of individual personalities than the usual attitude of considering the normal as an average standard animal. As Brown states, "The current method of dealing with normality is the method of standardization: the establishment of mean values with limits of variation or of other standards of measurement, and the separation of individuals into two classes, the normal and the abnormal. It is apparently assumed that either what happens within the limits of the normal is of no consequence or the methods available for drawing distinctions are inadequate." Every observer soon learns from even a limited experience with numbers of living animals that the average individual is rare or nonexistent, this average being only the theoretical mean of deviations in many directions.

When one sketches the average, not the composite, face from a group of faces, the drawing will probably be not a likeness of several of the faces but unlike all of them. In other words, the sketch may actually represent a face not in the group. The use of average is equally unsatisfactory in studying human constitutions; the averages may have little in common with any individual complex. As Brown states it for one instance: "From the point of view of the bearing of constitution on susceptibility to disease, we have to consider the factorial potentialities on the one hand, and the functional expression of these potentialities on the other." Certainly neither of these conceptions lends itself to treatment on the basis of averages.

Brown found in his studies on rabbits, and man is probably even more variable than the rabbit, that a four- or

five-fold difference in the weight of an endocrine gland or of a lymphoid organ, or a two-fold difference in the weights of parenchymatous organs, per unit of body weight, is by no means uncommon. Variations of 25 to 100 per cent in comparative weights of different organs per unit of body weight are ordinary occurrences. Figure 72 shows in a diagrammatic way the great weight differences among the organs in normal individuals as recorded by Brown. The smaller variations in the size of organs in different normal individuals are of the order of the differences in total body weight or stature of adult men, but in some instances the extremes among organ-sizes in normal individuals exceed the difference between the dwarf and the giant. Such marked discrepancies in organ weights suggest the important question of the relationship between the weight of an organ, or of a group of organs, and the weight of the body which they serve. In general the mass of organs in proportion to body weight was found to be distinctly greater for small than for larger individuals.

A small thyroid gland coördinating in function with a given group of organs may produce a thyroid balance in the constitution as a whole similar to that resulting from a much larger thyroid gland balanced against another organ relationship. These very different organic interrelationships, coördinations, or balances, exist in entirely normal individuals and there is probably no known mathematical expression which could indicate all their possibilities among a group of normal human constitutions.

The composition of the organ balance varies qualitatively as well as quantitatively with different ages and under different seasonal conditions. These variations represent

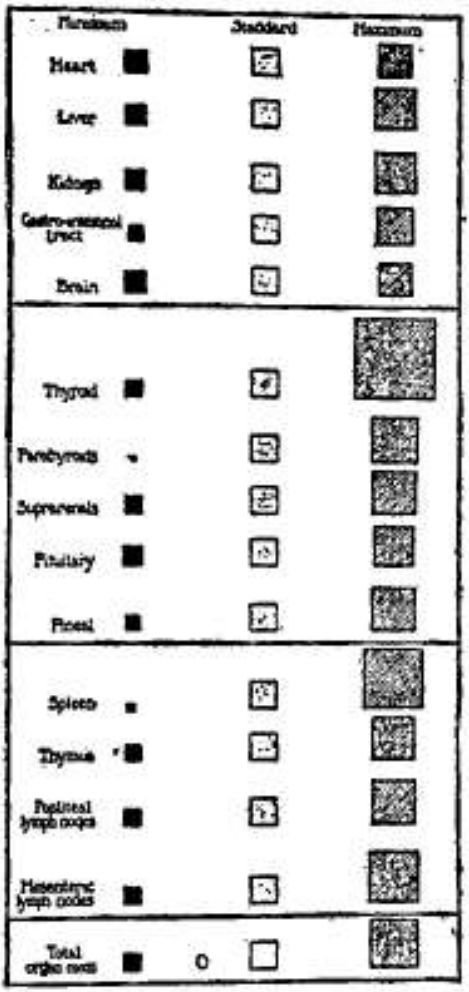


Fig. 72. Theoretical range of variation in organ size for perfectly normal individuals. The thyroid and parathyroid glands and the spleen vary enormously in mass per unit of body weight in normal specimens, while the brain, heart and liver are much more constant in their proportions. (After Wade Brown.)

not only physical differences but, of course, chemical differences also. Brown showed in his rabbits, that individual animals differ with respect to the mean levels of calcium, inorganic phosphorus, lecithin, and cholesterol, which they maintain in the blood, just as they do with respect to the weights of organs or to any physical character.

Changes in Functional Equilibrium among Normal Persons

It has been shown by Brown that under the influence of ultra-violet light the ratio between the chemical stuff lecithin and the inorganic phosphorus in the blood of an animal decreases, while the ratio of another substance, cholesterol, to the calcium increases. This relationship resulting from light stimulation simulates the conditions which prevail in summer, while the exclusion of light, with conditions analogous to those which exist in winter, gives the opposite effects.

Important data from Brown's experiments also show that changes in physical constitution parallel the clinical course of disease throughout, with periods of increase and decrease in organ balance corresponding with the periods of activity and quiescence of the lesions, terminating finally with the development of a state of organic equilibrium in the immune animal which differs from the equilibrium of the normal.

It was further learned that the course of disease may be influenced in a definite direction by the use of measures which disturb organic equilibrium directly, as by the removal of a part or the whole of some organ. Brown showed,

for example, that the removal of the thyroid gland greatly increased the activity or malignancy of a growing tumor and the severity of certain infections, while, strangely enough, the removal of only a part of the thyroid gland produced an oposite effect. The extirpation of sympathetic ganglia or of part of the nerves of the sympathetic nerve trunk in the neck also affects the course of disease by influencing the function of the thyroid gland.

Somewhat comparable results were obtained from experiments done in our laboratory at Cornell a few years ago by Papanicolaou and Bagg. These investigators exposed the thyroid gland in the neck of the female guinea-pig to direct radium emanations. After a certain interval it was found that the action of the radium had destroyed the most directly exposed areas of the gland but other portions survived and, apparently, became hyperactive as a consequence of the radium stimulation. This hyperactivity of the remaining parts of the thyroid gland seemed to stimulate an increased activity in the ovaries of these animals. Ovogenesis, the formation of new eggs in the ovary, was decidedly accelerated, almost returning in activity to the state of the developing foetal ovary. The rutting response or oestrous reactions were also modified and accentuated in these females.

On the other hand, it is well known that when the entire thyroid gland is removed from the guinea-pig, a completely opposite reaction to that just described occurs in the ovary, with connective tissue degeneration, cessation of the throwing-out of eggs or ovulation, and the oestrous reaction disappears.

From these experiments with guinea-pigs and those by

Wade Brown with rabbits, it is clearly shown that a direct change in organic equilibrium through the alteration of one organ induces new and definite responses in other distantly located organs, changing the general constitution of the individual. Many examples of this have already been cited in other connections in the previous chapters.

The Delicate Response and the Exaggerated Effects of Internal Secretions

As shown above, the entire personality of the normal individual may be promptly altered in significant ways by changes in functional coördination among the organs of the body. The glands of internal secretion respond most delicately to all modifications in organ balance, and thus they superficially appear to be the most important elements in determining the personality. Yet we should not lose sight of the very evident fact that the initial cause for personality changes is not necessarily in the glands of internal secretion themselves. For example, an acute disease may so modify the body chemistry as greatly to alter the organ balance, and a deficiency of the suprarenal gland with low blood pressure and general debility may result. This particular modification in the internal secretions is primarily due to the initial infection. We may say that the infection induced the personality change, and the glandular modification served simply as the means through which the change was expressed; yet, at the same time, the nature of the glandular reaction truly determines the particular kind of personality change. Mental anxiety and unusual nervous irritation inhibits both appetite for food

and normal digestion. This disturbance of metabolism affects the sympathetic system and the internal secretions and, if long continued, may derange the personality.

Different causes may induce one and the same effect by initiating the same secretory reactions. For example, if a person be injected with a certain dose of adrenalin the pulse will become quickened, the blood pressure will rise, respiration will become excited, the pupils of the eyes will dilate, "goose flesh" may appear on the skin and the hair will tend to rise owing to pilo-motor contraction, et cetera. All these reactions make up the excitement or effort syndrome. Again, if while looking from a window one sees a person meet with a violent accident on the street, the same syndrome—increased respiration, quickened pulse, cold sweat, dilation of the pupils, et cetera—will occur. This time the initiating stimulus was a visual impression conducted by the optic nerve to the central nervous system, instead of the injection of adrenalin. Again, one may be sitting quietly in a room; another person may enter and make a shocking remark which will produce in the hearer the same complex of symptoms as that which resulted from the adrenalin injection and the sight of the horrible accident. Thus the three entirely different causes provoke the same secretory and nervous responses.

Over-activity of the thyroid gland with extreme nervousness, derangement of the pituitary gland with alterations in body form, degeneration of the parathyroids with spasm and tetany, and other such glandular modifications, may result from acute disease as well as from minute chemical deficiencies in an originally normal body.

It is also true that the course of infectious disease may

be affected favorably or unfavorably by the use of chemical agents, which act not directly on the infecting organisms or parasite but on the host, such as the iodides in affecting the thyroid gland, or by conditions which involve nothing more than a difference in light environment.

Again, as Dr. Brown has stated: "It has been found that disease gives rise to changes in physical and chemical constitution comparable with those that occur in normal animals at different periods of the year or with variations in susceptibility to disease and, conversely, that disturbance of the normal constitutional equilibrium gives rise to decided changes in the efficiency of the reaction to disease. It has also been found that the changes in physical and chemical constitution, metabolic activity, and susceptibility to disease that are produced by environment are of the same nature as the differences presented by animals of different age groups." This quotation contains a suggestion which the present author holds to be most highly significant: namely, that resistance in the adult to certain childhood diseases is brought about in many cases as a developmental condition rather than as an acquired immunity due to a series of mild infections. For example, many adults may be highly resistant to diphtheria although they have never experienced the disease as children. Is this resistance due to the constitutionally different chemical balance of the adult as compared with the child, rather than to the immunizing effects of unknown mild infections which never actually induced the disease?

It is at least suggestive to find, as further evidence in this direction, that in many instances those adults infected with childhood diseases are somewhat arrested and them-

selves childlike in type. This is also usually true of persons who repeatedly experience the same childhood disease without being able to develop an immunity. The well-known arrested human type termed *status lymphaticus*, with a large persistent thymus body and a poorly-developed lymphatic system, frequently gives a record of repeated attacks of various diseases of childhood without immunity.

The Age Element in Organic Differences among Normal Individuals

We need not know the function of a single organ in order to show that individuals differ from one another in respect to their organic equipment. Or, again quoting from Brown, "that they *are* individuals and not standard machines or standard media, as physicians sometimes think, for the growth of disease germs or pathogenic microörganisms. It can be shown that variations in the mass and mass relations of organs are constantly occurring in response to demands made by the changing conditions of life and that these variations in organic constitution are accompanied by variations in chemical constitution, all of which may well be confined within the usual limits of the normal, for they are normally happening."

The same person is constitutionally a different chemical make-up at one age or life period from that which he or she may be during another period. The secretions and the chemical complex in the child after puberty obviously differ from those found in the baby's body. It is equally certain that the chemical constitution of a senile person, with degeneration of the sex-glands and general sclerosis, must

differ from that of a vigorous adult person with a complete range of internal secretions. It is a matter of fact that the same individual is constitutionally a changed animal complex at several different times during his existence, and his personal behavior is equally different at these several times.

From the standpoint of good health and strong personality, the above facts are of much significance, since susceptibility to disease differs so decidedly among slightly different individuals. The age changes in chemical state are probably the underlying reason why there are certain diseases typical of infancy, others of childhood, and still others commonly affecting adult life. The usual adult is constitutionally no longer readily susceptible to the diseases of childhood. The lack of susceptibility, as we have said above, may not be due simply to a gradually acquired immunity for diseases which the individual may never have actively experienced, but probably in many cases to an actual constitutional deviation from the childhood state.

Similar age reactions are found even in response to gross intestinal and body parasites. Ordinary mange in dogs, which is due to a parasitic mite, thrives only on the very young and the weakened old animals. Intestinal parasites such as round worms are abundant in puppies, while the adult dogs in adjoining runs and under the same surroundings may be free from such parasites. The individual is actually a different chemical medium at different ages and thus offers a changing environment to parasites. There is probably a developmental immunity to certain gross parasites and microbic infections which is comparable to the well-known species immunity against the parasites infecting

other animal kind. So, for instance, man does not contract dog distemper nor do adults show the rash reactions of babies.

The evidence is clear that normal individuals differ from one another in many respects on the quantitative basis. But these differences are of such a nature that they do not lend the individuals of a population to treatment on the basis of a single average or standard type. This suggests that there are actual qualitative as well as quantitative differences; if so, then normal individuals may possibly be segregated into two or more distinct types or classes. Should such distinct types exist they can naturally not be blended into a single average norm. We shall consider in the following chapter the possibility of the existence of such distinct types.

XV

PERSONALITY AND STRUCTURAL TYPES AMONG NORMAL INDIVIDUALS

DOES the ordinary population of normal persons permit of a division or break-up into several definite physical types, mental types or personality types differing from one another in quality rather than degree? Or is the normal population on this basis an unarrangeable mixture?

Classes and Castes in Human Communities

Everyone knows that a so-called normal community may be separated into classes or grades of physical strength, mental ability, or other characteristics, in which the individuals differ from one another simply in amounts or degrees. Our daily social performances tend to grade and arrange the population on this basis, and castes and classes develop in all communities.

In the United States we have a so-called upper class, middle class, and poorer class of persons, graded on the basis of the amount of property they have been able to accumulate and retain. This is not altogether a false method of grading, since the getting and accumulating of money has made a peculiarly wide appeal to the entire population of this country. But the division on this basis is due only to differences in degree, not in kind, among the competi-

tors, as is indicated by the fact that members of one class are constantly rising up or falling down into the other classes. A poor man may in a very short while settle himself on the top of the entire classification, as has been done during the last thirty years, while during the same short time a host of others have fallen from the top class into the bottom.

In other countries where somewhat different methods of class or caste distinctions have evolved, we find again proof of the lack of quality differences between the members of any two classes in their entirety from the fact that persons of the middle class are constantly being elevated to ranks of nobility, and peasants and workers often win their way into the substantial middle group, while members of the upper groups may fall into the lower classes.

Therefore, it is quite evident from historical record and the present state of human affairs that the struggle for existence and supremacy in artificial societies does not divide persons into qualitatively different groups, but separates them into definite classes of graded successfulness in accordance with their degrees of ability in the competitions concerned.

Our present interest from these observations is the conclusion, that if qualitative differences among *normal* personalities do exist they are not definitely significant in determining the individual's position in the community. In others words, qualitative differences in personality may exist which will cause two persons to accomplish the same thing in two different ways, but such differences do not seem to make it so that one person may accomplish a certain thing which is impossible for another qualitatively differ-

ent capable individual to do. The grouping of normal persons doing the same thing into good, fair, and poor performers results from differences in degrees of ability and accomplishment rather than from differences in kind or physical types among the individuals. Persons of two or more kinds or types may be in any one class.

Nevertheless, the above community grades give no final indication that there may not be various qualitatively different types among human beings which tend to separate them into another series of groups or classes. The community reaction may, however, alleviate one's sensitiveness in respect to finding oneself in any particular group of qualitative type. Neither the upper, middle nor lower class of human society has sifted out any one definite human type.

The Qualitatively Different Types of Normal Personalities

What then may be said of the presence of different qualitative types among normal men? Medical literature and particularly the recent reports on human constitution abound in the separation of diseased and abnormal persons into various qualitatively different classes. Since ancient times the normal population has also been thought of as consisting of qualitatively different kinds or types: the lean kind and the fat kind, the long slender and the short thick, the emotional and the phlegmatic, and more recently the high thyroid and the low thyroid types, and so on. All of the old and the new classifications are found in the end to be based primarily on the recognition of two normal adult

types. Anthropologists have recognized these as being most readily differentiated by the general shapes of the head or cranium, and on this basis they are classed as *dolichocephalic* or long-headed and *brachycephalic* or short-headed, according to the relation of length to width of their cranial vaults. In still commoner terms, they are the long-heads and the round-heads of our everyday acquaintance. Or, Bean from another point of view classes them as *hyperontomorphs* and *mesontomorphs*, that is, high and medium developmental types. Or, I have in a simpler fashion termed them the *linear* and the *lateral* types: one, as a rule, thin and linear, though not necessarily tall; the other, as a rule, wide and lateral, all the features and organs being spread and voluminous instead of linear. Thus the lean and the fat kind of common acquaintance are the hyper- and hypothyroid types of today.

These are probably two qualitatively different kinds of persons, and we shall presently enumerate a number of their contrasted features. The two types are found not only among the modern groups of men but among aboriginal and savage tribes. The North American Indians in certain regions, near the coast lines, were long-headed, while in other localities, the central western plains, they were round-headed. Anthropologists have recognized the existence of these two types for a great number of years, yet they have attempted practically no analysis of them. Most anthropologists, with limited experience in comparative anatomy and embryology and lacking the experimental method, have resorted largely to measurement and mathematics as a means of solving the problem of human form and type. The head shape and type in general has seemed to them a

fixed and unchangeable quality, and they have resorted only recently to growth studies and scarcely, if at all, to comparative morphology and the type conditions among lower mammals. Thus anthropologists have not explained why some heads are long and others wide, although they lay great stress on the fact that such is the case. Would it be possible for the same baby to develop either one, the long or the wide head? We have seen that growth disturbances from modified internal secretions in dogs may readily change a long skull type into a more rounded one.

Very little attempt has been made to associate type of behavior and psychology with shape; this correlation has been left almost entirely in the hands of fortune-tellers and phrenologists, whereas it should be recognized as a most serious and fruitful field for scientific investigation. We may some day be surprised to find that, within normal limits, brain shape is more significant for mental quality and ability than brain size. When we recall that the brain of the French anatomist, Cuvier, weighed almost 2000 grams, while the brain of another French academician, Anatole France, weighed only about 1100 grams, little more than half as large, brain size begins to lose some of its significance. The brain of certain prehistoric tribes of men weighed as much as that of Anatole France. Thus variation in brain weight does not correspond with disparity in brain function. The significant difference between prehistoric man and his accomplishments and the behavior of modern man is more probably associated with the progressive modification in brain form and contour than with increase in size. This statement is equally probable from a comparison of the brain sizes and shapes as we ascend the scale of ani-

mal intelligence. The more intelligent animals have brain regions and forms approaching the human and vice versa, while size is not so directly associated with the higher functions as we recognize them.

From another point of view, in understanding the reason for the superiority of human intelligence over that of other animals, not only size and shape of the brain are the fundamental factors concerned. The late Prof. L. Bolk of Amsterdam called attention to the fact that the human head and brain retain more of the immature and foetal proportions than those of any other mammal. The large relative size of the cranium as compared with the face in man is similar to the prenatal or foetal head proportions in many of the mammals.

In addition to this significant retention of the foetal head proportions, a second quite unique reaction has arisen during the evolution of man. His postnatal development and growth have been retarded and long-drawn-out as contrasted with the rather rapid development of all other mammals. The late attainment of the complete adult condition after over twenty years of age in the human being as compared with only a few years—probably about ten, though this is not accurately known—in the highest or man-like apes, about twelve months in the dog, and only three years in the horse, gives advantage to man in the extended length of the active learning time, which among ordinary individuals is largely confined to the periods of immaturity and childhood.

The slow attainment of adult size and lengthened immaturity in the human being are probably due to a specifically peculiar balance of the growth-regulating internal

secretions. There is certainly an inhibition in the development of the gonads and the secondary sexual characters, as is indicated by the rare pathological cases of suprarenal gland disease in which the child, only two or three years old, may become sexually mature with well-developed genitalia and almost adult secondary sexual characters. Other glandular disturbances are met which at times remove the inhibition on body growth and the child becomes precociously long and attains the height of the adult by the age of ten or twelve.

Theorizing from our studies of the nature of peculiar structural growths, we might surmise that this delay in human maturity has arisen as a consequence of a germinal mutation which primarily modified the usual mammalian coördination and balance among the internally secreting glands, and secondarily brought about prolonged immaturity and the lengthened period of learning time. This mutation possibly occurred some time during early human evolution and gave man the opportunity of lifting himself out of the animal wild. The earliest fossil remains of man-like beings, such as the Piltdown skull found in England in 1911 and the recent discoveries by Davidson Black in China, have been interpreted as coming from mature young persons of probably thirty years of age. It is possible, however, that these specimens lived at a time before the immaturity in human beings had become so prolonged. These fossil remains may possibly have been left by adult early men younger than ten years of age. Certainly the skeleton of a man-like ape nears adult size at ten years, and a horse is fully adult at three or four years; at one time during the evolution of man his skeleton may have developed as rap-

idly as those of other mammals of approximately his size.

From these general standpoints, the evolution of human intelligence has probably depended as largely upon the internal body chemistry and its influence in prolonging growth and development as upon the attainment of size and form in the brain itself.

Growth and Types

One premise we may depend upon, namely, that all structural form in animals results from a process of unequal growths. Growth equal in all directions from the originally spherical egg would perpetuate the spherical shape. Spheres may differ in size but in form all are alike. Should the growth processes be exactly the same in two specimens, their final structures will also be exactly similar while, whenever the growth processes in the two differ, the resemblance is modified. Thus the problem of human types is a problem of growth, and all individuals that may be grouped together under one type are individuals with closely similar growth histories. In previous chapters it was pointed out that in the embryo and foetus the type of structure largely depends upon the rate of growth. A rapid growth and development give one result and a slow growth produces, even in a twin individual, an entirely different result. The peculiar human adult and animal forms that have been described were also interpreted as due to modification of the usual growth processes by the actions of substances which affect metabolism and, therefore, growth rates. Certainly from the time of birth, numerous growth-affecting substances are being produced in the body, the action of

which regulates and modifies the rate and type of growth, their usual effects being simply to increase or decrease the rates of metabolism and thus to cause the individual to grow faster or slower.

It is necessary at this point to recall several propositions discussed in connection with embryonic development. In the first place, initial growth and rapid growth tend to produce linear structure, all plants and animals having this long-recognized primary tendency to form an axis or line of growth. Following this, a lateral growth in width takes place. Crudely stated, there is a tendency to attain first length and later width. Secondly, there is a certain degree of competition between these two tendencies so that as a rule the growth in width only expresses itself after the length growth has worn down and become slower.

It follows that any organ capable of affecting the rate of metabolism or oxidation would necessarily affect the growth rate, and must likewise affect the form and structure of the individual. The one organ in the vertebrate body which seems above all others to affect the rate of metabolism is the thyroid gland, and we know from convincing experimental proof that this gland also greatly affects the rate of growth and structural development. A very instructive fact in this connection is that the human child without a thyroid gland can only develop to the stage shown by the so-called cretin, a baby-like dwarf. This stage might be called the early larval condition of man. The most definite and clear-cut experiments done on the influence of the internal secretions in development are those which show that the thyroid is essential for the metamorphosis of the amphibian larva into the adult stage. The human cretin without thyroid will

not metamorphose or develop into an adult. Also the human individual with a subnormal amount of thyroid may be expected to be more child-like and less adult than the individual with a normal supply of the thyroid secretion. There is a great bulk of evidence to show that the amount or quality of thyroid secretion present in the developing individual is an enormously important element in determining the rate of its growth. The significance of this we have pointed out in other connections by showing that the rate of development is a factor in determining the quality and type of structural production.

The cretin is an abnormal or pathological individual. Its conditions would preclude the breeding of a race of such specimens. It is not in itself a type, cretinism being an arrested child-stage, but it furnishes an extreme growth condition which is most helpful in fully appreciating the influence of the thyroid gland on the growth of the so-called normal types of men.

The thyroid is probably not alone in its action. It, and also the growth rate, may be affected by many other organs but the point of primary importance is that the thyroid appears to be the specialized organ tending to control the rate of oxidation, and therefore of growth in the individual. A normally highly active thyroid gives fast-growing, rapidly differentiating structures, and linear rather than wide lateral type individuals. There is no evidence to indicate that one of these types is in general superior to the other; they are simply different.

It would be very difficult here to go into questions of the interactions among the internal glands, and it is only necessary for our present purpose to state that if a substance

such as the secretion of the thyroid does modify growth rate it may also tend to determine structural types. Since the rate of growth is the important thing in structural type, we should expect not more than two normal types which may grade into each other. The thyroid is so delicate in its response and is so probably different in its action in different environments that the two types may be quite well separated, the one being due to a highly active thyroid and the other to a less active thyroid. The high and low thyroid types differ not only quantitatively but qualitatively as well, since different thyroid secretions call forth different reactions from all other body organs, causing the chemical balance to differ in the two types. The intermediate ideally balanced or indifferent condition would be the most difficult to attain on the part of the sensitive gland.

The two groups into which almost all ordinary persons fall more or less exactly are, then, the *linear type* and the *lateral type*. The linear type is faster growing, high metabolizing, and thin but not necessarily tall; the lateral type is slower in maturing, and is stocky and rounder in form.

Characteristics of the Linear Type and the Lateral Type

Figure 73 represents in outline the common form of an infant placed between the outlines of these two recognized human types. An examination of this figure shows that when the person is linear in form the head is of course narrow or dolichocephalic. The interpupillary distance is short and the eyes are close together; the nose bridge is narrow and, therefore, generally high; the palate arch or

roof of the mouth is narrow and for the same reason highly arched; the lower jaw is small and narrow and usually not strongly developed. The teeth are as a rule crowded and somewhat ill-set. The neck is long and small in circumference, the shoulders are square, high and angular, the extremities are long and slender with long slender muscles and slender bones, the trunk is short, narrow, and tapering to the waist, the intercostal angle is quite acute, the stomach is long and narrow and somewhat vertical in position, extending to a low region in the abdomen, and the liver is generally small.

The shape of the eye-globe in persons of the linear type is such that they are usually far-sighted, though not abnormally so. They need no glasses on the street, unless for astigmatism or some defective eye condition. Usually, and particularly as children, they are under-weight for their height according to the crude average tables generally in use. They arrive at puberty early rather than late, and differentiate rapidly so that the males develop a large strong larynx and a low pitched bass or baritone voice. Their skin is thin and sensitive; as is also the epithelial lining of their digestive tracts. They are epithelial in nature rather than mesothelial, with thin muscles, thin fascia, and little fat. They are as a rule active, energetic, and nervous, quite self-conscious and thus constantly exerting considerable nervous control. When in normal health they rarely laugh aloud, when suddenly shocked they resist the reflex to jump, and they never scream. It is difficult for anyone to recall a shriek from a low-pitched voice, a scream being practically always shrill in tone. On these accounts the linear type passes for cool and calm, with steady nerve, while as a mat-

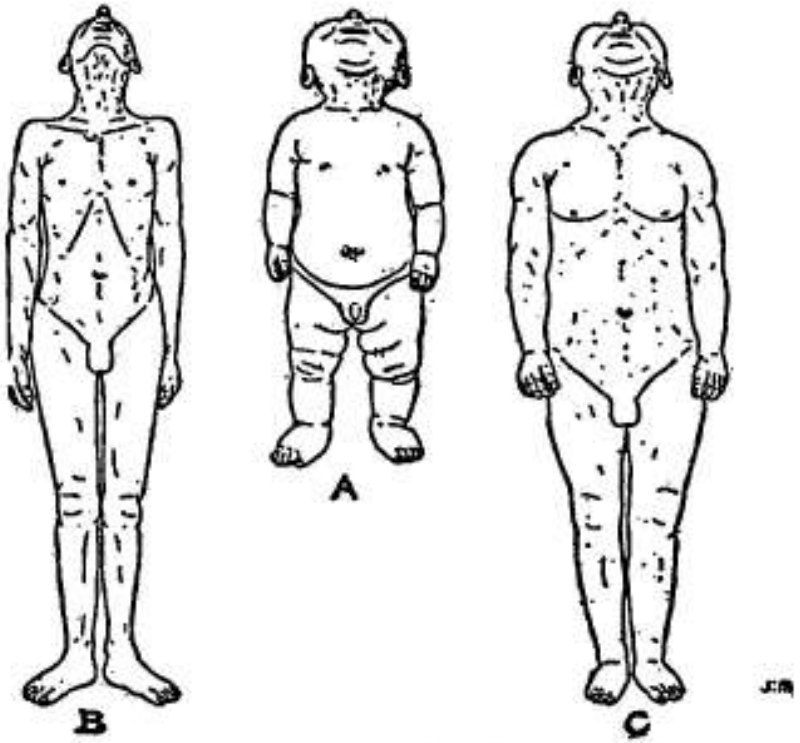


Fig. 73. The general outline of the infant, with the body proportions of the linear type outlined on the left and the lateral type on the right.

ter of fact the body is almost constantly held under nerve control and is actually nervous in the common sense, usually suffering more after a shock than on the occasion of it. When, for example, a street car collides with a truck a large fat person may jump and scream in a high-pitched voice while the thin person beside her sits quietly and calm. Later, however, the emotional person has no after-effect from the excitement, while the thin linear person is

nervous and unsteady as a result of the accident. Shell-shock was probably most common in the armies having most linear type persons.

The lateral type when fully expressed is the antithesis of the linear type in all the respects mentioned. The head grows wide (brachycephalic) and not long, the interpupillary distance is wide as the eyes are far apart, the nose bridge is wide and often, though not necessarily, low. The roof of the mouth or palate is wide and low-arched, the teeth are not crowded and are usually smoothly set, the lower jaw is large and strongly developed, the neck short and large in circumference, the shoulders smooth and sloping. The extremities are not proportionately long and are stocky, with thick bones and well proportioned muscles. The trunk is inclined to be long and full, not constricted but straight or bulging at the waist. The intercostal angle is quite obtuse. The stomach is large and tends to be transverse and high in position, the liver is generally large.

The eye-ball in the lateral type is so shaped as to be near-sighted instead of far-sighted, and such persons frequently use eyeglasses on the street. This type is well rounded and over-weight for its height, and also shows great fluctuations in weight, often gaining or losing as much as 15 or 20 pounds in a short space of time. Persons of the linear type, on the contrary, do not normally experience rapid weight changes but maintain a very constant weight, and may during the twenty years from about nineteen to thirty-nine vary only by a small number of pounds. The lateral type arrives at puberty a little later than the linear and is slower differentiating. The larynx or voice-box of the male does not develop so suddenly and does not usually

grow so large (the Adam's apple is not prominent) and the voice is thus high or tenor instead of bass. In men under thirty years old the deepest bass voices are almost always found among the thin linear individuals, the finest tenor voices among the round lateral type. Everyone recalls that the high tenor is a fat man while the heaviest bass is a linear type thin man.

The initial reaction of the linear type to any suggestion is apt to be contrary or negative; they often almost involuntarily decline things they on second thought are pleased to accept. The initial reaction of the lateral type, on the other hand, is positive but they often decline a suggestion on second thought. The linear type is more adventurous and often embarks without hesitation on an unknown trail, a trait which has caused them to set forth and discover the continents and islands of the world, while the lateral type is more inclined to follow well-thought-out plans and possesses a higher regard for details and preparedness.

The two types may differ in general in their choice of foods, the lateral type inclining towards a high carbohydrate diet, often choosing fatty foods and much sugar, while the linear type is more eager for lean meats and a general protein diet, usually eating little fat or sweets. Women, being as a rule more lateral in type than the male members of their immediate families, incline more towards the lateral tastes than their brothers.

The two types are more clearly differentiated in men than in women, since the growth and glandular reactions are more decided in the male than in the female and are also freer from physiological disturbances. Many more physical points of difference and contrast could be cited

for the two groups, but the above list is sufficient to make the distinctions clear.

The two types have long been recognized, as we have said, which is not surprising since, if the contrasting features are really of significant value, anyone studying the physical characters of men would have discovered them. The most recent and apparently important physical distinctions have been recorded by Bean. His data furnish in a statistical way a number of physical differences which might be added to those mentioned above. Our linear group Bean formerly termed hyperontomorph, meaning high developed structure, but he has since changed the term to *hyperphylomorph*, indicating a strong phyletic or hereditary origin. This change in terms means that Bean considers these types largely as fixed phyletic entities, rather than as ontogenetic or developmental results, as his former terms indicated. Our lateral type is close to his mesophylomorph. Finally, in considering the world races, he arranges in all five types and thus to some extent loses the two primary types. It is a usual procedure to think of the races as groups of separate types, and this accounts for Bean's change to heredity terms. But to this method of grouping end-products one must object from the developmental and growth standpoint. Thorough analysis of physical race differences is valuable, but it must be more clearly emphasized that there are frequently extreme type differences within the racial groups. These differences are often very probably of a genetic origin but they are complicated in other ways, and in all cases they are directly the result of definite growth and developmental reactions. The hereditary type is transmitted, but the expression or development of

the type depends upon numerous environmental influences, and although a feature may be definitely inherited it may never be developed or expressed. The Sebright bantam cock inherits the male plumage but is unable to develop it until he is castrated. Without this operation a casual observer might conclude that the rooster plumage had failed to be inherited, whereas it had only failed to be expressed.

In the same way the human types are modified by environment and the problem of expression or development is just as important as the involved questions of heredity in understanding them. The two types above outlined actually occur among all races and nations of men and are probably the only two common or normal human types. Some races or groups show a great majority of one type and only a few of the other. So that, in general, it may be said that one race is of the linear type and another of the lateral, whereas the ancestry or stock of the races may have been closely the same. The upper classes in England and Germany illustrate the point. Almost all the Englishmen of this caste are linear in type, thin and dolichocephalic, and not at all John-Bull-like, while almost all the Germans are of the lateral type, stocky and brachycephalic. Some Englishmen are, of course, decidedly lateral and some Germans decidedly linear in type, but all in all, the British may be called a linear type race, and the Germans a lateral type race.

We may go still further and claim that these types among the British and Germans are the results more largely of the effects on growth of the environments in which they live rather than of only the hereditary differences in the stocks. This position will be borne out if we consider the types in conjunction with the geographical distribution of

the peoples of the world. The linear types are usually found along the coastal plains, in maritime climates where there is a rich supply of iodine in the environment and where the thyroid gland is normally active or even hyperactive. The lateral types are largely central continentals living in an inland environment away from the iodine supply of the sea. The thyroid gland functions poorly in these central continental regions, colloidal goitre is common and in the extreme situations cretinism occurs. This is a brief general statement of type distribution, all that our present interest demands; a number of exceptional cases may occur to the reader but these when fully considered and analyzed may be fitted into the general scheme. The high volcanic islands, for instance, often have in certain of their central valleys lateral type peoples, but the environment may not be actually maritime although it is insular.

When we turn back to prehistoric man, the earliest skulls are decidedly dolichocephalic and are found in geologic coastal plains. The round-headed central continental type is probably the more recent human form. The most primitive man had a long skull, like the apes, and he probably lived in coastal valleys.

Geographic Distribution and Type

It is a well-recognized fact that when the distribution of an animal species becomes very extensive the species is frequently broken up into a number of varieties, each typical for a given geographic region. There are also certain similar characters developed by the varieties of different species in a given geographic area. The blue-jay has several

varieties, as has also the bob-white and other birds in different parts of the United States. The northern varieties of these birds are as a rule larger than the southern, the Florida types being often the smallest and frequently having longer feathers. The small mammals, squirrels and others, as well as large mammals, also show numerous geographic varieties. There are reasons to believe that food and other environmental conditions are the primary factors that have brought about these varieties.

A species of such wide distribution as the primitive man of many thousand years ago, with only limited means of world migration, must necessarily have broken up into the geographic varieties which existed at the beginning of historic times. But the species had in all of its ranges a tendency to produce either a majority of the linear type, long narrow individuals, or a majority of the lateral type, stocky round-headed persons. Whichever the tendency may have been, the result is probably due to the action of the environment on the function of the thyroid gland, and the type is the consequence of either a fast or slow rate of development. It is a growth reaction.

Age Modifications in Type

Between the ages of twenty and thirty, the linear type is always rather thin, but after thirty-five many individuals of this type become fat and rounder, and may at first sight be mistaken for lateral types, probably owing to some change in the glandular conditions. But on closer examination the head shape, interpupillary distance, tone of voice, and other characters that are not readily modified make the linear type recognizable even in this fat individual. The

young adult shows type in its most easily recognized and least modified form.

It will also be found on observing a group of men of about thirty-five or a little more, that a coarse growth of hair begins on parts which in youth were not so hairy or on which the hair was fine in texture. Strange coarse hairs grow in the eyebrows, on the pinna of the ears and at the entrance to the external auditory meatus. The beard becomes coarser and heavier, and coarser hair develops on the trunk and extremities. The man now possesses a more pronounced male hairiness than he did when under thirty. On first thought one might consider him to have fully arrived at the completely developed male state. This is not the case, however, since the gonads of such an individual have actually begun to decrease in their sexual power. The coarse hair growth is a plumage expression accompanying the decline in the male gonadal activity rather than the attainment of its zenith. The change is gradual but of exactly the same nature as that suddenly produced in the Sebright bantam by castration. In man this is to be recognized as an early indication of senility. It is, however, important that in man the hair growth reaction is not called forth by castration in youth but only follows a gradual degeneration of the gonads after middle life; this slower process, therefore, induces a different interaction among the other glands.

It is well known that castration generally favors an extra accumulation of fat in mammals. The ox is more readily fattened than the bull. At about the same time the coarse hair growth appears in man an accumulation of fat takes place. The anterior abdominal wall often becomes prominent and a decided increase in waist circumference occurs.

These mild symptoms possibly indicate a physiological castration which is gradually taking place. The structural changes occurring at the sex-decline or menopause in women are similar in character but more pronounced and rapid in their development than the above changes in men, probably because the physiological castration in women is much more complete than in the male. All these age reactions tend to distort the original types of such individuals and make them more difficult to recognize.

The Sex-Glands, Senility and Rejuvenation

The degeneration of the sex-glands and the accompanying structural changes during the senile periods of life have misled certain workers—Steinach in Vienna, Voronoff in France, and others—into claiming that the degenerating sex-gland is itself responsible for the aging reaction. Thus transplantations and grafting of sex-glands have been resorted to, both experimentally on lower mammals and surgically on man, with the idea of rejuvenating the individual. The only result has been an occasional temporary stimulation, but always without counteraction of the general aging symptoms. The sex-gland rejuvenation idea is based on an entirely erroneous conception. The degeneration of the gonad, either testis or ovary, in the aging body is one of the many symptoms of the senile complex, and being a symptom it can scarcely also be the causal factor in aging. Something in the body during middle age, no one knows what, initiates the degeneration of the gonads, and how can it be expected that this degenerating influence which overcomes the gonads in their own body could later be conquered by

a piece of engrafted gonad from a younger individual? Logically, the engrafted gonad will also succumb to the same aging influence which had been sufficiently great to cause the original degeneration of the body's own gonads. If these could not withstand the aging environment certainly newly introduced pieces of gonads would scarcely be more successful. Certainly anyone is highly optimistic who expects the implant to overcome the factors inducing the aging process. Rejuvenation, if a possible process, will be brought about by counteracting the senility-producing factors rather than by introducing new tissues similar to those that have already been degenerated through these influences.

There are some animals, such as turtles, crocodiles, and probably a few birds, in which the general body chemistry seems to be long maintained in the balanced adult state, and senile conditions do not develop. Some of these may live over a hundred years and, so far as is known, they reproduce throughout their lives. Their gonads are entirely capable of maintaining a functional state in the absence of the degenerating influences which arise in other animals. A further understanding of the functional balance in these individuals might aid us in the analysis of senility.

If the sex-glands possessed elements which could counteract the aging reaction there should be marked differences in the time of aging between normal animals and castrates without the gonads; but there is not. The ox, the castrated horse, and the capon do not age either faster or slower, so far as is known, than their normal prototypes the bull, the stallion, and the rooster.

The aging reaction is probably brought about by some gradual change in secretory balance among the organs of internal secretion which slowly alters the internal chemical complex of the individual. One of the earliest symptoms of age change is a slowing of the recuperative reaction of the sympathetic nervous system following acute shock. The severe test which brings out this symptom is illustrated by the prize fighter who at thirty may be as strong and as resistant as at twenty-two, yet, on being knocked to the floor, he does not recover and arise as quickly as at twenty-two; and because of this the man of thirty is apt to lose the fight to the one of twenty-two.

Only severe tests bring out the early symptoms of age, but by the late thirties a number of bodily reactions become evident which clearly separate a person of this age from the youthful adults of twenty-five. Quick adjustment to changed conditions is characteristic of youth, but the old man slowly arises from his couch and only gradually adjusts his circulation and bodily functions to the activities of the day.

Thus we observe that normal human beings are experiencing developmental and growth changes which are noticeably due to the usual fluctuations in function of the organs of internal secretion. The appearance of these very evident changes serves to illustrate the fact that if we study more closely the entire developmental history of the individual we will find that growth and structural expression are constantly being influenced by the amount and quality of the internal secretions that have been inherited in the breed to which the individual belongs.

Type Hybrids and Blends

Finally, there are many persons who do not properly fall into either of the well-recognized types, and are not truly intermediates or blends of the two types. These individuals may possess certain well marked, fully expressed features of the linear type along with other typically developed lateral features. They may be dolichocephalic in head shape and yet have near-sighted eyes, wide palate arches, and tenor voices. These combinations are at once out of harmony, and probably result from fluctuations and irregularities in growth-controlling secretions. The general endocrine complex is not harmonious and the glands are not properly proportioned functionally. There may be a linear type reaction at one period and a lateral type behavior at another. Such individuals are almost invariably found to be derived from parentage of opposite types; they are type hybrids or type mixtures. The fact that the purest type individuals are derived from two similarly pure type parents emphasizes the hereditary backgrounds concerned. But at the same time there is much evidence to indicate that environment may modify the growth-regulating mechanism and so tend to change the short or brachycephalic into the long or dolichocephalic head.

If two distinct types actually do exist to a significant extent in a wide population, we should fail to obtain a usually proportioned figure on averaging a large number of physical measurements from a general sample of the population. A striking illustration of this fact was derived from the accurate physical measurements made upon a great number of men in the army draft by Prof. C. B. Davenport of the

Carnegie Institution. From these data averages were obtained for each of the several measurements collected. A statue of the human figure was then built on the basis of these averages. This figure was not that of the usual young American as some would have expected it to be. The trunk was abnormally long, the arms disproportionately short, and the mid-point of the figure entirely out of position. Other unusual details made it that of a person one would rarely see. In averaging the accumulated measurements an unusual and disproportioned figure is produced instead of a combination of commonly seen proportions. This is just the result to be expected when measurements from two or more distinct form types are averaged.

The conclusion seems justified that a recognition of just two physical types is necessary in the formulation and development of the problem of variability in personality and form among normal human individuals.

XVI

THE PHYSICAL BASIS OF PERSONALITY

In Conclusion

WHAT is our present understanding of the physical basis of personality after considering the various problems and discussions as here presented? What is the actual significance of personality itself? Any conclusive answers to these questions cannot be stated as brief definitions. In fact, most of the foregoing pages have been employed in attempting to reply to them in such a way as to include the various factors and phases concerned. Nevertheless, certain deductions are permissible.

How does man differ from other animals, and are the results of experiments done on one animal applicable to another? Each animal species is different from all others, but not entirely different; the more closely related two animals are, the more similarities they show, but each possesses characteristic traits of its own. Experimental results obtained on one animal are often directly applicable to nearly related forms, but at times they are not, and the experimenter recognizes this fact and must put each case to test.

Man's most striking deviation from his nearest animal relatives is in intellectual achievement. There is no difference comparable to it between any other animal species.

We have surmised something as to what evolutionary change in the bodily nature of man could have initiated this supreme deviation. And strangely enough, what seems to be the most plausible possibility yet offered involves two developmental inhibitions. The first of these is uniquely human and results in the retention of head proportions comparable to those found in the foetal stages of the higher mammals. This gives the disproportionately large cranium and big brain with the small facial region, as compared with the reverse adult proportions of small cranium and excessive facial development among the other mammals. And still further, as Huxley remarked, the higher races of men have a larger brain and a smaller jaw than their lower "big-jawed brothers." The highest apes failed to retain this large-brained foetal proportion. The mutation which brought about the large brain was limited to ancestral man.

The second advantage man attains is an exaggerated prolongation of childhood and the stages of immaturity to more than twenty years, as compared with the much more rapid postnatal development of all other mammals. This retardation extends enormously the learning period for man, which among all mammals is largely confined to childhood and immaturity. The prolongation of immaturity can be theoretically accounted for on the basis of a germinal mutation which occurred during human evolution and modified the coördination of internal secretions in such a way as to retard the attainment of sexual maturity for about ten years, and to set the completion of adult size and proportions at more than twenty years, as long as the entire life-time of many of the larger mammals. Very early

ancestral man, probably like other mammals of his size, attained the adult condition within a few years, possibly as few as four or five.

All the great class of mammals is in some ways similar to us and every observer of them is frequently attracted by structural or functional expression much like his own. It is widely recognized that the different races of the human species, the white, the yellow, and the black, show in general different racial personalities. And within the white and yellow race there are well-known nationalistic differences in personality. An Englishman, a German, and a Frenchman are more different in physical appearance and in their personalities than three Englishmen would ordinarily be. Finally within the same national group, and within the same community, and actually within the same family, all members show individually distinct personalities. The point is, that the differences between the personalities in a family are as truly dependent upon physically different backgrounds as are the larger diversities among the personalities shown by members of the various animal classes.

We have followed in the foregoing pages the details in the origin of physical constitution upon which characteristic personality depends. For each individual a definite hereditary composition is formed by the union of an egg and a male sperm-cell at fertilization. This composition is not the same for a number of individuals, but is in the minutiae of its detail unique for each individual.

The physical basis of the individual, the fertilized egg, has within itself the potentiality which gives rise to the completed personality. In order to develop this personality, however, a long series of interactions between the orig-

inal basis and the surrounding environment is essential. We have attempted to consider something of the manifold variations and deviations which arise from the interactions between the germinal basis and the developmental environments. And we have found that the influences of the surrounding elements are important factors in determining the nature and success of the final personality. There is no question here of the degree of importance between the genetic background and the developmental environment; neither is sufficient without the other. Without genetic basis there is no individual, and without a suitably arranged complexity of environment the complete genetic basis is unable to produce the normal individual. The interaction between the individual and the environment is continuous from the germinal beginning to the end of life, and it is mutual: each modifies and affects the other. The individual and the environment are not separate; they are parts of a larger arrangement.

We have found that during both prenatal and postnatal development, peculiar stuffs are produced within the individual which tend to characterize its internal environment. The production and action of these stuffs seem to vary for different genetic constitutions, as is indicated by peculiar hereditary growth-responses which are secondarily dependent upon internal secretions. Our experiments on the inheritance of various peculiar structures and types among dog breeds aim at an analysis of these important reactions.

The presence of exaggerated differences among human personalities has led us to an examination of normal personalities, in order to determine whether minor differences among people could be in any way classified and explained.

This examination of normal persons seems to show that there are qualitatively different types of personalities resulting from two different patterns of growth reaction. These have been termed the linear or long-headed type, and the lateral or wide-headed type. The first is apparently the older human pattern, all prehistoric remains showing long-type skulls and the man-like apes being long-headed. The lateral type with wide skull is the more recent and may possibly have arisen as a response to central continental environments acting upon man as he migrated inland from his place of probable origin on the coastal plains. This supposition is partially suggested by the probability that the maritime environments tend to give a higher functional thyroid reaction and the linear type of growth which is in general associated with an active thyroid gland. In the central continental environments, colloidal goitre and thyroid disturbance frequently occur, and in general the thyroid gland is physiologically less active and the person develops the lateral and more rounded type. These two human types exist among both savage and civilized men, and among all races, and have long been recognized by anthropologists. However, an analysis of the genetic basis for their differences and a study of their developmental reactions has not yet been accomplished.

There are many variations in both types, and there are numerous type hybrids and blends. In spite of these, a careful investigation of human personalities from the physical basis will doubtless reveal many valuable facts and enable us far better to analyze and understand individual traits and behaviors. In Herbert Spencer's words, "The equilibrations of those nervous actions which constitute

what we know as mental life may be classified in like manner with those which constitute what we distinguish as bodily life. We may deal with them in the same order." Surely an understanding of this relation between form and behavior will be of vast importance to the psychologist, to the physician, and to all people as members of a community who must respond to the personalities about them.

BIBLIOGRAPHY

Adams, A. Elizabeth, 1930. Studies on Sexual Conditions in Triturus Viridescens. The Effects of Ovarian Grafts in Castrated Males. Jour. Exp. Zool., Vol. 55.

Adolph, E. F., 1930. Living Water. Williams & Wilkins, Baltimore.

Babcock, E. B., and Clausen, R. E., 1918. Genetics in Relation to Agriculture (New York).

Baltzer, F., 1910. Ueber die Beziehung zwischen dem Chromatin und der Entwicklung und Vererbungsrichtung bei Echinodermenbastarden. Arch. f. Zellf., Vol. 5.

Bagg, H. J., and Papanicolaou, G. N., 1924. Reactions in the Female Reproductive System following Irradiation in the Thyroids. Science, Vol. 59.

Bardeen, C. R., 1907. Abnormal Development of Toad Ova fertilized by Spermatozoa exposed to the Roentgen Rays. Jour. Exp. Zool., Vol. 4.

Bascom, K., 1923. Interstitial Cells in Cattle. Am. Jour. Anat., Vol. 31.

Bateson, W., 1913. Mendel's Principles of Heredity, third impression, Cambridge (Eng.) and New York.

Bateson, W., and Punnett, R. C., 1911. On the Interrelations of Genetic Factors, Proc. Roy. Soc., Vol. 84.

—— ——, 1911. On Gametic Series Involving Reduplication of Certain Terms. Jour. Gen., Vol. 1.

Bean, R. B., 1923. The Two European Types. Am. Jour. Anat., Vol. 31.

——, 1925. Types of Man in the Yellow-Brown Race. Am. Jour. Anat., Vol. 35.

Belar, Karl, 1929 Züchtung und Cytologie. Der Züchter, Vol. 1.

Benoit, M. J., 1923. Sur la Structure Histologique d'un Organe de Nature Testiculaire Developpée Spontanément chez une Poule Ovariotomisée. C. rend. Acad. des Sciences 177.

——, 1924. Sur la Signification de la Glande Génitale Rudimentaire Droite chez la Poule. C. rend. Acad. des Sciences 178.

Bissonnette, Th. H., 1928. Notes on Multiple Pregnancies in Cattle, with Special Reference to Three Cases of Prenatal Triplets and the Free-Martins Involved. Am. Jour. Anat., Vol. 42.

Boring, A. M., and Morgan, T. H., 1918. Lutear Cells and Hen-feathering. Jour. Gen. Phys., Vol. 1.

Bouin, M., et Ancel, P., 1904. Recherches sur la Structure et la Signification de la Glande Interstitielle dans le Testicule Normal et Ectopique du Cheval. Arch. de Zool. exp. et gén., Vol. 4.

Boveri, Th., 1888. Die Befruchtung und Teilung des Eies von Ascaris. Jenaische Zeitsch., Vol. 22.

——, 1903. Ueber den Einfluss der Samenzelle auf die Larvencharaktere der Echiniden. Arch. Ent. der Organismen, Vol. 16.

——, 1909. Die Blastomerenkerne von Ascaris megalocephala und die Theorie der Chromosomen-Individualität. Arch. Zellf., Vol. 3.

Bridges, C. B., 1913. Non-disjunction of the Sex-chromosomes of Drosophila. Jour. Exp. Zool., Vol. 15.
——, 1914. Direct Proof through Non-disjunction that the Sex-linked Genes of Drosophila are Borne by the X-chromosome. Science, Vol. 40.
——, 1915. A Linkage Variation in Drosophila. Jour. Exp. Zool., Vol. 19.
——, 1916. Non-disjunction as a Proof of the Chromosome Theory of Heredity. Genetics, Vol. 1.
——, 1917. An Intrinsic Difficulty for the Variable Force Hypothesis of Crossing Over. Amer. Nat., Vol. 51.
——, 1919. Specific Modifiers of Eosin Eye Color of Drosophila. Jour. Exp. Zool., Vol. 28.
——, 1921. Triploid Intersexes in Drosophila melanogaster. Science, Vol. 54.
——, 1925. Sex in Relation to Chromosomes and Genes. Am. Nat., Vol. 59.
Bridges, C. B., and Morgan, T. H., 1919. The Second Chromosome Group of Mutant Characters. Carnegie Publ. No. 278, Part II.
Brown, Wade H., 1928–29. Constitutional Variation and Susceptibility to Disease. The Harvey Lectures (New York).
Burns, R. K., 1925. The Sex of Parabiotic Twins in Amphibia. Jour. Exp. Zool., Vol. 2.
——, 1927. Some Results of the Transplantation of Larval Gonads in Urodele Amphibians. Anat. Rec., Vol. 37.
Burr, H. S., 1920. The Transplantation of the Cerebral Hemispheres of Amblystoma. Jour. Exp. Zool., Vol. 30.
——, 1923. Experimental Hyperplasia of the Cerebral Hemispheres in Amblystoma. Anat. Rec., Vol. 25.

Carothers, E. E., 1913. The Mendelian Ratio in Relation to Certain Orthopteran Chromosomes. Jour. Morph., Vol. 24.
——, 1917. The Segregation and Recombination of Homologous Chromosomes Found in Two Genera of Acrididae (Orthoptera). Jour. Morph., Vol. 28.
Castle, W. E., 1906. The Origin of a Polydactylous Race of Guinea-pigs. Carnegie Inst. Wash., Publ. No. 49.
——, 1916. Genetics and Eugenics (New York)
——, 1919. Is the Arrangement of the Genes in the Chromosome Linear? Proc. Nat. Acad. Sci., Vol. 5.
——, 1928. The Fate of Unborn Rabbit Embryos. Am. Jour. Anat., Vol. 42.
Castle, W. E., and Phillips, J. C., 1909. A Successful Ovarian Transplantation in the Guinea-pig, and its Bearing on Problems of Genetics. Science, N. S., Vol. 30, No. 766.
—— ——, 1911. On Germinal Transplantation in Vertebrates. Carnegie Inst. Wash., Publ. No. 144.
—— ——, 1913. Further Experiments on Ovarian Transplantation in Guinea-pigs. Science, Vol. 38.
Caullery, M., 1920. Les Problèmes de la Sexualité (Paris).
Coghill, G. E., 1924. Correlated Anatomical and Physiological Studies of the Growth of the nervous system in Amphibia. IV. Rates of proliferation and differentiation in the central nervous system of Amblystoma. Jour. Comp. Neur., Vol. 37.
Cole, L. J., 1924. The Effect of Feeding Thyroid on the Plumage of the Fowl. Jour. Agr. Research, Vol. 29.
Cole, L. J., and Lippincott, W. A., 1919. The Relation of Plumage to Ovarian Condition in a Barred Plymouth Rock Pullet. Biol. Bull., Vol. 36.

Conklin, E. G., 1915. Heredity and Environment. Princeton Univ. Press (Princeton, N. J.).
——, 1917. The Share of Egg and Sperm in Heredity. Proc. Nat. Acad. Sci., Vol. 2.
Corner, G. W., 1923. The Problem of Embryonic Pathology in Mammals—Intrauterine Mortality in the Pig. Am. Jour. Anat., Vol. 31.
Correns, C., 1901. Bastarde zwischen Maisrassen. Biblioth. Botanica, Vol. 53.
——, 1909. Zur Kenntniss der Rolle von Kern und Plasma bei der Vererbung. Zeit. Abst. Vererb., Vol. 2.
——, 1910. Der Uebergang aus dem homozygotischen in einen heterozygotischen Zustand in selben Individuum bei buntblättrigen und gestreiftblühenden. Mirabilis-Sippen. Ber. Deutsch. Ges., Vol. 28.
Correns, C., and Goldschmidt, R., 1913. Die Vererbung und Bestimmung des Geschlechtes (Berlin).
Crew, F. A. E., 1922. A Suggestion as to the Cause of the Aspermatic Condition of the Imperfectly Descended Testis. Jour. of Anatomy, Vol. 56.
——, 1923. The Significance of an Achondroplasia-like Condition met with in Cattle. Proc. Roy. Soc., B, Vol. 95.
Cushing, Harvey, 1912. The Pituitary Body and its Disorders. Lippincott, Philadelphia.

Darwin, C., 1859. The Origin of Species by Means of Natural Selection, or the Preservation of Favored Races in the Struggle for Life (London).
——, 1868. Animals and Plants under Domestication. Sec. Ed., New York.
Davenport, C. B., 1912. Sex-limited Inheritance in Poultry. Jour. Exp. Zool., Vol. 13.
Davenport, G. C. and C. B., 1909. Heredity of Hair Color in Man. Am. Nat., Vol. 43.
Detwiler, S. R., 1923. Experiments on the Reversal of the Spinal Cord in Amblystoma embryos at the Level of the Anterior Limb. Jour. Exp. Zool., Vol. 38.
——, 1924. The Effects of Replacing the Cephalic End of the Embryonic Spinal Cord by an Extraneous Medulla in Amblystoma. Proc. Nat. Acad. Sci., Vol. 10.
——, 1925. An Experimental Study of Cellular Proliferation in the Anterior End of the Spinal Cord of Amblystoma. Jour. Exp. Zool., Vol. 42.
——, 1929. Transplantation of Anterior-limb Mesoderm from Amblystoma Embryo in the Slit-blastopore Stage. Jour. Exp. Zool., Vol. 52.
Domm, L. V., 1929. Spermatogenesis following early ovariotomy in the Brown Leghorn Fowl. Arch. f. Entwmech., Bd. 119.
Doncaster, L., 1914. On the Relations between Chromosomes, Sex-limited Transmission and Sex-Determination in Abraxas grossulariata. Jour. Genet., Vol. 4.
——, 1914. Chromosomes, Heredity, and Sex. Quart. Jour. Micr. Sc.

East, E. M., 1909. The Distinction between Heredity and Development in Inbreeding. Am. Nat., Vol. 43.
——, 1910. A Mendelian Interpretation of Variation that is Apparently Continuous. Ibid., Vol. 44.
Evans, H. M., 1925. Invariable Occurrence of Male Sterility with Dietaries Lacking Fat Soluble Vitamine E. Proc. Nat. Acad. of Sci., Vol. 11.
Evans, H. M., and Burr, G. O., 1925. The Anti-sterility Vitamine Fat Soluble E. Proc. Nat. Ac. of Sci., Vol. 11.

Galton, F., 1892. Hereditary Genius (London).
——, 1897. The Average Contribution of Each of Several Ancestors to the Total Heritage of the Offspring. Proc. Roy. Soc. Lond., Vol. 61.
Geinitz, B., 1915. Über Abweichungen bei der Eireifung von Ascaris. Arch. Zellforsch., Vol. 13.
Godlewski, E., 1906. Untersuchungen über die Bastardierung der Echiniden- und Chrinoidenfamilie. Arch. Ent.-mec., Vol. 20.
——, 1914. Physiologie der Zeugung. Fischer, Jena.
Goldschmidt, R., 1912. Bemerkungen zur Vererbung des Geschlechtspolymorphismus. Zeits. Abst. Vererb., Vol. 8.
——, 1916. Experimental Intersexuality and the Sex Problem. Am. Nat., Vol. 20.
——, 1920. Untersuchungen zur Entwicklungsphysiologie des Flügelmosters der Schmetterlinge. Arch. f. Entwicklungsmech., Vol. 47.
——, 1920. Die quantitativen Grundlagen von Vererbung und Artbildung. Roux' Vortr. und Aufs., Vol. 24.
——, 1927. Physiologische Theorie der Vererbung (Berlin).
Goodale, H. D., 1911. Some Results of Castration in Ducks. Biol. Bull., Vol. 20.
——, 1913. Castration in relation to the Secondary Sexual Characters of Brown Leghorns. Am. Nat., Vol. 47.
——, 1916. Gonadectomy in Relation to the Secondary Sexual Characters of Some Domestic Birds. Carnegie Inst., Wash., Publ. No. 243.
Guyer, M. F., 1909. Atavism in Guinea-chicken Hybrids. Jour. Exp. Zool., Vol. 7.

Harrison, Ross G., 1910. The Development of Peripheral Nerves in Altered Surroundings. Arch. f. Entwmech., Bd. 30.
——, 1924. Some Unexpected Results of the Heteroplastic Transplantation of Limbs. Proc. Nat. Ac. Sci., Vol. 10, No. 2.
——, 1929. Correlation in the Development and Growth of the Eye Studied by Means of Heteroplastic Transplantation. Arch. f. Entwmech. d. Org., Bd. 120.
Heap, W., 1890 and 1897. On the Transplantation and Growth of Mammalian Ova within a Uterine Foster-Mother. Proc. Roy. Soc., Vols. 48 and 61.
Henking, H., 1891. Untersuchungen über die ersten Entwicklungsvorgänge in den Eiern der Insekten. Zeits. f. wiss. Zool., Vol. 51.
——, 1891, 1892. Über Spermatogenese und deren Beziehung zur Eientwicklung bei Pyrrhocoris apterus. Zeitschr. wiss. Zool., Vols., 51, 54.
Herbst, Curt, 1929. Die Physiologie des Kernes als Vererbungssubstanz. Handbuch der Normalen und Pathologischen Physiologie (Berlin).
Herlant, M., 1913. Étude sur les bases cytologiques du mécanisme de la parthénogenèse expérimentale chez les Amphibiens. Archives de Biologie, Vol. 28.
Hertwig, O., 1910. Neue Untersuchungen über die Wirkung der Radiumstrahlung auf die Entwicklung tierischer Eier. Sitz. d. Kgl. Preuss. Akad. d. Wissenschaften, Vol. 29.
Hogben, L. T., and Crew, F. A. E., 1923. Studies on Internal Secretion. II.—Endocrine Activity in Foetal and Embryonic Life. The British Jour. of Exp. Biology, Vol. 1.
Huge, M. A., 1915. The Influence of Temperature on the Development of a Mendelian Character. Jour. Exp. Zool., Vol. 18.
Humphrey, R. R., 1928. The Development of Potencies of the Intermediate

Mesoderm of Amblystoma when Transplanted into Ventrolateral Sites in other Embryos: the Primordial Germ Cells of Such Grafts and their Rôle in the Development of a Gonad. Anat. Rec., Vol. 40.

Jennings, H. S., 1911. Heredity and Personality. Science, Vol. 34.
——, 1913. The Effect of Conjugation in Paramecium. Jour. Exp. Zool., Vol. 14.
——, 1924. Heredity and Environment. The Scientific Monthly, Vol. 19.
Johannsen, W., 1911. The Genotype Conception of Heredity. Am. Nat., Vol. 45.

Keller, K. und Tandler, J., 1920. Zur Frage der sterilen Zwillingskälber. Wiener tierärztl. Monatsschr., Vol. 7.
Koppanyi, T., 1923. Die Replantation von Augen. VI. Wechsel der Augen- und Körperfarbe. Arch. f. Entwmech. d. Org., Bd. 99.

Lang, A., 1912. Vererbungswissenschaftliche Miszellen. Zeits. Abst. Vererb., Vol. 8.
Lewis, W. H., 1906. On the Origin and Differentiation of the Otic Vesicle in Amphibian Embryos. Anat. Rec., Vol. 1.
Lillie, F. R., 1917. The Free-martin; a Study of the Action of Sex Hormones in the Foetal Life of Cattle. The Jour. of Exp. Zool., Vol. 23, No. 2.
——, 1917. Sex-Determination and Sex-Differentiation in Mammals. Proc. Nat. Acad. Sci., Vol. 3.
——, 1923. Supplementary Notes on Twins in Cattle. Biol. Bulletin, Vol. 44, No. 2.
Lipschütz, A., 1924. The Internal Secretions of the Sex Glands (Cambridge and Baltimore).
Loeb, J., 1913. Artificial Parthenogenesis and Fertilization (Chicago).
——, 1916. The Organism as a Whole (New York).
——, 1918. Further Experiments on the Sex of Parthenogenetic Frogs. Proc. Nat. Ac. Sci., Vol. 4.
——, 1923. Theory of Regeneration Based on Mass Action. Jour. of Gen. Physiology, Vol. 5, No. 6.

MacDougal, D. T., 1911. Alterations in Heredity Induced by Ovarian Treatments. Bot. Gaz., Vol. 51.
McClung, C. E., 1902. The Accessory Chromosome—Sex-Determinant? Biol. Bull., Vol. 3.
——, 1905. The Chromosome Complex of Orthopteran Spermatocytes. Biol. Bull., Vol. 9.
——, 1914. A Comparative Study of the Chromosomes in Orthopteran Spermatogenesis. Jour. Morph., Vol. 25.
McDowell, E. C., and Lord, E. M., 1926. The Relative Viability of Male and Female Mouse Embryos. Am. Jour. Anat., Vol. 37.
Mall, F. P., 1908. A Study of the Causes Underlying the Origin of Human Monsters. Jour. Morph., Vol. 19.
Mangold, O., 1929. Das Determinationsproblem. Zweiter Teil. Die paarigen Extremitäten der Wirbeltiere in der Entwicklung. Ergebnisse d. Biol., Bd. 5.
Marshall, F. H. A., 1922. The Physiology of Reproduction. 2nd edition (London).

Mendel, G., 1865. Versuche über Pflanzen-hybriden. Verh. d. Naturf. Vereins in Brünn, Vol. 4.
Meyer, Arthur W., 1917. Intra-uterine Absorption of Ova. Anat. Record, Vol. 12.
——, 1919. Uterine, Tubal and Ovarian Lysis and Resorption of Conceptuses. Biol. Bull., Vol. 36.
——, 1921. Frequency and Cause of Abortion. Am. Jour. Obstet., Vol. 2.
Moore, C. R., 1922. The Effects of Gonadectomy in the Guinea-pig, on Growth, Bone Lengths and Weight of Organs of Internal Secretion. Biol. Bull., Vol. 43.
Morgan, L. V., 1925. Polyploidy in Drosophila melanogaster with Two Attached X-chromosomes. Genetics, Vol. 10.
Morgan, T. H., 1910. Chromosomes and Heredity. Am. Nat., Vol. 44.
——, 1911. An Attempt to Analyze the Constitution of the Chromosomes on the Basis of Sex-linked Inheritance in Drosophila. Jour. Exp. Zool., Vol. 11.
——, 1914. Two Sex-linked Lethal Factors in Drosophila and Their Influence on the Sex Ratio. Jour. Exp. Zool., Vol. 17.
——, 1915. Localization of Hereditary Material in the Germ-cells. Proc. Nat. Acad. Sci., Vol. 1.
——, 1915. The Rôle of the Environment in the Realization of a Sex-linked Mendelian Character in Drosophila. Am. Nat., Vol. 49.
——, 1917. The Theory of the Gene. Am. Nat., Vol. 51.
——, 1919. The Genetic and the Operative Evidence Relating to Secondary Sexual Characters. Carnegie Inst., Wash., Publ. No. 285.
——, 1922. Croonian Lecture on the Mechanism of Heredity. Proc. Roy. Soc., B. Vol. 94.
——, 1923. The Modern Theory of Genetics and the Problem of Embryonic Development. Physiological Reviews, Vol. 3, No. 4.
——, 1924. Human Inheritance. The Am. Naturalist, Vol. 58.
Morgan, T. H., and Bridges, C. B., 1916. Sex-linked Inheritance in Drosophila. Carnegie Inst., Wash., Publ. 237.
—— ——, 1919. The Origin of Gynandromorphs. Carnegie Publ. No. 278, Part I.
Morgan, T. H., Sturtevant, A. H., Muller, H. J., and Bridges, C. B. 1915. The Mechanism of Mendelian Heredity (New York).
Muller, H. J., 1914. A Gene for the Fourth Chromosome of Drosophila. Jour. Exp. Zool., Vol. 17.
——, 1916. The Mechanism of Crossing Over. Am. Nat., Vol. 50.
——, 1929. The First Cytological Demonstration of a Translocation in Drosophila. The American Naturalist, Vol. 63.
Muller, H. J., and Painter, T. S., 1929. The Cytological Expression of Changes in Gene Alignment Produced by X-rays in Drosophila. The American Naturalist, Vol. 63.

Newman, H. H., 1917. The Biology of Twins. The University of Chicago Science Series (Chicago).
Newman, H. H., and Patterson, J. T., 1909. A Case of Normal Identical Quadruplets in the Nine-banded Armadillo. Biol. Bull., Vol. 17.
—— ——, 1911. The Limits of Hereditary Control in Armadillo Quadruplets. Jour. Morph., Vol. 22.
Nicholas, J. S., 1922. The Effect of the Rotation of the Area Surrounding the Limb Bud. Anat. Rec., Vol. 23.

——, 1924. Regulation of Posture in the Fore Limb of Amblystoma punctatum. Jour. Exp. Zool., Vol. 46.
——, 1929. Movements in Transplanted Limbs. Proc. Soc. Exp. Biol. and Med., Vol. 26.
Nonidez, J. F., 1920. Studies on the Gonads of the Fowl. I. Hematopoetic Processes in the Gonads of Embryos and Mature Birds. Am. Jour. of Anat., Vol. 28.
——, 1922, 1924. Studies on the Gonads of the Fowl., Am. Jour. Anat., Vols. 31 and 34.

Painter, T. S., and Muller, H. J., Parallel Cytology and Genetics of Induced Translocations and Deletions in Drosophila. Jour. of Heredity, Vol. 20, No. 6.
Patterson, J. T., 1927. Polyembryony in Animals. The Quart. Rev. Biol., Vol. 2.
——, 1929. X-rays and Somatic Mutations. Jour. of Heredity. Vol. 20, No. 6.
Pearl, R., 1917. The Experimental Modification of Germ Cells. Parts I, II, III. Jour. Exp. Zool., Vol. 22.
Pende, Nicola, 1922. Das Gesetz der Morphogenetischen Korrelation von Viola und die Grundlagen der Pathologie des Wachstums und der Konstitution. Zeitschrift für Konstitutionslehre, Vol. 8.
Pezard, A., 1927. Les Hormones Sexuelles et l'hérédité Mendélienne chez les Gallinacés. Z. f. ind. Abst. u. Vererbungsl., Vol. 46.
Plough, H. H., 1917. The Effect of Temperature on Crossing Over. Jour. Exp. Zool., Vol. 24.
Ponse, K., 1924. L'organe de Bidder et le Déterminisme des Charactères Sexuels Secondaires du Crapaud (Bufo vulgaris). Rev. suisse de zool., Vol. 31.
Punnett, R. C., 1911. Mendelism, third ed. (New York).

Riddle, Oscar, 1917. The Theory of Sex as Stated in Terms of Results of Studies on Pigeons. Science, n. s., Vol. 46.
——, 1924. Sex in the Right and Left Sides of the Bird's Body. Amer. Phil. Soc., Vol. 68.
——, 1925. Reciprocal Size Changes of Gonads and Thyroids in Relation to Season and Ovulation in Pigeons. Am. Jour. Physiol., Vol. 73.
——, 1928. Internal Secretions in Evolution and Reproduction. Sci. Monthly, Vol. 26.
Roux, W., 1881. Kampf der Theile. Leipzig.
——, 1883. Ueber die Bedeutung der Kerntheilungsfiguren. Engelmann, Leipzig.

Schleip, W., 1912. Geschlechtsbestimmende Ursachen im Tierreich. Ergebn. u. Fortscher. d. Zool., Vol. 3.
Shull, A. F., 1925. Sex and the Parthenogenetic-bisexual Cycle. Am. Nat., Vol. 59.
Spemann, H., 1912. Über die Entwicklung umgedrehter Hirnteile bei Amphibienembryonen. Zool. Jahrb., Suppl. Bd. 15.
——, 1925. Some Factors of Animal Development. The British Jour. of Exp. Biology, Vol. 2.
Spencer, Herbert, 1868. First Principles. New York.

Stark, M. B., 1918. An Hereditary Tumor in the Fruit Fly, Drosophila. Jour. Cancer Research, Vol. 3.
Steinach, E., 1910. Geschlechtstrieb und echte sekundäre Geschlechtsmerkmale als Folge der innersekretorischen Funktion der Keimdrüsen. Zentralbl. f. Physiol., Vol. 24.
——, 1916. Pubertätsdrüse und Zwitterbildung. Arch. Entw.-Mech., Vol. 42.
Stern, C., 1927. Ein genetischer und cytologischer Beweis für Vererbung im Y-Chromosom von Drosophila melanogaster. Zeitschr. ind. Abst. u. Vererbungsl., Vol. 44.
Stevens, N. M., 1905. Studies in Spermatogenesis with Especial Reference to the "Accessory Chromosome." Carnegie Inst., Wash., Publ. No. 36.
Stieve, H., 1924. Beobachtungen über den rechten Eierstock und den rechten Legdarm des Hühnerbabichts und einiger anderer Raubvögel. Morph. Jahrbuch., Vol. 54.
Stockard, C. R., 1907. The Artificial Production of a Single Median Cyclopean Eye in the Fish Embryo by Means of Sea Water Solutions of Magnesium Chloride. Archiv. für Entwicklungsmechanik der Organismen, Vol. 23.
——, 1907. The Influence of External Factors, Chemical and Physical, on the Development of Fundulus Heteroclitus. Jour. Exp. Zool., Vol. 4.
——, 1908. Studies of Tissue Growth. I. An Experimental Study of the Rate of Regeneration in Cassiopea Xamachana (Bigelow). Publ. of the Carnegie Inst., Wash., No. 103.
——, 1909. The Development of Artificially Produced Cyclopean Fish,—"The Magnesium Embryo" Jour. Exp. Zool., Vol. 6.
——, 1909. Studies of Tissue Growth: II. Functional Activity, Form Regulation, Level of the Cut, and Degree of Injury as Factors in Determining the Rate of Regeneration. The Reaction of Regenerating Tissue in the Old Body. Jour. Exp. Zool., Vol. 6.
——, 1909. The Artificial Production of One-Eyed Monsters and Other Defects, which Occur in Nature, by the Use of Chemicals. Anat. Record, Vol. 3.
——, 1909. The Influence of Alcohol and Other Anaesthetics on Developing Embryos. Proc. Soc. Exp. Biol. & Med., Vol. 7.
——, 1910. The Independent Origin and Development of the Crystalline Lens. Am. Jour. Anat., Vol. 10.
——, 1910. The Influence of Alcohol and Other Anaesthetics on Embryonic Development. Am. Jour. Anat., Vol. 10.
——, 1910. Studies of Tissue Growth. III. The Rate of Regenerative Growth in Different Salt Solutions. IV. The Influence of Regenerating Tissue on the Animal Body. Arch. f. Entwick.-Mech. d. Org., Vol. 29.
——, 1911. The Fate of Ovarian Tissues when Planted on Different Organs. Arch. f. Entwick.-Mech. d. Organ, Vol. 32.
——, 1911. The Experimental Production of Various Eye Abnormalities and an Analysis of the Development of the Primary Parts of the Eye. Arch. f. Vergl. Ophthal., Vol. 1.
——, 1912. Is the Control of Embryonic Development a Practical Problem? Proc. Am. Phil. Soc., Vol. 51.
——, 1912. An Experimental Study of Racial Degeneration in Mammals Treated with Alcohol. Arch. Internal Med., Vol. 10.
——, 1913. An Experimental Study of the Position of the Optic Anlage in Amblystoma Punctatum, with a Discussion of Certain Eye Defects. Am. Jour. Anat., Vol. 15.

——, 1914. The Artificial Production of Eye Abnormalities in the Chick Embryo. Anat. Record, Vol. 8.
——, 1914. Injuries to Germ-Cells. Jour. of Heredity, Vol. 5.
——, 1919. Developmental Rate and the Formation of Embryonic Structures. Proc. Soc. Exp. Biol. & Med., Vol. 16.
——, 1920. Effect of Underfeeding on Ovulation and the Oestrous Rhythm in Guinea-pigs. Proc. Soc. Exp. Biol. & Med., Vol. 17.
——, 1921. Developmental Rate and Structural Expression: An Experimental Study of Twins, "Double Monsters" and Single Deformities, and the Interaction among Embryonic Organs during their Origin and Development. Am. Jour. Anat., Vol. 28.
——, 1921. A Probable Explanation of Polyembryony in the Armadillo. Am. Naturalist, Vol. 15.
——, 1921–22. The Significance of Modifications in Body Structure. Harvey Soc. Lectures (New York).
——, 1922. Alcohol as a Selective Agent in the Improvement of Racial Stock. British Med. Jour. (Aug.)
——, 1923. Experimental Modification of the Germ-plasm and its Bearing on the Inheritance of Acquired Characters. Am. Philos. Soc., Vol. 62, No. 5.
——, 1923. Human Types and Growth Reactions. Am. Jour. of Anat., Vol. 31, No. 3.
——, 1924. The Structures of the Vertebrate Eye as an Index of Developmental Deficiencies: With the Bearing on Recent Inheritance Studies. Am. Naturalist, Vol. 58.
——, 1926. The Gonads and Sex Physiology. Trans. Congress Am. Physicians & Surgeons, Vol. 13.
——, 1926. Constitution and Type in Relation to Disease. Medicine, Vol. 5.
——, 1927. Extra Toes in the Guinea-pig an Atavistic Condition and its Genetic Significance. Anat. Record, Vol. 35.
——, 1927. Hormones and Structural Development. Beaumont Foundation Lectures (Detroit), Series VI (Williams & Wilkins, Baltimore).
——, 1928. Inheritance of Localized Dwarfism and Achondroplasia in Dogs. Anat. Record, Vol. 38.
——, 1928. Hormones of the Sex Glands—What they mean for Growth and Development. "Chemistry in Medicine," Chemical Foundation, New York.
——, 1928. Present Status of the Problem of So-called Rejuvenation. Bull. N. Y. Acad. of Med., Vol. 4, No. 12.
——, 1928. Rickets in Dogs as Probably Related to Sex. Am. Jour. of Diseases of Children, Vol. 36.
——, 1929. The Trend of Morphology. Science, N. S., Vol. 69.
——, 1930. The Presence of a Factorial Basis for Characters Lost in Evolution: the Atavistic Reappearance of Digits in Mammals. Am. Jour. Anat., Vol. 45.
——, 1930. The Problem of Development in Adult Constitution. Address at Dedication of Medical School, Univ. of Va., Charlottesville.
Stockard, C. R., and Papanicolaou, G. N., 1917. The Existence of a Typical Oestrous Cycle in the Guinea-pig, with a Study of Its Histological and Physiological Changes. Am. Jour. Anat., Vol. 22.
—— ——, 1918. Further Studies on the Modification of the Germ Cells in Mammals; the Effect of Alcohol on Treated Guinea-pigs and their Descendants. Jour. Exp. Zool., Vol. 26.
Stone, L. S., 1930. Heteroplastic Transplantation of Eyes between the Larvae of Two Species of Amblystoma. Jour. Exp. Zool., Vol. 55.

Stone, L. S., and Uesber, N. T., 1927. Return of Vision and Other Observations in Replanted Amphibian Eyes. Proc. Soc. Exp. Biol. and Med., Vol. 25.
Streeter, G. L., 1906. Some Experiments on the Developing Ear Vesicle of the Tadpole with relation to Equilibration. Jour. Exp. Zool., Vol. 3.
——, 1924. Single-ovum Twins in the Pig. Am. Jour. Anat., Vol. 34.
Sturtevant, A. H., 1915. The Behavior of the Chromosomes as Studied through Linkage. Zeit. Abst. Vererb., Vol. 13.
——, 1917. Genetic Factors Affecting the Strength of Linkage in Drosophila. Nat. Acad. Sci., Vol. 3.
——, 1917. Crossing Over without Chiasmatype. Genetics, Vol. 2.
——, 1919. Inherited Linkage Variations in the Second Chromosome. Carnegie Publ. No. 278, Part III.
Sturtevant, A. H., Bridges, C. B., and Morgan, T. H., 1919. The Spatial Relations of Genes. Proceed. Nat. Acad., Vol. 5.
Swett, F. H., 1926. On the Production of Double Limbs in Amphibians. Jour. Exp. Zool., Vol. 44.
——, 1927. Differentiation of the Amphibian Limb. Jour. Exp. Zool., Vol. 47.
Swingle, W. W., 1926. The Determination of Sex in Animals. Physiol. Rev., Vol. 6.

Tandler, J. und Gross, S., 1909. Über den Einfluss der Kastration auf den Organismus. I. Beschreibung eines Eunuchenskeletes. Archiv. f. Entw.-Mech., Vol. 27.
—— ——, 1910. II. Die Skopzen. Arch. f. Entw.-Mech., Vol. 30, Part 2.
—— ——, 1913. Die biologischen Grundlagen der sekundären Geschlechtscharaktere. Berlin.
Tandler, J. und Keller, K., 1910. IV. Die Körperform der weiblichen. Frühkastraten des Rindes. Arch. f. Entw.-Mech., Vol. 31.
—— ——, 1911. Über das Verhalten des Chorions bei verschiedengeschlechtlicher Zwillingsgravidität des Rindes und über die Morphologie des Genitales der weiblichen Tiere, welche einer solchen Gravidität entstammen. D. Tierärztl. Wochenschr. 19.
Torrey, H. B., 1925. Thyroid Feeding and Secondary Sex Characters in Rhode Island Red Chicks. Biol. Bull., Vol. 49.
Torrey, H. B. and Horning, B., 1922. Hen-feathering Induced in the Male Fowl by Feeding Thyroid. Proc. Soc. Exp. Biol. and Med., Vol. 19.
Tschermak, E., 1900. Ueber künstliche Kreuzung bei Pisum sativum. Zeit. landw. Versuch. Oest.
Twitty, V. C., and Schwind, J. L., 1928. Growth of Heteroplastically transplanted Eyes and Limbs in Amblystoma. Proc. Soc. Exp. Biol. and Med., Vol. 25.

Uhlenhuth, E., 1912. Die Transplantation des Amphibienauges. Arch. f. Entwmech. d. Org., Bd. 36.

Vogt, W., 1926. Über Wachstum und Gestaltungsbewegungen am hinteren Körperende der Amphibien. Anat. Anz., Bd. 61.
——, 1929. Gestaltungsanalyse am Amphibienkeim mit örtlicher Vitalfärbung. II. Gastrulation und Mesodermbildung bei Urodelen und Anuren. Arch. f. Entwick.-Mech., Vol. 120.
De Vries, H., 1901. Die Mutationstheorie (Leipzig).
——, 1905. Species and Varieties; Their Origin by Mutation (Chicago).

Weismann, A., 1893. The Germ-plasm, translation by W. N. Parker, New York.
——, 1904. The Evolution Theory. Trans., J. A. Thomson, London.
——, 1913. Vorträge über Deszendenztheorie, Jena.
Willier, B. H., 1921. Structures and Homologies of Free-martin Gonads. Jour. of Exp. Zool., Vol. 35.
Wilson, E. B., 1905. Studies on Chromosomes, I and II. Jour. Exp. Zool., Vol. 2.
——, 1911. The Sex-chromosomes. Arch. Mikr. Anat., Vol. 77.
——, 1914. Croonian Lecture: The Bearing of Cytological Research on Heredity. Proc. Roy. Soc., Vol. 88.
——, 1925. The Cell in Development and Heredity (New York).
Witschi, E., 1921. Der Hermaphroditismus der Frösche und seine Bedeutung für das Geschlechtsproblem und die Lehre von der inneren Sekretion der Keimdrüsen. Arch. f. Entw.-Mech., Vol. 49.
——, 1923. Über die Genetische Konstitution der Froschzwitter. Biol. Zentralbl., Vol. 43.
——, 1923. Über geographische Variation und Artbildung. Revue suisse de Zool., Vol. 30.
——, 1927. Sex Reversal in Parabiotic Twins of the American Woodfrog, Rana sylvatica. Biol. Bull., Vol. 52.
——, 1929. Bestimmung und Vererbung des Geschlechts bei Tieren (Berlin).

Yatsu, N., 1921. Changes in reproductive organs of Parabiotic Rats. Anat. Rec., Vol. 21.

Zeleny, C., and Senay, C. T., 1915. Variation in Head Length of Spermatozoa in Seven Additional Species of Insects. Jour. Exp. Zool., Vol. 19.

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