

CHROMOSOMES AND HEREDITY

T. H. MORGAN

Columbia University

Morgan, T. H. 1910. Chromosomes and heredity.
The American Naturalist, 44:449–496.

ESP

ELECTRONIC SCHOLARLY PUBLISHING

[HTTP://WWW.ESP.ORG](http://www.esp.org)

Electronic Scholarly Publishing Project

Foundations Series — Classical Genetics

Series Editor: Robert J. Robbins

The ESP Foundations of Classical Genetics project has received support from the ELSI component of the United States Department of Energy Human Genome Project. ESP also welcomes help from volunteers and collaborators, who recommend works for publication, provide access to original materials, and assist with technical and production work. If you are interested in volunteering, or are otherwise interested in the project, contact the series editor: *rrobbins@fhcrc.org*.

Bibliographical Note

This ESP edition, first electronically published in 2003, is a newly typeset, unabridged version, based on the 1910 edition. Unless explicitly noted, all footnotes and endnotes are as they appeared in the original work. Some of the graphics have been redone for this electronic version.

Production Credits

Scanning of originals: ESP staff
OCRing of originals: ESP staff
Typesetting: ESP staff
Proofreading/Copyediting: ESP staff
Graphics work: ESP staff
Copyfitting/Final production: ESP staff

© 2003, Electronic Scholarly Publishing Project

<http://www.esp.org>

This electronic edition is made freely available for educational or scholarly purposes, provided that this copyright notice is included.

The manuscript may not be reprinted or redistributed for commercial purposes without permission.

Morgan, T. H. 1910. Chromosomes and heredity.
The American Naturalist, 44:449–496.

CHROMOSOMES AND HEREDITY

T. H. MORGAN

Columbia University

THE INDIVIDUALITY OF THE CHROMOSOMES

We have come to look upon the problem of heredity as identical with the problem of development. The word heredity stands for those properties of the germ-cells that find their expression in the developing and developed organism. When we speak of the transmission of characters from parent to offspring, we are speaking metaphorically; for we now realize that it is not characters that are transmitted to the child from the body of the parent, but that the parent carries over the material common to both parent and offspring. This point of view is so generally accepted to-day that I hesitate to restate it. It will serve at least to show that in what I am about to say regarding heredity and the germ-cells I shall ignore entirely the possibility that characters first acquired by the body are transmitted to the germ. Were there sufficient evidence to establish this view, our problem would be affected in so far as that we should not only have to account for the way in which the fertilized egg produces the characters of the adult, but also for the way in which the characters of the adult modify the germ-cells.

The modern literature of development and heredity is permeated through and through by two contending or contrasting views as to how the germ produces the characters of the individual. One school looks upon the egg and sperm as containing *samples* or *particles* of all the characters of the species, race, line, or even of the individual. This view I shall speak of as the *particulate theory of development*.

The other school interprets the egg or sperm as a kind of material capable of progressing in definite ways as it passes through a series of stages that we call its development. I shall call this view the *theory of*

© 2003, Electronic Scholarly Publishing Project

<http://www.esp.org>

This electronic edition is made freely available for educational or scholarly purposes, provided that this copyright notice is included.

The manuscript may not be reprinted or redistributed for commercial purposes without permission.

physico-chemical reaction, or briefly the reaction theory. The resemblance of this comparison to the traditional theories of preformation and epigenesis is obvious, and I should willingly make the substitution of terms were it not that the terms preformation and epigenesis have certain historical implications, and, as I wish to emphasize certain things not necessarily implied in the historical usage, I prefer descriptive terms other than these overladen with so many traditions.

A few preliminary considerations will serve to clear the way for the detailed examination to follow:

The particulate theory may appear more tangible, definite and concrete because it seems to make a more direct appeal to a material basis of development and heredity. The theory of physico-chemical reaction may seem more vague and elusive, since the responses and reactions to which it must appeal are as yet little known. But this distinction is not one of much importance. For the particulate theory requires as elaborate a series of processes or changes to account for the distribution of the postulated particles and their development into characters as does the reaction theory itself, and on the other hand the reaction theory may rest its claims on as definite a physical or material basis as does the other view. One theory lays emphasis on the material particles of development, the other on the changes or activities in the same material. Both views assume that there is something in the egg that is responsible for every detail of character that later develops out of the egg. Since we do not know what this something is, it must be admitted at the outset that the distinction between the two is largely theoretical and possibly temperamental. To some minds it appears that to admit that every detail of character is represented by the egg must mean that something material in the sense of some actual particle that stands for each detail must be present. To other minds it seems only necessary to admit that eggs are made of different materials in order that the outcome of the development may be different, and that these differences between eggs, while leading to differences in the end product, need not be conceived as different material particles in the sense that the particles become the ultimate characters that differ.

Both views postulate an initial difference in the egg, but one view conceives the differences in the egg to be associated with particles that are in some way directly responsible for the different characters, while the other view conceives adult characters to be the product of an elaborate series of processes and that the material differences in different eggs are too remotely connected with the end product of their development for us to think of those differences in terms of special or separate particles except in the purest symbolic fashion. Whichever

view we adopt will depend first upon which conception seems more likely to open up further lines of profitable investigation, and second which conception seems better in accord with the body of evidence at hand concerning the process of development.

It may be said in general that the particulate theory is the more picturesque or artistic conception of the developmental process. As a theory it has in the past dealt largely in symbolism and is inclined to make hard and fast distinctions. It seems to better satisfy a class or type of mind that asks for a finalistic solution, even though the solution be purely formal. But the very intellectual security that follows in the train of such theories seems to me less stimulating for further research than does the restlessness of spirit that is associated with the alternative conception. The purely adventurous character of any explanation offered by the reaction theory seems more in accord with the modern spirit of scientific theory. But when we lay aside these generalities concerning the two theories and descend to particulars we may find at times very real distinctions between the two views. For example:

The original conception of preformation postulated an actual material embryo in the egg; epigenesis denied the existence of that embryo, and justified its denial. Here surely there was a real distinction.

But the problem has refined itself in modern times. We no longer look for an actual embryo preformed but we look for samples of each part, which samples by increasing in size and joining suitably to other parts make the embryo. This is modern preformation. Is it not a question of fact whether such samples exist in the egg? The contrasting theory looks upon the germ-cells as consisting of one fundamental material, or at most of a few materials that change as development proceeds, until finally the end-product of the changes are the kinds of materials that we know to differ chemically in a number of ways. It seems to me that there is here also a real difference between the two views, and that the one can be as clearly formulated as the other: I propose, therefore, to examine further these contrasting views in the light of our present opinions concerning the egg and its mode of development.

The *modern* theory of particulate inheritance goes back no further than the discovery that the sperm transmits equally with the egg the characters of the race; and with the discovery that the most conspicuous thing that the sperm brings into the egg is the nucleus of the male cell or more specifically its chromatin. Around these simple statements the whole edifice has been erected. We owe to Weismann more than to any other biologist, the peculiar trend that this speculation has followed. It has seemed to many biologists that the only interpretation of the facts just stated could be that special turn that Weismann has given to them.

By a curious twist of logic Roux brought the chromosomes into the discussion. He argued that the karyokinetic figure is an instrument of such a sort that we must suppose its function to be that of nicely separating at each division the different kinds of materials of which the chromosomes are composed, or supposed to be composed. Were it only necessary, he argued, to divide the chromatin quantitatively into equal parts a far simpler mechanism ought to suffice. Weismann took this argument in good faith, and built up his theory upon it.

But if one thing seems more certain than anything else in modern cytological work it is that in most cases the karyokinetic figure divides the chromatin of the chromosomes into exactly equal parts, irrespective of what the fate of the cells is to be. We find that the chromosomes in the different tissues are identical as far as our methods reach. Observation gives a positive denial to the Roux-Weismann assumption. In fact, Roux himself has later abandoned this position. We find in many quarters a strong disinclination to the view that the chromosomes are responsible *in this sense* for the process of development.

This feeling has interested me a good deal in recent years, especially since I myself have felt the same disinclination to reduce the problem of development to the action of specific particles in the chromosomes. In my own case and possibly in the minds of others this hesitation is due in the first place to a distaste for the particular form of this theory that Weismann has made so pronounced a feature of his speculations, and in the second place to a feeling that it is unsafe or unwise to reduce the problem of heredity and development to a single element in the cell; when we have every evidence that in embryonic development the responsive action of the cytoplasm is the real seat of the changes going on at this time, while the chromosomes remain apparently constant throughout the process.

The feeling against the view that ascribes everything to the chromosomes has been increased also by the assumption that unit characters in heredity are preformed; especially since those who assume such characters to be the basis of heredity have as a class — with some exceptions, however — shown a strong predilection towards locating their indivisible units in the chromosomes.

These and other conditions have combined to produce two opposing views and the chromosomes have come to be the chief bone of contention. I shall attempt, therefore, to limit my discussion to this topic, at the risk of appearing to take rather a narrow point of view.

We can trace to the important work of Boveri a great deal in our modern conception of the idea of the chromosomes in heredity and development. We owe to Boveri the current conception of the individuality of the chromosomes; we owe to him the discovery of facts

that go to show in a sense the independence of the chromosomes of the cytoplasm in which they lie; and most important of all we owe to him the idea that the chromosomes may be individually different and that development depends on the presence in the cells of samples of each kind of chromosome. Let us take up these points in turn.

Individuality is a word with vague meanings. Boveri has, however, defined very precisely the limited way in which he applies this term to the chromosomes. Whether we agree that the facts show the chromosomes to possess this kind of individuality is a question to be further examined, but admitting differences of view possible Boveri's careful analysis of the situations must excite our admiration and respect. Wilson's expression, the genetic continuity of the chromosomes, seems, however, to better express Boveri's attitude than the word individuality used by Boveri himself so far as the facts of direct observation are concerned; but if we extend this term to include Boveri's deductions from certain experimental work, then the word individuality means something more than genetic continuity.

Applied to the chromosomes, individuality means that the chromosome that passes into the resting nucleus is substantially the same that comes out at the next division. This interpretation has met with some opposition. Every cytologist is familiar with the fusion of the chromatin threads in the resting nucleus. If they fuse, what guarantee is there that they will separate again along the exact lines of union? If the separation is not exact the materials of the chromosomes would, before long, become completely intermixed. It is this difficulty that has created a presumption against the theory of the individuality of the chromosomes.

Despite the supposed objection the fact remains indisputable that in cells where the chromosomes can be distinguished by their distinctive sizes, the same sized bodies emerge after every supposed fusion in the resting nuclei. The most convincing evidence for individuality in this sense is that brought forward by Boveri's study of the position and shape of the chromosomes as they emerge from the nucleus at the two-cell stage of *Ascaris*. He shows that there is often a remarkable agreement between the chromosomes in the two sister cells which can only be explained on the grounds that the chromosomes have retained in the resting stage the same form and position that they had when they went into the resting nucleus, and this arrangement can be traced back to the way in which the chromosomes divided in the segmentation spindle,

This evidence points to the conclusion that the central part at least of the chromosomes has not been lost by fusion in the resting stage. It is important to note that we can not explain their reappearance after

each resting stage by means of the assumption that they differ chemically and segregate according to their kinds of materials, because in each nucleus there are two chromosomes of the same sort, one paternal the other maternal in origin, but identical otherwise. The pairs may lie in any position with regard to each other in the resting nucleus. Hence like chromosomes they might often interlace, and there is no guarantee that later these materials would move into the two original chromosomes rather than concentrate around one of the two centers. It has been suggested by Hertwig and held also by others, especially by Fick, that the formation of the chromosomes and of the network represents a kind of crystallization process that is regulated by the amount of chromatin present. This suggestion also meets with serious objections, for, were it true, we should expect, I think, to find that the chromosomes would assume definite positions with regard to each other. The evidence shows clearly that this is not the case, as seen best when chromosomes of different sizes exist. The arrangement is varied in different cells of the same individual and in only a few cases do certain chromosomes lie in a definite position in the equatorial plate — in the center of the plate, for example, as seen in the spermatocyte divisions of certain insects. We can only fall back, therefore, on the evidence, brought forward by Rabl and demonstrated in the clearest way by Boveri, showing that the position of the chromosomes in the new division is determined by the position of the chromatin in the last division, and assume that in some way the center of the old chromosomes becomes the center of the new.

Putting the facts together, they go far towards showing that the central axis of the chromosome is not lost in the resting nucleus, but remains to become the center of the next chromosome. Here perhaps we find a clue to the genetic continuity, or individuality. If we look upon the spinning process of the chromosome as a process by means of which its peripheral substance is thrown out into the nucleus to form the reticulum, and assume that most of it fails to return the next time the chromosome becomes distinct, we have an hypothesis in conformity with many facts at least, and also a view that makes simpler, perhaps, our interpretation of the meaning of the process. On this view the materials set free by the chromosomes remain behind in part when the nuclear wall is dissolved, and become a part of the cytoplasm of the cell. In this way chromatin materials set free at each breaking down of the nucleus reach the cytoplasm, and in time may come to represent a large part of the cytoplasmic substance. If we look upon the chromosomes as organs for producing the fundamental organic material out of substances absorbed by the cytoplasm — in a word if we look upon the chromosomes as assimilating centers of the

cell we can understand the enormous increase of chromatin in the early stages of development of the embryo, and also how in time their products set free in the cell may come to have a controlling influence on the reactions and responses of the cytoplasm of the cells.

Any one who has observed the dissolution of the enormous germinal vesicle will sympathize with such an interpretation. A relatively large part of the nucleus is thrown out into the cell; for, the chromosomes form a relatively small part of the entire germinal vesicle.

The impression, often given in popular works on the cell, that the nuclear sap alone is set free at the dissolution of the nuclear wall, and that this nuclear sap is only a watery fluid without significance in the cell, is probably erroneous. On the contrary, there is set free not only a fluid, but a large mass of material that may in part represent some of the nuclear network, and much of this material at once assumes the same staining capacity as the rest of the cytoplasm.

Individuality of the chromosomes means, therefore, in this sense genetic continuity from cell to cell of a portion of each of the original chromosomes. This interpretation will apply whether we consider the chromosomes as made up of entirely different materials, or of partly different materials, or even if they are all identical in chemical composition. Let us turn then to the next most important question. Have we evidence to show whether the chromosomes are identical in chemical composition or whether they are different?

We may dismiss at once, I believe, the evidence based on the similarity of the staining capacities of the chromosomes. With the rarest exceptions they all stain alike. Such methods as are used are too crude to throw any light on the question of their possible differences. The stains that we employ do little more than differentiate basic from acid bodies and in this regard the chromosomes belong to the acid group. Their finer differences, if such exist, would not appear by the methods used.

The most striking evidence that can be cited to show that the chromosomes are different is based on their size relations. These are constant. Does this mean that the chromosomes are therefore different? I do not believe that such evidence is of any value one way or the other. If the size of the chromosomes is referable to their genetic continuity, the facts can be accounted for without recourse to the assumption of chemical difference.

Fortunately we have some evidence from embryology that has seemed to many embryologists to indicate that the chromosomes differ in their physiological behavior; from which we may infer that they

differ chemically. I refer to Boveri's brilliant experiments with the dispermic eggs of the sea urchin.

When two spermatozoa enter simultaneously the egg of the sea urchin each brings in its own center or aster from which two centers are formed. These two centers form a triaster (one being excluded) or a tetraster about the three pronuclei (two male, one female). When the nuclei dissolve each sets free its 18 chromosomes, producing $18 \times 3 = 54$ chromosomes which are distributed to the three poles of the triaster, or to the four poles of the tetraster. The distribution is, as a rule, irregular in the sense that some centers get more than others. The protoplasm then divides into three or into four equal parts, the axis of division corresponding with that of the egg axis as in normal division.

From these eggs embryos develop; many of them are abnormal, but a few are normal. Normal embryos develop more often from the eggs that divided at once into three, than from those that divided into four. Boveri points out that the chance is greater in the three-fold type that each cell gets at least one set of the chromosomes than in the four-fold type — hence he argues the greater frequency of normal development.

Boveri's chief results, however, were obtained by isolating the three blastomeres of the three-fold type and the four blastomeres of the four-fold type. Under these circumstances one or two or three of the isolated blastomeres may produce a normal embryo, but, as a rule, not more than one normal embryo develops, although as stated, cases of two or three embryos are also found. This result can be explained on the ground that only those blastomeres develop normally in which one full complement or set of chromosomes is present. Boveri concludes that normal development is dependent on the presence of at least one set of chromosomes. Hence the evidence points to the conclusion, he believes, that the chromosomes are different; and that one of each kind must be present to insure a normal process of development.

That the results are not due to cytoplasmic differences is shown by the fact that the plane of first division passes through the axis of the egg, so that each blastomere gets a part of the different regions of the egg. That the result is not due to the size of the blastomere is shown by a comparison with isolated blastomeres of eggs that have divided normally. Moreover, experiments with fertilized egg-fragments show that normal development is not dependent on a prescribed size relation between the nucleus and the cytoplasm.

Other objections that have been raised have also been successfully met by Boveri and I can not but think, therefore, that until more valid objections can be found, Boveri has made good his point.

The experiment of fertilizing non-nucleated fragments of the egg has demonstrated that a single set of chromosomes suffices to produce normal development. Artificial parthenogenesis in the sea urchin has also shown that the single set of chromosomes in the female pronucleus is capable of giving rise to normal embryos. It follows that as a result of normal fertilization a double set of chromosomes is present in the embryo — two of each kind of chromosomes — and this fact is of significance in heredity.

Boveri has added further evidence in favor of his conclusion from an experiment in which normally fertilized eggs are put under pressure just as the cleavage is about to appear. The cytoplasm division often fails to take place. A single cell may sometimes contain two nuclei and such cells not infrequently later form polyasters. These may cause inequalities in the distribution of the chromosomes, and the abnormal development that sometimes follows can be explained in the same way as in the case of the dispermic eggs. Boveri asks what can these cases have in common unless it is the inequality in distribution of the chromosomes.

Driesch has argued that, since in the normal development the plane of bilaterality corresponds with the first (Boveri) or second (Driesch) plane of cleavage, the three-fold or four-fold types may fail to produce this effect at the right moment. But it is not evident, even if it is true that a bilaterality exists in the egg, that the embryo might not still produce it independently of the cleavage. In the case of the four-fold type an opportunity is, in fact, furnished for the normal relation to appear, yet this type produces fewer normal embryos than does the three-fold type. Moreover, the development of symmetrical embryos for the one-half and one-fourth blastomeres shows that the egg has remarkable regulatory powers in this regard. Again radially symmetrical embryos have been produced by Herbst in lithium solutions, yet these do not appear in embryos from dispermic eggs.

This evidence goes far towards establishing in some form the probability of Boveri's argument. It seems to me more cogent and convincing than that brought forward by his opponents. It does not, I think, prove that the chromosomes are entirely unlike and does not, obviously, prove that each character of the embryo is located in a particular chromosome. But the evidence makes probable the view that the different chromosomes may have somewhat different functions, and that normal development depends on the normal interactions of the materials produced by the entire constellation of chromosomes.

Boveri himself is far from ascribing to the chromosomes the intricacies of the Weismannian conception. He has clearly stated that his conception of their individuality does not require that each

chromosome represents a distinct character of the individual, or even an exclusive bundle of such characters. He concedes, that whatever it is in them that stands for the characters of the adult may be distributed to all of the chromosomes in some species, and that in different species the materials may be differently assorted.

It should indeed be pointed out that Boveri's evidence seems to prove too much for that form of the particulate theory that ascribes unit characters to chromosomes, for it indicates, I think, that individual chromosomes do not in any sense contain either preformed germs or determinants, or unit characters, or even stand for the production of particular organs in any sense.

Were this the case we should expect the isolated blastomeres of the dispermic eggs to produce different kinds of organs, heterogeneously united. It can not fairly be argued in reply to this point that such development would be a physical impossibility; for, we are familiar with the fact that teeth, hair, bones, etc., may form in various teratomata, and this shows that individual organs may develop independently of the rest of the organism with which they are normally connected. This side of the question has not, I believe, been sufficiently considered by Boveri.

It is true that Boveri has pointed out that embryos that develop from dispermic eggs are often imperfect or asymmetrical and interprets this as due to the inequalities of distribution of the chromosomes. His figures, however, give the impression that the abnormalities are due to imperfections in the relations of the parts rather than to dislocation of organs as his view in the strictest sense seems to require. It should not be forgotten that eggs normally fertilized if kept under unfavorable conditions so that they develop abnormally show similar imperfections. Were his results really due to dislocations, *i.e.*, mal-assortments of chromosomes, we should anticipate a far greater mosaic type of development, I think, than actually appears.

In conclusion we must consider the behavior of the chromosomes at that period in their existence that has seemed to most cytologists the most critical time in their history, especially in relation to their behavior in heredity. I refer to the so-called synapsis, when the total number of chromosomes becomes reduced to one half the number characteristic of the body-cells. The most significant fact in this reduction is that like-chromosomes pair, or unite, as first made probable by Montgomery, and since confirmed on an extensive scale by several other writers, notably by McClung, Wilson, Stevens, Schreiner, etc.

It may appear that we can most easily interpret this process as due to like materials running together or fusing in consequence of the

likeness of the materials themselves. But that the process is something more than this seems probable from the fact that such union takes place at no other time in the innumerable resting stages, except at this particular one, just prior to polar-body formation in the egg, and at the corresponding period in the spermatogenesis. The actual apposition of the thread-like chromosomes that has been described by many observers does not suggest a simple physical fusion or running into a lump of like materials, but rather the approach and fusion of definite cell constituents. The line of separation persists for some time in some species, according to certain observers, and may, according to Brauer and others, remain evident until the next division occurs, when the threads again separate to pass to different parts of the spindle.

The mechanism appears to be such, on this interpretation, that like chromosomes are at this time separated and pass into daughter cells. If this is the correct interpretation the process is one of profound significance for students of heredity.

It is true that in most cases a separation between the united pairs can no longer be detected and this has been interpreted to mean that an actual fusion takes place as complete as when two drops of water unite into one. If so there would be no grounds left for assuming when the next division occurs, that the united halves actually separate again; for the splitting might occur along any axis of the double chromosome as far as we know. I should not care to make any dogmatic statements in regard to this question in the present unsettled state of our knowledge; but whether we assume the separation to be along the line of union or whether in any other plane the conclusion will have, as I said, a deep interest for the student of heredity.

There is one additional piece of evidence that may be cited in favor of the non-fusion interpretation. In some insects one pair of chromosomes does not enter into synapsis. These remain apart in the nucleus in some species or simply touch each other without fusion in others. In both cases the pair enters the spindle and its members pass to opposite poles.

Even more remarkable are such forms as *Acholla*, in which one large chromosome has as its mate five smaller ones. None of them fuse in synapsis, but they meet on the spindle and four go to one pole and one — the larger one — to the opposite.

It may be argued that these cases show that the “purpose” of the synapsis is only to bring together similar chromosomes in order that they may be again separated. It can not be denied that these cases give a certain plausibility to this interpretation, yet they are exceptional cases, and it is unsafe to generalize from them to other chromosomes that we know to behave differently. Moreover, this method of “touch and go”

appears to be so much simpler than the elaborate changes involved in synezeis, that one may well ask whether synezeis may not have a deeper significance than the mere apposition of like chromosomes. In fact the process seems well suited to bring into close and intimate fusion the pairs of chromosomes instead of simple apposition as appears in the sporadic instances cited above. The situation calls, at least, for a suspension of judgment until we have more evidence.

The number of chromosomes in closely related forms presents one of the most puzzling problems when we attempt to apply the chromosome view to the facts of heredity. The case of the thread worm of the horse, *Ascaris megalcephala*, is the best-known case. In some localities the worms have four chromosomes for their full number, in other localities only two. The animals are identical externally, and occasionally where both forms exist crosses occur. In such hybrids three chromosomes are found in the embryo, but unfortunately no adult worms have as yet been seen with three chromosomes. Such a worm would offer an exceptional opportunity to study the reduction problem. In other groups similar variations in numbers are known between closely related species. For example, one of the phylloxerans has 44 and another 12 chromosomes, yet the two species differ only in minor points, and every structure in one has its counterpart in the other. If the chromosomes are the bearers of the hereditary characters how can such facts be interpreted?

If we think of each chromosome in the one species as containing the unit characters of a leg, or a wing, or an eye, how are the same characters distributed in the other species? Evidently a complete redistribution of such units must be conceived. If genetic continuity is to be extended also to the origin in time of the unit characters in species, it seems to me inconceivable that so vital a question as the assortment of these characters should so readily change in closely similar, and probably closely related species. Difficult as it is to interpret this relation, the simplest view would be to assume that it makes no difference how the chromatin is assorted in the chromosomes, so long as the sum total of the materials is present.

From this point of view the individuality of the chromosomes is a matter of secondary importance; for, the same or equivalent material may be represented by two or by forty chromosomes. Individuality or genetic continuity (*i.e.*, *ontogenetic* not *phylogenetic*) has no further significance, from this standpoint, than that it insures for each species the transmission to all the cells of the body of a given amount of materials or possibly a definite amount of all the different kinds.

We may next proceed to examine into the relation of the chromosomes in Mendelian inheritance from the point of view reached in the preceding discussion.

CHROMOSOMES AND MENDELISM

It has become generally accepted by students of Mendelian inheritance that some kind of "segregation" is the key to the numerical results that play an all-important part in the Mendelian theory of heredity. The discovery that there occurs in the formation of the germ-cells a process that supplies the machinery by means of which segregation might take place has aroused expectation to a high pitch of interest in the application of the observations of cytology to the conclusions in regard to Mendelian segregation. It is true that there is much diversity of opinion as to the value of cytological study, in its present imperfect state of development, to Mendelism, and this divergence relates unfortunately to the very nature of the processes involved.

Mendel realized that the numerical proportions that appear in the second hybrid generation could be explained, if, in the formation of the germ cells or gametes, a separation of the constituent elements, or characters of the hybrid occurs. These paired characters that separate Bateson has called allelomorphs.

A process takes place in the germ-cells, at the so-called maturation divisions, that may possibly offer a clue as to how the paired characters in the germ cells of the hybrid separate. Prior to this division there are two chromosomes of each kind; one member of each pair being maternal in origin and the other paternal. The members of each pair come together just before maturation division, reducing the number of chromosomes to half. Later these paired chromosomes divide so that each germ-cell gets one half of each pair.

Sutton first pointed out in 1903 that if each character that Mendelizes is carried by a particular chromosome the mechanism of reduction gives an explanation of the way in which there may come to be two kinds of germ cells with respect to each particular pair of characters. This hypothesis has been championed by Wilson in 1903, and later by Boveri in 1904.* If we analyze the facts further we find that the hypothesis requires in order that pure gametes are to be formed by the hybrid that each particular character, or whatever it is that

* In 1902 Boveri referred to a possible relation between reduction and inheritance in hybrids, but he did not point out how this idea could be applied to explain the numerical results of Mendelism.

produces the character, be confined to a single chromosome; otherwise the separation will not be complete and pure gametes will not be formed. Do the facts of reduction fulfil this condition?

When the reduction in the number of the chromosomes takes place we find that the homologous pairs of chromosomes fuse completely, so far as we can judge by our modern methods of technique. Observation gives no evidence in most cases that the chromosomes only adhere side by side, but on the contrary conjugation appears to be a complete fusion, and if this is what really takes place, what guarantee is there that subsequently the members of a pair will separate along their line of fusion? It seems all the more remarkable that such a process should take place, if, as is often assumed, the separation division is not the first, but the second division of the paired chromosome. In other words it is admitted that in such cases the first division is at right angles to the plane of union, and that only at the second division does separation or segregation occur. In fact the assumption of separation is largely gratuitous, and is the outcome of certain theoretical postulates of Weismann's theories — postulates that rest in part on questionable evidence.

All that we really know is that in some cases two longitudinal divisions of the chromosomes occur,* whose relation to the plane of fusion is largely hypothetical. If, however, it be assumed that the chromosomes simply come to lie side by side (or even end to end) and later separate the process of synapsis, as it is called, is merely "touch and go" and has no deeper significance. If, on the other hand, it be assumed that the synapsis is a true fusion of the combining elements, there are no reasons to suppose that the chromosomes separate later into their constituent parts. The expectation is rather that once completely fused they do not necessarily separate at the plane of fusion to give the pure elements that combined.

It is, however, the assumption that the chromosomes do separate along their line of union that has appeared to some writers to have important bearing on the theory of Mendelian theory of pure gametes. Let us therefore assume for the moment that the separation takes place in this way. Since the number of chromosomes is relatively small and the characters of the individual are very numerous, it follows on the theory that many characters must be contained in the same chromosome. Consequently many characters must Mendelize together. Do the facts conform to this requisite of the hypotheses? It seems to me that they do not. A few characters, it is true, seem to go together, but

* For the sake of simplicity I have left out of account here the possibility of end-to-end union.

their number is small, and it is by no means evident that their combination is due to a common chromosome. It is true that in no one species do we know much concerning the behavior of many characters, but so far as we do know them there is no evidence that they Mendelize in groups commensurate with the number of chromosomes. In two cases, in fact, viz., in *Pisum* and in *Antirrhinum* it appears that the number of the characters that have been shown to Mendelize separately is greater than the number of their chromosomes.

This has seemed a fatal objection to the chromosome view, but it may not be so, as Spillman has argued, so long as it has not yet been shown that all of the dominant characters may be present at the same time. But even admitting this possible way of eluding the objection, the other point raised above concerning the absence of groupings of characters in Mendelian inheritance seems a fatal objection to the chromosome theory, so long as that theory attempts to locate each character in a special chromosome. We shall have occasion to return to this point later.

In recent years most workers in Mendelian inheritance have adopted a new method of formulating their theory. Characters that Mendelize are no longer allelomorphous to each other, but each character has for its pair the absence of that character. This is the presence and absence theory. We can apply this hypothesis to the chromosome theory. For examples, let us assume a new variety or race arises by the loss of a character from that chromosome that has heretofore carried it. The chromosome still remains in existence, since it may carry many other characters besides the one that was lost, and it becomes in the hybrid the mate of the one still retaining that character. If now separation occurs, two classes of germ-cells result, one with and the other without the character; and the observed numerical proportions follow. There is nothing in this assumption that meets with any greater difficulty on the chromosome separation hypothesis than on the earlier view of paired allelomorphs, but it meets with the same difficulties, and as an assumption is neither more nor less in accord with the postulated mechanism.

More recently, still another interpretation has been suggested by Shull and by Spillman. It is a quantitative conception, and I shall try to point out some of its applications to the chromosomes.

Let me recall once again the familiar fact that in animals and plants two homologous chromosomes of each kind are present in every cell. This gives the diploid number. One of each kind suffices to produce the character in some cases, but each is nevertheless present in double. We might think of the doubleness as a sort of reserve and the double group be conceived as a "mechanism of safety." That the double number is

not always necessary for the formation of the characters is shown in embryos that develop from non-nucleated fragments of eggs. These embryos have all the characters peculiar to their species. The importance of the double set is illustrated, however, in certain hybrids. The best case is that of the hybrid between horned and hornless races of sheep. The male hybrids from this union have horns, the female hybrids lack horns, irrespective of the way in which the first cross was made, *i.e.*, the results are the same whether the mother was horned and the father hornless, or the mother hornless and the male horned. Bateson interprets this to mean that one dose of horns in the male hybrids suffices to call forth horns; but one dose in the female hybrids is insufficient to call forth horns. In terms of chromosomes this may mean that one horn-bearing chromosome suffices in the male to call forth horns, but in the females one chromosome is not enough.

When these hybrids are inbred they produce in the second generation four kinds of individuals, horned males and females; hornless males and females. The numerical results appear to coincide with the assumption made above in regard to the number of doses of chromosomes necessary to call forth horns in the two sexes. For in the second generation there will occur a certain number of combinations in which females will contain two doses of horns and these females should be horned.

The case of color blindness in man appears to follow the same rule, for here also females may transmit the character without developing it, while males, if they have it at all, develop color blindness. One dose of color blindness in males makes the male color blind; one dose in females is insufficient. The rarity of color-blind females is explicable on this view.

These results may be significant for the chromosome hypothesis since the interpretation seems to imply that the amount of a given material, or chromatin, perhaps, is an important element in the determination of the development of characters. If the interpretation is correct it means that a character will not develop even when its primordia or forerunners are present, unless a sufficient amount of that material be present. And, on the other hand, in other individuals a smaller amount of the same material suffices to call forth the unfolding of a given structure.

The same interpretation seems to have a wide application to the characters of the first generation of hybrids, and in all heterozygous individuals that are in nature identical (*i.e.*, heterozygous) with the first generation hybrids. It is known that in several cases the dominant character does not reach its full development in the first generation, as Correns showed for *Mirabilis Jalapa*. Such cases can be explained on

the ground that one dose is not enough. The reappearance in the second generation of individuals with the full dominant character is in harmony with this assumption, for in one fourth of the individuals two doses of dominance are expected.

In mice, too, the heterozygous form between black and chocolate often shows black or chocolate areas in the fur, and in the same mouse a region may be at first black and later chocolate, or *vice versa*. It appears that the condition of the mouse at the time when the molt takes place determines whether the hair contains the one or the other pigment in excess. Thus external conditions or internal states may regulate dominance in hybrid forms.

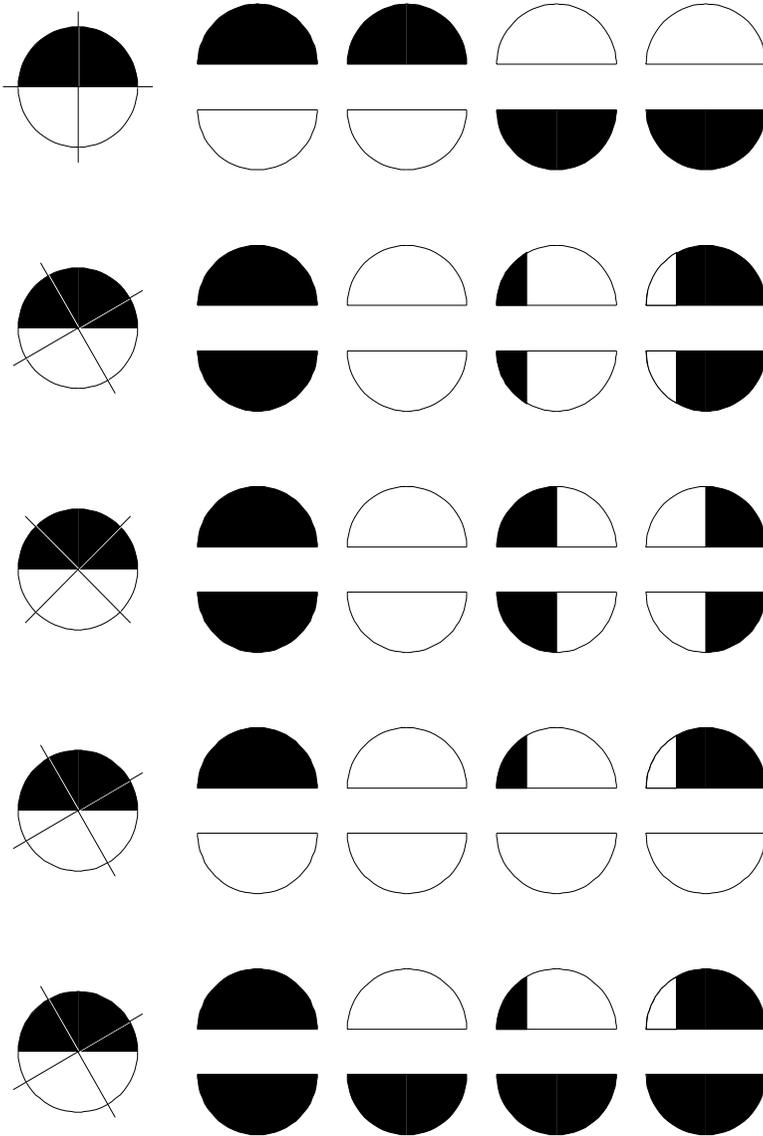
Such facts lead to a consideration of how far quantitative relations are factors in heredity, and how far the chromosomes support such an interpretation. If, as we have seen, the development of a character depends on the amount of a given material rather than on its presence or total absence as the theory of pure gametes demands, may not this view give an interpretation of the rôle of the chromosomes in inheritance?

Let us see where such an interpretation leads. By means of diagram A, I have tried to indicate one way in which a quantitative interpretation of the facts of Mendelian inheritance might be explained. In the hybrid the pair of fused chromosomes, representing the presence and absence of a character, is represented by the black and white semicircles fused together. Should their separation occur along the line of fusion (first line) as demanded by the theory of pure gametes there will result after two divisions two chromosomes bearing the positive character (or briefly the black chromosomes), and two without (or the white chromosomes). These are represented for the egg in the upper line by the four semi-circles; and the similar cells for the male by the four similar semi-circles in the line below. Chance combinations will give three classes of individuals in the proportion of 1: 2: 1; or three with the dominant to one with the recessive character.*

But should the pair of chromosomes fuse and not separate at the line of fusion, the results are shown in the second line, where the intersecting lines indicate the plane of division. Again four classes of gametes result, as shown in the upper line. If the same sort of division occurs in the male, and fortuitous combinations result, there will be the same three classes of individuals as before, which gives the ratio of three dominant to one recessive.†

* In this scheme when one of the two chromosomes of the pair is black the combined action is black.

† It is assumed here that when as much or more than the volume of one member of the pair is black the result is black.



The only division that will not give this result is that when the planes of division lie exactly at 45 degrees to the plane of fusion, as shown in the third line. Here the results give 11 dominant to 5 recessive, but this is so near the three to one proportion that it offers no serious drawback to the result when we consider how seldom this division will occur.

The two remaining lines show the results of back-crossing between the hybrid (F_1) with the recessive (fourth line); and with dominant (fifth line). They give the expected proportions.*

In all of the preceding cases except the first the gametes are not pure, as a rule, but nevertheless produce two classes of individuals that may be sharply defined. This scheme seems to work as well as the pure gamete assumption; it avoids certain difficulties encountered by the latter; and appears to explain further a class of cases inexplicable on the pure gamete hypothesis; namely the graded series of forms so often met with in experience and so often ignored or roughly classified by Mendelian workers.

Again, for simplicity it has been assumed that varieties or races lacking a character lack entirely the kind of activity that calls forth that character. But there is no need to make this limitation. If in some cases the lack of character may in reality be due to total absence of action, there are other cases which can be explained on the chromosome basis if we assume that the absence of a character is due to incomplete or insufficient activity of its chromosomes varying from 1 to 50, to put the matter graphically. Let us assume 25 per cent. of activity takes place. Such an individual paired to a dominant will give dominance in the first generation (due to the 50 per cent. of the dominant plus 25 per cent. of the recessive). Chance splitting of the fused chromosomes after synapsis in the hybrid will give two classes of gametes, but one class will contain numerically more than 50 per cent. of character-forming materials. Consequently there will be more individuals of the dominant race than the theory of pure gametes and equal division demands.

The converse case is also worthy of consideration. If one individual is just able to produce a given color or material by the combined activity of its two chromosomes, but no more than just able to do so, and the other individual totally lacks all power, the first hybrids will also fail to produce the character. Their chromosomes combined and divided at random in the germ cell will produce a much larger number of gametes that fall below the standard than of those that rise to a point sufficient to give the character when combined — in consequence the recessives will be greatly in excess.

These considerations may seem to throw light on the question of potencies of different individuals — a question that is coming more into the foreground. We can see from the point of view here suggested how individuals alike externally may differ very greatly in their power to transmit their peculiarities to hybrid offspring.

* Provided when more than half of a chromosome of a pair is black the result is black.

This conclusion is especially applicable to cases where the full development of a character can only appear when two groups of chromosomes (to take the simplest case) are necessary to produce a character; or, to take the more extended view, when excessive amounts of chromatin must be present. It is now well established that certain races lacking a character nevertheless dominate in the first generation when crossed with a race possessing a character. In such cases the failure of dominance may be due to insufficient chromatin of the positive kind rather than due to an inhibiting factor as sometimes assumed.

As regards blending, it is evident that this relation must result from the combined action of the two parental contributions to the hybrid; the blending is the sum of both effects. Such cases differ from Mendelian cases in the first generation only in that one influence does not exclude the other. In the second generation separation into two classes of individuals does not occur, but a great variety of forms appear: Nevertheless the individuals may show a tendency to group around the two parental and the hybrid classes, as Castle has shown for long and short hair. In this sense blended inheritance shows gradations into alternate inheritance. The chief difference between the two, I repeat, is found in the compatibility of the contrasted characters. So far as the chromosomes are concerned the results need not be referred to any special kind of fusion of the combining elements, but simply to the way in which the effects become patent. Alternate inheritance and blended inheritance appear only to be extremes of the same process.

This brings us to the inheritance of the spotted condition, a class which has been a serious difficulty on the assumption of Mendelian dominance and segregation of pure characters. The most striking case is that of spotted animals or striped plants. Some regions of the body are colored, other regions white, *i.e.*, they lack pigment. On the assumption that the individual has the capacity to produce pigment the presence of white spots is inexplicable; on the assumption that the individual lacks the power to produce pigment the colored spots are inexplicable. A spotting factor is therefore assumed whose presence accounts for spots. Its allelomorph is a uniform coat whose presence does away with spots. A more refined juggling would be difficult to imagine, especially when the presence of color is explained by the presence of an enzyme and a color producer, and its absence to the lack of one of these. Yet after appealing to a purely physiological principle to explain color versus no color, the explanation is thrown overboard in the case of spotted animals and a mystical spotting factor is set up as an explanation. The humor of the situation grows when one thinks that the spotting factor may produce a few white hairs on the tip of the tail, or a coat nearly

entirely white. To be logical there should be as many spotting factors as there are hairs on the body.

It has been shown that the spotted condition does not follow by simply crossing a uniform color and an albino — unless that albino has been derived from spotted ancestors. Hence spotting is not due to combinations of this sort, but is due to a condition peculiar to certain races. How can we interpret this peculiarity? The great difficulty of explaining this class of cases must be admitted, but I think that a possible interpretation may be found in the following direction, although I am far from wanting to urge that it is the only possible interpretation. The absence of a character, color in the present instance must be due to local conditions; certain regions are like the hornless female hybrid sheep. It is well known that injuries to the skin may cause the cessation of formation of colored hair and the production of white hair. Similarly in colored animals, certain regions are more prone to lack pigment than other regions. In rodents for example, the belly, the tip of the tail and the forehead seem to be such regions even in animals that would be classed as uniformly colored. It follows that if in certain races these regions are particularly deficient in their power to produce pigment a spotted race will arise. Crossing with an albino race does not increase the extent of the spotted area in the hybrid. On the contrary, if the white animal has been derived from a race uniform in pigment production in these regions the hybrid will be uniform, *i.e.*, not spotted at all, although one parent was spotted.

It may appear that this view has simply introduced the spotting factor in a new guise. In a sense this is true, but it recognizes a condition that is ignored by those who make use of a spotted factor, for it rests on the assumption that whether pigment develops in certain regions depends not only on whether pigment producing factors are present or absent in the germ cells, but on the modifications of such inheritance by local conditions. My conclusion is, moreover, of a piece with our general knowledge of development of different organs of the same embryos.

Why, it may be asked, can not the spotted character be explained on the assumption of weakened power in these spotted races to produce color; or why is it not due to loss of chromosomes in the early blastomeres of the germ cells in certain regions?

The first alternative must be rejected, I believe, for were the power of color production weakening in spotted animals, the ratio being lower than 50 per cent., we should still have to invoke local action to account for the results. Moreover, there is no evidence that color production is less intense here.

The other alternative can be answered on more general grounds. If Mendelian characters are due to the presence or absence of a specific chromosome, as Sutton's hypothesis assumes, how can we account for the fact that the tissues and organs of an animal differ from each other when they all contain the same chromosome complex. Bateson has called attention to this weakness of the single-chromosome-single-character hypothesis. For on such a view the chromosomes should be sorted out in the soma until each region gets its proper kind. The facts are the reverse. However important therefore the chromosomes are in transmitting the full quota of hereditary traits, we must be prepared to admit that the evidence is entirely in favor of the view that the differentiation of the body is due to other factors that modify the cells in one way or in another. This consideration is, to my mind, a convincing proof that we have to deal with two sets of factors — the common inheritance of all the cells to produce all the kinds of tissues and organs in the body, and the limitation of that property in the course of development. If the former is due to the chromosomes and the unspecialized parts of the cytoplasm, the latter may be due to the local changes that the relation of the parts to each other calls forth. It might even be argued that since in the development we find no evidence of a sorting out of the chromosomes that produce special parts, the individual chromosomes can not stand each as the representative of those parts, but rather that each part needs the entire set of chromosomes for its normal life. However tempting such an argument may be for those who have reached on other grounds the conclusion that this is the more probable interpretation of the chromosomes, the argument will not appear conclusive to those who do not accept such a general standpoint, for they may justly claim that we know too little about the possibilities of chromosomal behavior to make this sort of a demand of them. The consideration is nevertheless, I think, worth consideration.

The most serious, and probably fatal, objection to the quantitative view outlined above is found in the later possibilities of the mixed chromosomes. If the longitudinal division is fortuitous in the synaptic pair it must also be assumed to be fortuitous in the later splittings of the same chromosomes in the embryo. The results would give a mosaic of cells in some of which one and in other cells another character will predominate. We should expect therefore a sort of piebald or chimaera type to result. The difficulty is not minimized by referring the results to all of the chromosomes instead of to a single one.

Unless we refer the problems of heredity to principles apart from a material basis our only hope at present of a scientific solution of the problem is to rely on such a basis. There are three ways, however, in

which we may make use of such a physical material conception of "segregation." First, by postulating material particles in the chromosomes of the germ cells qualitatively different — particles that are sorted out at the reduction period. Our analysis has shown that there are serious difficulties for this interpretation. Second, by postulating a quantitative factor as the basis of segregation; here also difficulties are met with. Third, by assuming initial differences in the germ cells of the hybrids due to the same kind of differences that become patent in the development of the embryonic organs where the results are not referable to segregation of chromatic materials, but due to regional differences or state of equilibrium — the result of reactions between the cells. Here it seems to me we find the most promising direction in which to look for further light on the subject. For example, the formation successively of brown, yellow and black pigment by the follicle cells of a gray mouse suggests that a similar process may take place in the germ cells of hybrids. In the somatic cells no one supposes that the differences are due to loss of chromatin, or to a segregation, otherwise, of materials. On the contrary, the presumption is in favor of the view that the effects are produced not by segregation, but by the relation of the cells to each other, or to the whole. If this comparison be admitted, it follows that at some stage in the history of the germ cells of the hybrid similar effects may take place in regard to each kind of the inherited qualities (not characters). In this connection it should be recalled that the germ cells of the hybrid have had a long history before maturing. If the chromosomes are the essential elements in producing or maintaining the material constitution of the cells there has been an abundant opportunity for the chromosomes to have produced general effects of this kind. The way in which the cells react will depend on the changes that the chromosomes have produced in them. In other words, at some period in their history when the germ cells have become, as it were, hybrid throughout they develop one or another of each of the alternate possibilities to a greater or to a less degree. Since the same sort of process occurs in groups of somatic cells where it results from the responsive action of the parts on each other, so let us suppose in the germ cells of the hybrid a similar relation determines the fate of its different potentialities.

Our general conclusion is, therefore, that the essential process in the formation of the two kinds of gametes of hybrids in respect to each pair of contrasted characters, is a reaction or response in the cells, and is not due to a material segregation of the two kinds of materials contributed by the germ cells of the two parents. The reaction differs in the germ cells of the hybrid from that of either of the parental types because the material basis of the germ cells differs owing to its dual

origin. The results are due, however, to difference in reaction, and not to a separation of mixed materials. The general point of view that underlies this conclusion is epigenetic, while the contrasting view, that of separation of materials, is essentially one of preformation.

CHROMOSOMES AND SEX.

In recent years two converging lines of evidence have led the most sanguine of us to hope that before long we shall know, in part, at least, the answer to the outstanding riddle of the ages, the determination of sex. These two lines of research are the experimental study of sex inheritance, and the microscopic study of the germ cells. Both have led to the conclusion that sex is not, as has been so often supposed, determined by the external conditions to which the parents, or the eggs, or embryos are subjected, but that there exists an automatic process in the egg and sperm by which equality of the two sexes is attained.

Before I bring this evidence forward, I must stop for a moment to point out how the idea that sex is determined by external conditions arose, for this view is by no means defunct. In fact it is a widely current belief at the present time. One might, in fact, appear to justify himself in holding such a view, not only by quoting the names of those who have advocated it or still maintain it, but even by referring to a considerable number of experiments that have been claimed to be in favor of such an interpretation.

Landois stated in 1867 that he could produce male or female butterflies at will by regulating the amount of food of the caterpillars. Similar statements were made later by others; but the futility of the experiments became manifest when it was found that the character of the sexual organs is already determined when the caterpillar hatches from the egg.

It has been claimed that the sex of the frog could be determined by the quantity of food, or by the kind of food supplied to the tadpole. More extensive work has disproven completely this statement also.

Statistical studies, especially those of Düsing, are often cited to show that in man, and in some of the domesticated animals, the nourishment of the parents affects the sex of the offspring. But here again other statisticians have found evidence of the opposite results. The careful experiments of Cuénot and of Schultze on mice have positively shown that no such relation exists in these animals.

There are two groups of animals that seemed for a long time to furnish evidence in favor of the view that sex is determined by the environment. I must refer to these in more detail.

The plant lice, or aphids, produce throughout the summer by means of parthenogenesis a series of parthenogenetic females. In the autumn, when the food begins to fail, there appear males — and *sexual females*. If the aphids and their food plants are brought into the green house the males and sexual females may not appear, but the animals go on reproducing by parthenogenesis. It seems, therefore, that external conditions determine the appearance of males and are therefore sex determining, since the parthenogenetic forms are ranked as females.

It has become apparent in recent years that these results have nothing to do with sex determination in the sense that external conditions determine the production of males or females. The results show that external conditions cause the cessation of the parthenogenetic reproduction and the beginning of sexual reproduction, *i.e.*, the appearance of males and sexual females. Whether the one, or the other, seems not to be determined by the environment, but to some internal mechanism to which I shall refer later.

In the rotifer, *Hydatina senta*, Maupas claimed that temperature determines sex. Later Nussbaum tried to show that food conditions determine sex in this animal. Still more recently both views have been disproven. It has been shown in the first place that here, as in the aphids, the external conditions affect the life-cycle in such a way that parthenogenesis ceases and sexual reproduction begins. Recently A. F. Shull has determined that if the animals are kept in old culture water, *i.e.*, water in which the food has been kept — parthenogenesis goes on indefinitely. At least nineteen generations of purely parthenogenetic individuals have been reared.

But if at any time individuals are taken out of this culture medium and put into spring water, males and sexual females appear. By diluting the spring water with varying amounts of culture water the number of sexual forms that appear is directly proportional to the dilution.

In this animal the individual that produces the male eggs is the same individual that produces the sexual egg. If she is early fertilized by a male, her eggs produce sexual females. It is clear here that external conditions change the cycle but do not determine sex. This brief review will suffice to clear away the traditional evidence supposed to support the view that sex is determined by the environment.

Let us pass now to the results that seem to show that there is an internal automatic mechanism that regulates the production of males and females. I shall take up the botanical evidence first.

Correns' experiments with two species of *Bryonia*, may be examined. *Bryonia dioica* is dioecious; *B. alba* monoecious. Correns' main experiment shows that when *dioica* ♀ is crossed with *alba* ♂, all of the offspring are females, but when *alba* ♀ is crossed with *dioica* ♂,

half the offspring are male and half female. The results can be explained by three assumptions. First that the male condition dominates the female, second that the dioecious condition dominates the monoecious; third, that the female is homozygous in regard to sex and the male heterozygous.

These conclusions are opposed to the interpretation of other workers that make the female the dominant condition. It is also not clear from G. H. Shull's recent work on a more extensive scale that the dioecious condition can be assumed in general to be dominant.

Whatever the correct interpretation may be, these facts show at least that by treating sex as a character that segregates in the gametes, as Mendelian characters in general are assumed to do, the results can be accounted for, provided one sex is assumed to be always heterozygous and the other homozygous.

The experiments of Elie and Emile Marchal on dioecious mosses are equally interesting. They used species with separate sexes. When spores from a single capsule are sown some produce female, others male protonemata. The sporophyte generation that produces the spores has arisen from a fertilized egg; the formation of the spores is a non-sexual process. The sporophyte contains the full number of chromosomes, and this number is reduced to half in each spore, not by union of chromosomes, but by halving the total number.*

The protonemata or gametophytes produce the male or the female organs separately. Fragments of a protonema regenerate a new individual having always the same sex, under all the possible external conditions to which the Marchals subjected them. Obviously the sex of the protonema *once* determined can not be changed, and the presumption is in favor of the view that the sex of each spore is determined at some time in its formation.

The tissues of the sporophyte itself should contain the potentiality of both sexes. Owing to the power of regeneration possessed by this tissue, it is possible to test such a view. Pieces of the sporophyte regenerate protonemata — each thread arises from a single cell of the piece; a cell presumably having the full number of chromosomes. These regenerated protonemata produce moss plants that are either male, or female, or hermaphroditic. They seem to be all potentially hermaphrodites, but in some plants only the male organs develop — especially those that first appear; in other plants only female organs. If the suggestion just hazarded is correct, namely, that all the plants are hermaphroditic, and the males and females are due to the failure of the

* Although union may have preceded the reduction in number as in ordinary synapsis in plants and animals.

other sex to develop, we raise a large issue; namely, whether males and females may not in general be potential hermaphrodites with only one sex developed, or whether the sexes are separated into pure male and pure female forms, as is assumed in so many of the most recent speculations concerning sex. This topic will come up later for fuller consideration.

As I said, the presumption is that the regenerated protonemata from this sporophyte have the diploid number of chromosomes, and when the spores are formed the number is reduced. Have the sex characters separated when the chromosomes are reduced? We have no means of knowing, but two important points should be noted: first, that the male or the female is produced with the reduced number of chromosomes present; second, that an approach to the same result is reached in the regenerated forms with the entire number present. Sex here is not connected with the half number, or the whole number. Any attempt to solve the problem of sex in the mosses along these lines must assume that some unknown or unseen chromosomal element is separated at the time of formation of the spores.

Furthermore, since hermaphroditic species of mosses and ferns produce both male and female gametes on the same plant that has the reduced number of chromosomes, it would be necessary to assume in such cases that some kind of chromosomal separation takes place in different regions of the same protonema to give rise to male or to female organs. The only other alternative would be to assume that the kind of gamete formed, male or female, is determined by the regional differences in the protonema or prothallium, and that no separation of chromatin precedes this effect. If such effects can be produced in this way, may it not be that similar processes occur in the unisexual species? I shall return to this topic again.

Blakeslee's brilliant experiments with moulds also bring out many important points connected with sex determination, although nothing is known as yet concerning the changes in the chromatin. He finds in *Phycomyces* that some mycelia are male (or — strains as he calls them) and that these produce non-sexual spores of the same sex indefinitely. Other mycelia are female (+ strains) and produce only female spores. Male mycelia will not conjugate with mycelia of the same sign, but readily with the female mycelia. In fact, their sexual behavior is the only way of distinguishing the two kinds of mycelia. On the other hand, the sexual spore or zygosporangium produces a sporophyte that in turn produces spores; some of which are male, others female.

In striking contrast to this case is that of *Mucor mucedo*. Here also male (–) or female (+) mycelia are found which unite to form the sexual spore. This produces the sporangiophore bearing a sporangium

whose spores are all of one or of the other sex, *i.e.*; all the spores from the single sporangium give rise to males; all the spores from another sporangium gave rise to females. Despite the fact that the zygosporium is formed by the union of the two mycelia, male and female, the spores are not mixed, but represent only one sex. Blakeslee points out that this is the same condition found in dioecious flowering plants, such as the Lombardy poplar, when one seed gives rise to a male tree, another seed to a female tree. In these cases the evidence points to the view that there is no separation of sex units, but a suppression of one sex or the other. In other words that the basis of sex is the hermaphrodite condition and the unisexual form is due to the suppression of one of the dual possibilities, and not to a separation of unit characters that stand for male and female.

Let us next turn to the experimental evidence in the animal kingdom. Since the experiments of Doncaster and Raynor on the current moth, *Abraxas grossulariata*, bid fair for years to come to occupy the foremost place in speculations concerning sex I shall bring forward this evidence first.

This species has a rare sport known as *Abraxas lacticolor*. No intermediate forms between the two exist and none arise from crossing. In nature female specimens only of *lacticolor* have ever been found, although males have been produced artificially by suitable combinations, as will be seen below.

TABLE I
Abraxas CROSSES, DONCASTER'S INTERPRETATION

	Parents	Constitution	Gametes	Offspring
Cross 1	Lact. Female	LL ♀ ♂	L ♀, L ♂	GL ♀ ♂ = gross. female
	Gross. male	GG ♂ ♂	G ♂, G ♂	GL ♂ ♂ = gross. male
Cross 2	Heterozygous Female	GL ♀ ♂	L ♀, G ♂	GL ♀ ♂ = gross. female
		GL ♂ ♂	G ♂, L ♂	LL ♀ ♂ = lact. female
	Heterozygous male	GL ♂ ♂	G ♂, L ♂	GL ♂ ♂ = gross. male
		GL ♀ ♂	L ♀, G ♂	GG ♂ ♂ = gross. male
Cross 3	Lact. Female	LL ♀ ♂	L ♀, L ♂	GL ♀ ♂ = gross. female
	Heterozygous male	GL ♂ ♂	G ♂, L ♂	LL ♀ ♂ = lact. female
Cross 4	Heterozygous Female	GL ♀ ♂	L ♀, G ♂	GL ♂ ♂ = gross. male
	Lact. male	LL ♂ ♂	L ♂, L ♂	LL ♂ ♂ = lact. male

No less than four hypotheses have been already advanced to explain these facts. Doncaster assumed, at first, that each sex produced

male and female gametes; that in the first hybrid generation the male gametes bear the *grossulariata* character and the female the *lacticolor*; that in the male no such coupling occurs. Bateson and Punnett simplified this hypothesis by assuming that the female is heterozygous for sex, the male homozygous; that femaleness is dominant to maleness; that in the hybrids the character for femaleness and that for *grossulariata* repel each other so that each germ cell gets one or the other. The results are summed up in Table I.

Castle pointed out that Wilson's sex-hypothesis, that two X chromosomes stand for femaleness and one X for maleness, will not explain the case of *Abraxas*, but that by the hypothesis of one X standing for femaleness and no X for maleness, the results can be explained; provided Bateson's assumption of repulsion is also employed. Thus if in the Bateson-Punnett table (above) the male signs are omitted, and X put in for the female signs, the results just stated follow, as the next table shows. It will be observed that Castle has simply omitted the male and female signs and substituted X for femaleness. When it is absent the male is assumed to develop.

TABLE II
Abraxas CROSSES, CASTLE'S INTERPRETATION

	Parents	Constitution	Gametes	Offspring
Cross 1	Lact. female Gross. male	LLX GG	LX, L G, G	GLX = gross. female GL = gross. male
Cross 2	Heterozygous female Heterozygous male	GLX GL	LX, G G, L	GLX = gross. female LLX = lact. female GL = gross. male GG = gross. male
Cross 3	Lact. female Heterozygous male	LLX GL	LX, L G, L	GLX = gross. female LLX = lact. female GL = gross. male LL = lact. male
Cross 4	Heterozygous female Lact. male	GLX LL	LX, G L, L	LLX = lact. female GL = gross. male

More recently Spillman has suggested a simpler explanation that avoids in a sense the postulate of repulsion of femaleness and *grossulariata*. According to Spillman, if the character for *grossulariata* be represented by "G" and femaleness by "X," then if G (or L) and X when they meet behave as ordinary allelomorphs, the results can be accounted for. The next table shows how Spillman's scheme applies to *Abraxas*. It is apparent that he has further simplified Castle's table by

omitting one L whenever it occurs with another G or L. This arrangement avoids the necessity of the assumption that femaleness is repelled by X (as on the Bateson-Punnett scheme) because the X that was repelled has become the allelomorph of the G that is present and allelomorphs are supposed to move to opposite poles.

TABLE III

Abraxas CROSSES, SPILLMAN'S INTERPRETATION

Parents	Constitution	Gametes	Offspring
Lact. female	LX	L X	GX = gross. female
Gross. male	GG	G G	GL = gross. male
Heterozygous female	GX	G X	GX = gross. female
Heterozygous male	GL	G L	LX = lact. female
			GG = gross. male
			GL = gross. male
Lact. female	LX	L X	GX = gross. female
Heterozygous male	GL	G L	LX = lact. female
			GL = gross. male
			LL = lact. male
Heterozygous female	GX	G X	LX = lact. female
Lact. male	LL	L L	GL = gross. male

It will be observed that in this table the "heterozygous female" is GX. She is therefore not heterozygous for *lacticolor* unless *lacticolor* is absence of G.

The case of *Abraxas* finds a parallel in three characters in fowls and one in canaries.

The pink eyed cinnamon canary crossed with the black eyed green canary gives the following results:

P. ♀ × B. ♂ = 100 per cent. Black eyed ♂ + ♀,

B. ♀ × P. ♂ = 50 per cent. Black eyed ♂ + 50 per cent. Pink eyed ♀
+ 4 per cent. black eyed ♀.

Analysis shows (if we reject the 4 per cent. unexplained anomaly), that the facts can be explained in the same way as in *Abraxas*.

The barred condition of the feathers of Plymouth Rock fowls is inherited in the same way as the next table shows when crossed with Langshan.

Ply. ♀ × Lang. ♂ = 50 per cent. Ply. ♂ + 50 per cent. Lang. ♀,

Lang. ♀ × Ply. ♂ = 100 per cent. ♂ and ♀.

There are two varieties of Game Bantams which according to Hagerdoorn give similar results.

Bankiva ♀ × Brown red ♂ = 50 per cent. Bankiva ♂ +
50 per cent. Brown red ♀,

Brown red ♀ × Bank. ♂ = 100 per cent. Bankiva ♂ and ♀.

Finally yellow shanks and blue shanks in fowls are inherited apparently in like fashion.

Yellow ♀ × Black ♂ = 100 per cent. Yellow ♂ and ♀,

Black ♀ × Yellow ♂ = 50 per cent. Yellow ♀ + 50 per cent. Black ♂.

These facts are of extraordinary interest, for they show that certain characters behave in certain ways that can be explained on the Mendelian formulae provided that sex is likewise treated in the same way. It may seem unfortunate that we have so many possible ways of explaining the same facts, and the case might be turned to ridicule on that score, but the explanations are only variations of the same hypothesis. Whatever the final decision may be it is interesting and important to find that the inheritance of sex can be treated by the same methods used for other alternate characters and gives consistent results. Let us be as sceptical as we will, yet the facts will impress themselves on any one who takes the pains to think them over.

Such are the experimental results. Looked at not too critically they show that by the time that reduction of the chromosomes occurs, or after that event, there seems to exist a distinction between the cells, so that half of the cells are destined to become males and half females. But, as has been said, unless we assume this process to take place in one sex only the results can not be explained.

Let us turn then to the evidence which the study of the germ cells has revealed, which shows that in certain forms exactly such a process occurs in one sex and not in the other. I may say at once that the evidence relates to the chromosomes of germ-cells.

Only a few years ago it was generally held that the number of chromosomes in each species of animals is constant for all individuals of the species. Every cell in the body contained the same number.

We now know, however, that in some species of animals, the female contains one more chromosome than does the male, and we have a complete account of the mechanism by means of which this difference arises.

In *Anasa tristis* and in *Protenor*, and in a number of other insects, as shown by Wilson, one chromosome in the male has no mate. At one division it passes to one pole of the spindle, so that one of the two

resulting cells has one more chromosome than the other. This chromosome is the accessory, or the odd, or the sex chromosome, or, as Wilson has called it, the X-element. At the other division it, like the other chromosomes, divides into two parts, so that both of the derived cells from this division have the same number of chromosomes. In the egg the X-element has a pair, another X to all appearances. Thus there are two X's in the unripe egg, and one in the sperm-mother cell. These three are apparently identical, and their perturbations I have called the problem of the three chromosomes. Chance matings between the two classes of sperm and the eggs (all alike) give the results shown in the following scheme.

<i>Sperm.</i>	<i>Egg.</i>	<i>Individual</i>
X	→ X	XX female
<i>or</i>		
O	→ X	XO male

The egg that is fertilized by a sperm containing the accessory produces a female; the egg fertilized by a sperm without the accessory produces a male.

In a few insects, as in *Tenebrio*, the X-chromosome has a smaller chromosome for its mate, as shown by Stevens. This has been called by Wilson the Y-chromosome. Two classes of sperm are produced with an equal number of chromosomes, but in one class the X-element is present, and in the other its smaller mate the Y-chromosome.

All of the eggs of *Tenebrio* have two X's, one of which is lost in the polar body, so that only one remains, the egg that is fertilized by a sperm bearing the X-chromosome produces a female, the egg fertilized by the sperm bearing the Y-chromosome produces a male. The following scheme shows the results graphically.

<i>Sperm.</i>	<i>Egg.</i>	<i>Individual</i>
X	X	XX female
<i>or</i>		
Y	X	XY male

In a third class of insects the X-chromosome has a mate of equal size; consequently all of the sperm, have the same number of chromosomes of the same sizes. Since we can not here distinguish X from Y, we may assume either that Y is the same as X, in which case we should have the problem of the four X's; or we may assume that despite their similarity in size they are nevertheless qualitatively different. In this case we should still speak of one of them as Y, and imagine that when a sperm bearing a Y enters an egg a male results. In favor of the latter interpretation Wilson has pointed out that an

unbroken series of forms exists at one end of which the X-chromosome has no partner, in the middle of the series a partner of unequal size, toward the other end of the series a partner of nearly equal size, and at the end of the series a partner of equal size. If we are justified in attributing the male sex to no X, or to Y, it may seem that when Y can no longer be distinguished by its size it may still be responsible for the production of maleness. On the other hand, if X and Y do not in themselves produce sex, but simply accompany more profound changes, they are only indices of what is taking place and the graded series has no important significance.

These cases all apply to the group of insects. The criticism has been made that we are not justified in extending these conclusions to other groups where no such difference in number of chromosomes exist.

Quite recently surprising results have been obtained in groups other than the insects, that go far toward meeting the criticism just referred to.

First Baltzer has found in the sea urchins that there are specific chromosomes found only in the female. The *spermatozoa* are all alike, but the *eggs* are of two classes. In principle the outcome is the same except in so far as it shows that the sex element may be confined either to the male or to the female. Second, Guyer has found in the fowl that there is an odd chromosome in the male. This is the first case reported for the vertebrates, but the chromosomes in the group are so numerous or the cells so small that failure to detect two classes of sperm in this group (if they exist) is not surprising. Lastly, the all-important outstanding case of *Ascaris* has been brought into line by the announcement within the last few weeks by Boveri of the discovery of an accessory in this group. In one of the nematode worms of the pheasant he has found that there are two classes of sperm, one with one more chromosomes than the other. Correspondingly, there are two kinds of embryo, male and female, differing by one chromosome in every cell.

In the classic case of the nematode of the horse, *Ascaris megalcephala*, the reduced number of chromosomes is *one* in one variety and *two* in another, it has been found by one of Boveri's students that about half the embryos contain one more chromosome than the other half. This chromosome is attached to one of the others in the early stage and hence does not appear as single.

This discovery shows that even when no accessory is found it may still be a part of one of the other chromosomes — and being confined to one sex fulfills all the conditions of the sex mechanism.

The conclusions arrived at from a study of these unisexual animals have been confirmed in the parthenogenetic phylloxerans and aphids.

Two years ago I found that in the phylloxerans two classes of spermatozoa are present; *one* is a rudimentary sperm, and corresponds to the male-producing of other insects. The other sperm contains the accessory, and it alone is functional. Hence all the fertilized eggs should be female. This has been known for a long time to be the case.

The female is the stem-mother of the summer brood of parthenogenetic individuals. They all contain the full number of chromosomes and are females. At the time when males appear a peculiar process occurs. When the male egg gives off its single polar body one (or two) whole chromosomes lag behind the others (that divide) and are thrown out into the polar body. Hence this egg contains two less chromosomes and it develops into the male. In the sexual female no such reduction takes place.

Here then we find a mechanism in the male to produce only females, but also another mechanism in the parthenogenetic female for producing males. The facts make out a strong case in favor of the view that we have probably found the mechanism by means of which sex is determined.

When we try to analyze the results, however, I mean when we try to make clear to ourselves how the accessory determines sex, we fail to make good a consistent story of the process.

If we assume, as Wilson and I have done, that the result is purely *quantitative* in that the *female* develops because the egg fertilized by the female producing sperm contains one more chromosome than the egg that becomes a male; when we make this assumption, we seem to leave unexplained how sex is determined in a large number of cases when the odd chromosome has a partner of equal size.

On the other hand, if we assume that the accessory is a *qualitative* agent producing females in this way; then the mate of the accessory, or one of the corresponding chromosomes in the female, must be male-producing. To make this mechanism "go" we must assume *selective* fertilization; for which at present there is no evidence.

I shall try to indicate in the barest outline the further analysis of the two statements just made.

When the accessory has no mate, as in the examples just given, we have the problem of the three X-chromosomes. The following situation then develops.

(A) The three X's are identical as everything we know about them indicates. Their position on the reduction spindle both in the male and female is so far as we know fortuitous. It follows then the female results when two X's meet in the same egg, and a male when only one

X is present. This is the simplest explanation yet found that is strictly in conformity with observed relations for this class. It encounters five difficulties: first, it does not seem to apply when the accessory has a mate of equal size, if that mate be another X (see below); second, sex in hermaphroditic forms is not apparent on this view; third, the mate of the accessory when it exists, if it is not an X but a Y element, is ignored; fourth, in *Acholla* the Y element is larger than the combined X elements all taken together; fifth, it may seem to reduce the male to a less highly developed form than the female in the sense that it lacks a quantitative factor and leaves unexplained the characters peculiar to the male.

(B) If the three X's are not identical, but consist of two female and one male element, and if they are undirected on the spindle, the results can be explained only by assuming selective fertilization. The assumption meets with a flat contradiction in that it must assume that the only X in the male is a female X. Were it assumed to be a male X, the scheme will not work out. Moreover, there is no evidence for selective fertilization.

(C) If the three X's are not identical, but male and female, and are directed on the maturation spindles, equality of males and females will result only on the assumption of selective fertilization. Three assumptions, all unknown, are necessary to work out this scheme.

Let us turn our attention to the class with three X's and one Y. I take the simplest case for analysis in which all three X's are assumed to be alike. The sperm, bearing the X, fertilizing any egg (for all eggs have an X), produces a female, the sperm bearing the Y fertilizing any egg produces a male. We know this, in fact, to happen whenever we can identify Y. This scheme meets with no difficulties on its own account, and appeals (with certain modifications) more directly to my mind than any other; but it meets with a difficulty when no Y is present; and also when Y is the same size as X, if this size relation identifies Y with X. Unless these points can be met the hypothesis is insufficient to meet the situation. I shall return to these difficulties in a moment and try to meet them. This is the extreme application of the particulate theory, and has the advantages and disadvantages of its kind.

On the other hand, there is no need to assume that X is the *sex chromosome* in the sense of carrying sex. The use of this term, I fear, prejudices the situation by the very aptness of the application. It may be that X only means more X, and that this is a factor in sex determination. The only criticism that I have to offer of this view is that it ignores the Y element, and thereby makes the male condition the result of the absence of something which, if present, turns the embryo

into a female. It seems to me that there is no warrant for considering the male in this sense a lacking female. The physiology and the biology of the males offer much to contradict such a view of his composition. I should also object to the above conclusion on the general grounds that it refers a particular character to a single chromosome.

Can we meet these objections if we admit that when the Y chromosome is absent the things that it stands for are redistributed, or are present in the other chromosomes whether equally or unequally distributed there need not be decided? Correspondingly, the materials of the X chromosome may be supposed to be distributed in part also to the other chromosomes. The production of male or female will then be determined by the preponderance of the amount of X or of Y in any given combination.

The groups with an accessory represent from this point of view an extreme form of distribution of the X material; while those with a Y show a like distribution of the Y material, but in neither case need we imagine all of this material present in a given chromosome, *i.e.*, in X or in Y. But this assumption also meets with difficulties in another direction, for we should be obliged to assume that the chromosomes carrying the Y element pass to the opposite pole at one division from those bearing the X element and we have as yet no evidence to support such a view.

These are some of the difficulties of interpretation:

Science advances by carefully weighing all of the evidence at her command. When a decision is not warranted by the facts, experience teaches that it is wise to suspend judgment, until the evidence can be put to further test. This is the position we are in to-day concerning the interpretation of the mechanism that we have found by means of which sex is determined. I could, by ignoring the difficulties and by emphasizing the important discoveries that have been made, have implied that the problem of sex determination has been solved. I have tried rather to weigh the evidence, as it stands, in the spirit of the judge rather than in that of the advocate. One point at least I hope to have made evident, that we have discovered in the microscopic study of the germ cells a mechanism that is connected in some way with sex determination; and I have tried to show, also, that this mechanism accords precisely with that the experimental results seem to call for. The old view that sex is determined by external conditions is entirely disproven, and we have discovered an internal mechanism by means of which the equality of the sexes where equality exists is attained. We see how the results are automatically reached even if we can not entirely understand the details of the process. These discoveries mark a distinct advance in our study of this difficult problem.