

CHAPTER XIV

SEX-CHROMOSOMES AND SEX-LINKED INHERITANCE

THE discovery that the female in certain species of animals has two X-chromosomes and the male has only one X-chromosome, either with a Y-chromosome in addition (Stevens) or without the Y (Wilson), established a view first suggested by McClung that the difference between the sexes is connected with the distribution of particular chromosomes. Two interpretations of the facts have been proposed: The first, and most obvious one, was that the presence of two sex-chromosomes (XX), in connection with the rest of the cell complex, causes a female to develop; while only one sex-chromosome (X) in connection with the rest of the cell causes a male to develop; the second interpretation was that of XX and X are merely indices of sex, *i.e.*, that the sex-chromosomes follow sex and do not determine sex.

It is now possible to show that sex follows the chromosomes and not the reverse, because if a "female producing" sperm (X) fertilizes an egg without an X (as exceptionally occurs) an XO individual is produced that is a male, whereas if this same sperm had fertilized an egg with an X, giving an XX individual, a female would be the result. Conversely when a "male producing" Y-sperm fertilizes an egg with two X's (as exceptionally occurs) an individual is produced that is a female, despite the presence in her of a Y-chromosome.

THE SEX-CHROMOSOME

It will be convenient to treat the XX-XY type of combination first. I shall follow the usual custom of calling both X and Y sex-chromosomes.

At the time when the polar bodies are extruded from the egg, the two X's separate, one passing out, the other remaining in the egg. Every egg is left with one X (Fig. 68).

In the male, the X and Y conjugate and separate at one of the maturation divisions, so that each sperm contains either an X- or a Y-chromosome (Fig. 68). Fertilization of any egg (X) by an X-bearing sperm produces a female

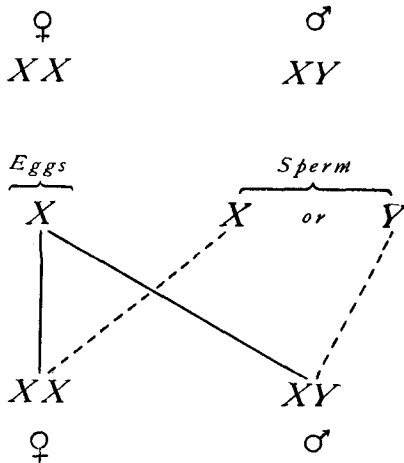


FIG. 68.—Scheme showing the relation of the sex-chromosome to sex-determination. XX-XY type.

(XX). Fertilization of any egg (X) by a Y-bearing sperm produces a male (XY).

Since the two kinds of spermatozoa are produced in equal numbers, females and males will be equal in number. The mechanism is self-perpetuating.

THE INHERITANCE OF FACTORS CARRIED BY THE SEX-CHROMOSOMES IN THE DROSOPHILA TYPE

Since the son gets his one X-chromosome from his mother, and the Y from his father, he inherits factors carried by the sex-chromosomes in a different way from

the way in which he inherits the factors carried by the other chromosomes (autosomes), because X and Y differ from each other in a way in which no other chromosomes differ.

The recessive gene for white eyes (w) in *Drosophila* is carried by the X -chromosome. It is inherited in the following way (Fig. 69): When a male with white eyes (w) is mated to a red-eyed female (WW), the F_1 sons and daughters have red eyes. When these are bred to each other, all the daughters have red eyes (50 per cent.), half the sons have red eyes (25 per cent.) and half the sons have white eyes (25 per cent.). The ratio, irrespective of sex, is three red to one white, but the white-eyed flies are found only amongst the males. In the diagram (Fig. 69), the relation of these results to the sex-chromosomes is shown. The X -chromosome that carries the normal gene (wild type) which gives red eyes is indicated by W . The X -chromosome that carries the gene for white eyes is indicated by w . The rod with a bent end stands for the Y -chromosome.

The F_1 daughters contain one of each kind of X -chromosome. The F_1 sons only one kind. The recombinations that give the F_2 results are shown in the middle of the lower part of the diagram. Half of the females are seen to be homozygous for the wild-type gene (W). They should never transmit white eyes, and they do not. The other half of the females are heterozygous (Ww), and if mated to a white-eyed male should give 50 per cent. red-eyed males and females, and 50 per cent. white-eyed males and females. This they do. The red F_2 sons (W) should never transmit white eyes, nor the white-eyed sons (w) transmit red eyes. These relations are also known to hold.

The reciprocal cross (Fig. 70), *viz.*, a white-eyed female (ww) to a red-eyed male (W) gives red-eyed daughters (wW) and white-eyed sons (w). If these F_1 's

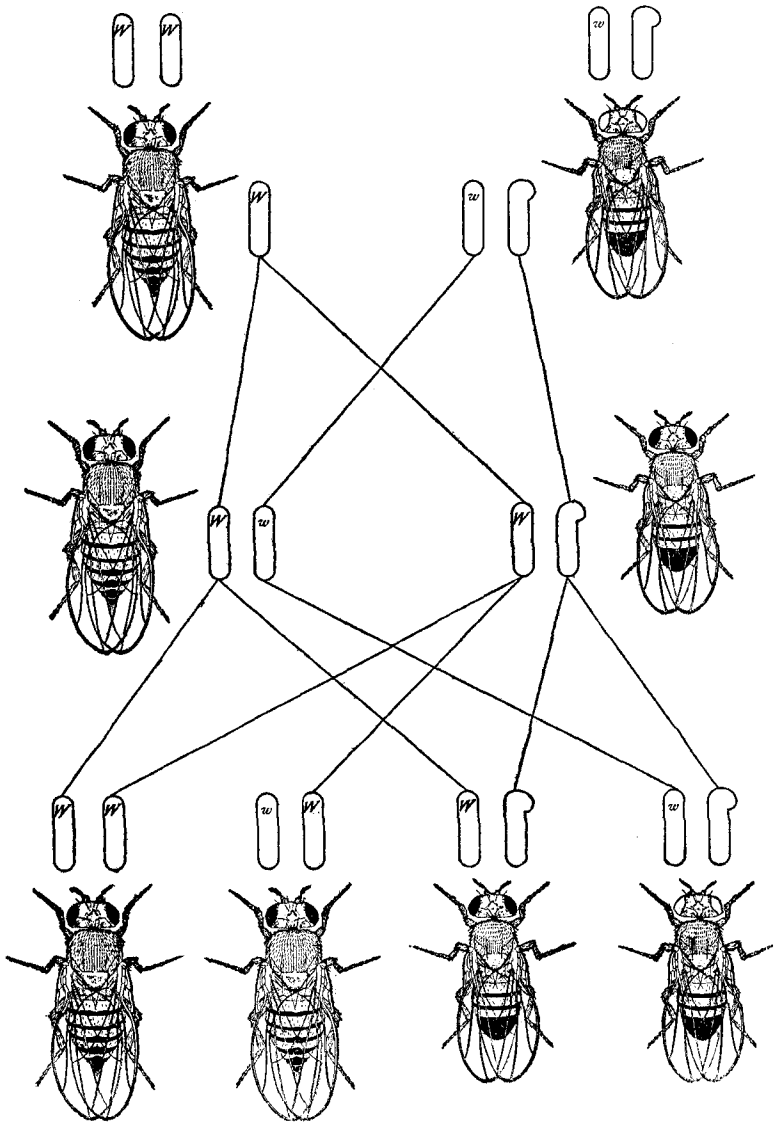


FIG. 69.—Cross between white-eyed male and a red-eyed female of the vinegar fly.

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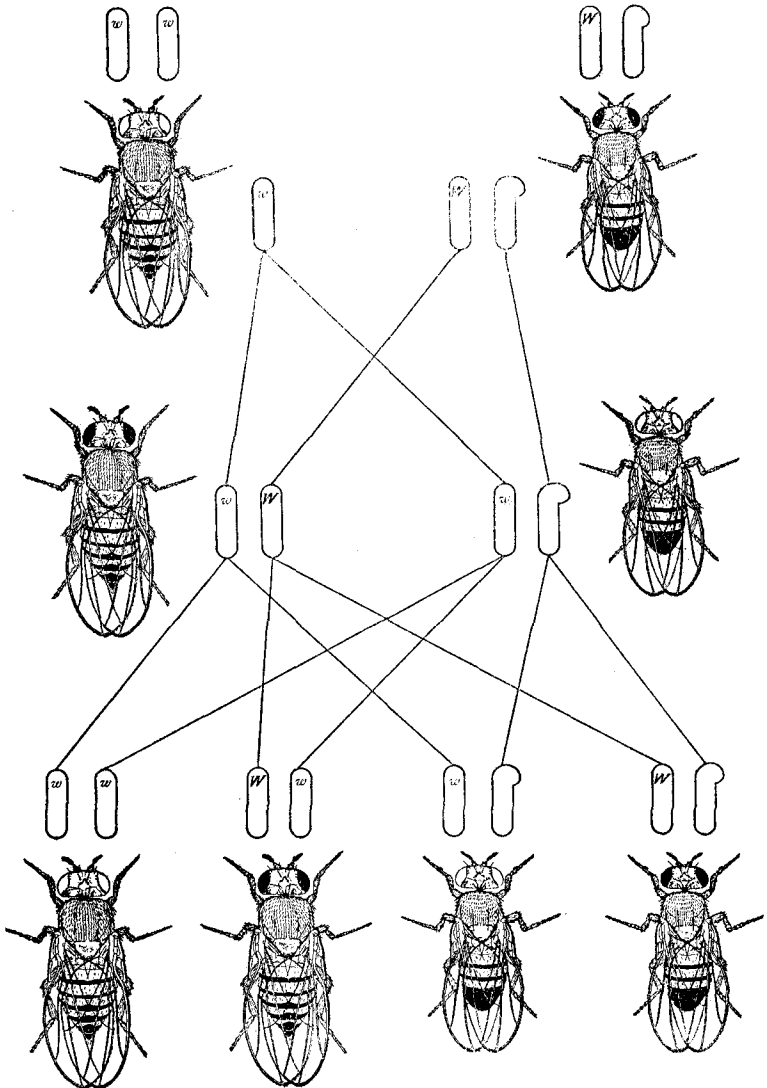


FIG. 70.—Cross between white-eyed female and a red-eyed male of the vinegar fly.

are bred together, the results are as follows: Half the daughters have white eyes (ww), half red eyes (wW); half the sons have white eyes (w), half red eyes (W). It will be seen that the red-eyed F_2 daughters are all heterozygous, and should give 50 per cent. white and 50 per cent. red offspring if mated to white-eyed males. This occurs.

Similar illustrations might be given for any of the 50 sex-linked characters of *Drosophila*. Of these the sex-linked lethals form the most interesting cases and will be spoken of in another connection.

Despite the fact that the results in one of the two foregoing crosses gave a 3:1 ratio, and in its reciprocal a 1:1 ratio, the results in both cases conform to Mendel's first law of segregation. The peculiarity of the 1:1 ratio is due to the fact that the P_1 red-eyed male is in a sense heterozygous for the wild-type eye color (since he has but one X-chromosome that carries the factor for red eyes). Since in the second cross the F_1 male gets no red-producing X from either parent, he is pure for white eyes in the sense that he has an X bearing the factor for white eyes and a Y that bears no factor making red. Hence this F_1 cross is exactly like a back-cross of a heterozygous female to a recessive male, and gives the same numerical result, *viz.*, 1:1.

Cases of sex-linked inheritance of this kind are also known in man. Color blindness in man appears to follow exactly the same procedure as sex-linked inheritance in the vinegar fly—at least certain kinds of color blindness have been shown to do so. Hæmophilia also is sex-linked, and there are four or five other defects in man that appear to come under this head. According to several accounts there is an unpaired sex-chromosome (or two of them) in man, which is also called for by the genetic evidence relating to sex-linkage in man, but since the female number of chromosomes in man is stated by Guyer to be 24, and by von Winiwarter to be 48, it is unsafe as yet to appeal

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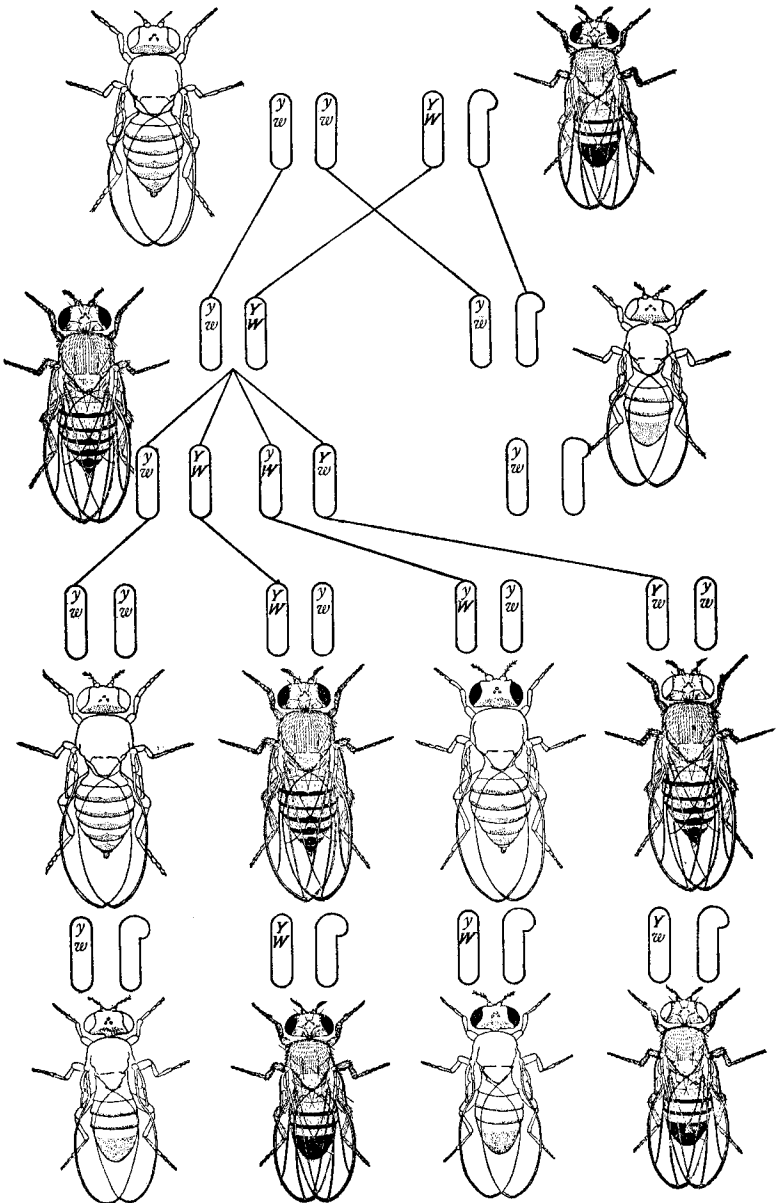


FIG. 71.—Cross between a yellow, white-eyed female and a wild-type ("gray"), red-eyed male.

to this evidence as showing the identity of the sex-determining mechanism of man and the vinegar fly.

When two or more sex-linked characters are involved at the same time, the situation is different only in so far as crossing over may take place in the female. It will be simpler to consider such a cross and its reciprocal in the reverse order from that just given. If a female with yellow wings (yy) and white eyes (ww) is crossed to a wild-type male, "gray" wings (Y) and red eyes (W), the sons are yellow white and the daughters are gray red (Fig. 71). When these are inbred there are four types in F_2 (ignoring sex), *viz.*, the two original combinations yellow white and gray red, and the two crossover combinations yellow red and gray white. They occur in the following ratios:

| | | | |
|--------------|----------|-------------|------------|
| Yellow white | Gray red | Yellow red | Gray white |
| 99 per cent. | | 1 per cent. | |

In this case the F_1 male acts as a double recessive, revealing the amount of crossing over in the F_1 female. Since neither his female-producing nor his male-producing sperms carry factors that cover up the characters carried by the four classes of gametes in the F_1 female, all four classes of her gametes are revealed in their numerical proportions. Reciprocally, when a male with yellow wings (y) and white eyes (w) is crossed to a wild-type female (gray (YY) red (WW)), both sons and daughters are gray red, because both get the dominating genes for these characters carried by the X-chromosome received from the mother. If these F_1 's are inbred (Fig. 72), the F_2 females are gray red, since each contains an X with the two dominant genes derived from the father whose genes have remained completely linked, as there is no crossing over in the male. On the other hand, there are four kinds of F_2 males: yellow white; gray red; yellow red; gray white; because each male shows the

character of his single X-chromosome, and there are four kinds of these chromosomes in his mother on account of crossing over in the female. The other sex-chromosome, the Y, has no dominating influence.

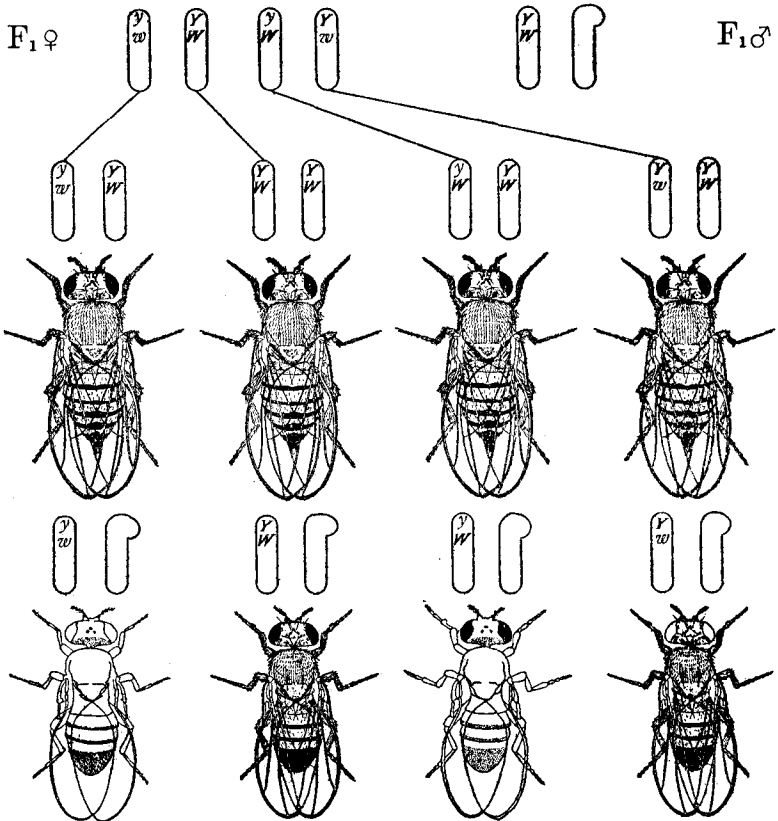


FIG. 72.—The F₂ results from the reciprocal cross of that shown in Fig. 71.

SEX-LINKED INHERITANCE OF THE ABRAXAS TYPE

In certain moths and birds it has been shown by the genetic evidence that the female is heterozygous for sex-linked factors. The cytological evidence, as far as it goes, supports this evidence, but for birds the material is so

difficult to interpret that Guyer's conclusions do not seem to me as yet to be on as secure grounds as those of Seiler's for moths. Both descriptions give, however, the bases for a consistent explanation of sex-linked inheritance in this type ($WZ-ZZ$).

Since we do not know as yet whether the same or different sex factors are involved in the *Drosophila* and in the *Abraxas* types, it seems best not to use the same sym-

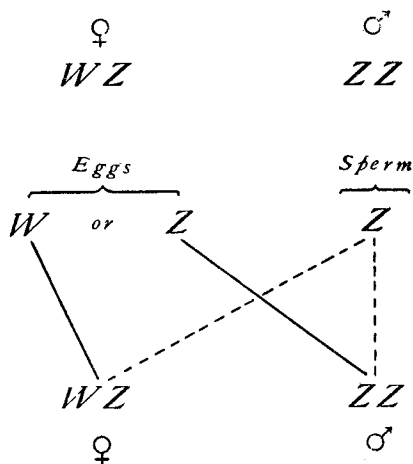


FIG. 73.—Scheme showing the relation of the sex-chromosomes of the moth (and of the bird) in sex-determination. $WZ-ZZ$ type.

bolis in both for the sex-factors. If in both types a single sex-factor is concerned, and if it is the same in both, the conditions that make for a female in one case and for a male in the other must be due to a difference in the rest of the hereditary complex that reverses the reaction. It would appear simpler to assume that the sex-factor itself is different in the two cases. If there is more than one factor for sex, the two types may have some in common, but the theoretical situation would remain the same. For our present purpose these possible distinctions are of no importance.

If the sex-chromosome that carries the sex-linked genes in birds and moths be symbolized by Z , and its homologue that occurs in the female by W , the scheme for sex-determination is that shown in Fig. 73: The eggs of the female extrude either one or the other sex-chromosome. If Z stays in, and this egg is fertilized by a sperm (Z -bearing

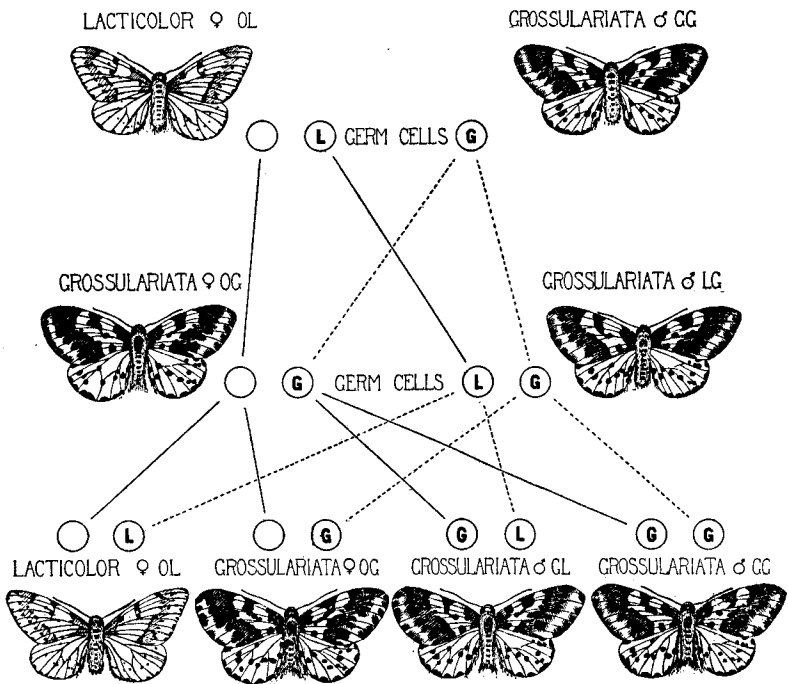


FIG. 74.—Cross between *Abraxas lacticolor* female and *grossulariata* male.

also) a male (ZZ) is produced; if W stays in, and the egg is fertilized by a Z -bearing sperm, a female (WZ) is produced. The way in which sex-linked characters are transmitted may be illustrated by the inheritance of a color difference in the currant moth *Abraxas*. The wild species (*grossulariata*) has a mutational variety called *lacticolor*, that differs from the former by having less

black pigment in the wings. When a dark (grossulariata) male is mated to a light (lacticolor) female, both sons and daughters are dark (Fig. 74). If these are inbred all the F_2 sons are dark, half the daughters are dark, half light. As the diagram shows, the distribution of the Z-chromosome furnishes the mechanism by means of which we can

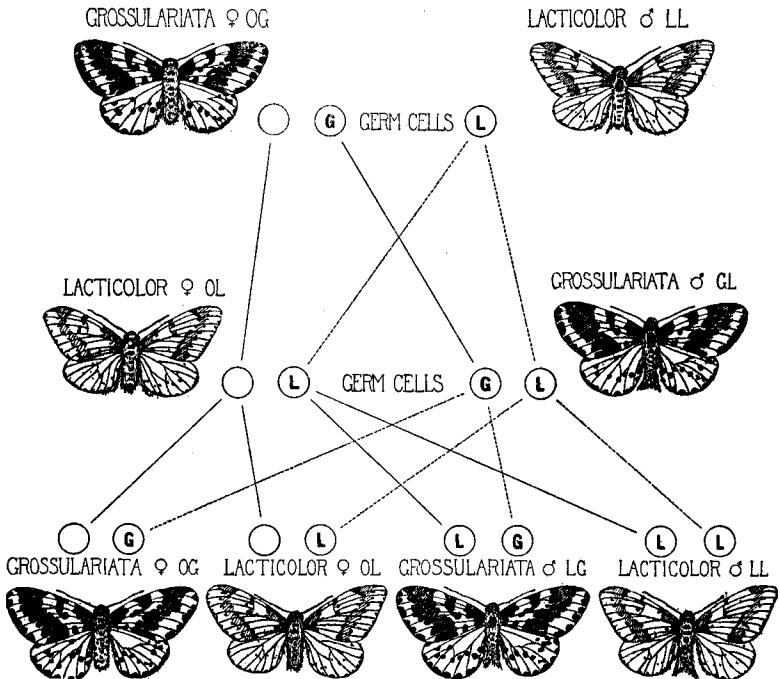


FIG. 75.—Cross between *Abraxas grossulariata* female and *lacticolor* male.

explain, as in *Drosophila*, the process of sex-linked inheritance in this moth.

The reciprocal cross is shown in the next diagram (Fig. 75) in which a dark (gross.) female is mated to a light (lact.) male. The daughters are light like the father, the sons dark like the mother—criss-cross inheritance. The daughters get their one Z-chromosome carrying the light

factor from their father, the sons get in addition to a light Z from their father a dark dominating Z from their mother. When the F_1 's are bred together four classes result in the proportion of 1:1:1:1, when sex is taken into consideration, or in the ratio 1:1 for the color differences alone.

According to Doncaster, the male and the female *Abraaxas* have each 56 chromosomes, *i.e.*, the female is ZW rather than ZO ; but as yet the sex-chromosomes as such have not been identified. That sex is connected with such chromosomes is not only established by sex-linked inheritance, but is also indicated by an aberrant race of *Abraaxas* found by Doncaster. The males of the race had the normal number of chromosomes (56), but the females had only 55 chromosomes. Doncaster found that in these females an unpaired chromosome, presumably the Z -chromosome, was more often thrown out into the polar body than left in the egg, so that most of the resulting eggs had only 27 chromosomes. Any egg of this kind fertilized by a spermatozoön should give a 55-chromosome individual, *i.e.*, a female. The few eggs that retained the unpaired Z -chromosome, fertilized by a Z -spermatozoön, would be expected to give rise to the rare males, which like normal males have 56 chromosomes. The excess of females is thus accounted for, and incidentally the results show that the W -chromosome carries no essential factors for the life of the individual, since females without it develop and look like normal females. Probably it is empty as is the Y of *Drosophila*.

In poultry there are several cases of sex-linked inheritance that follow the *Abraaxas* type. One of the most striking cases is the cross between Barred Plymouth Rock and Langshan. When a barred male is crossed to a black female, the sons and daughters are barred (Fig. 76). Barring is dominant to black. Two such F_1 's, inbred, give all barred males; half the hens are barred, half are black. It may be said here that the black grandmother transmits

her black color to only half of her grandsons. The chromosomal explanation can obviously be worked out on the same scheme as in *Abraaxas* (Fig. 77). But if Guyer's recent account of spermatogenesis in birds is correct, the situation is different. Guyer describes the ripening of the sperm as follows: There are 18 chromosomes in the male, including two large *Z*'s ($16 + 2$). After synapsis there are 9 double chromosomes in the first spermatocyte, all of which, except *ZZ* separate at the first maturation division, 8 going to one pole and 8 to the other. One

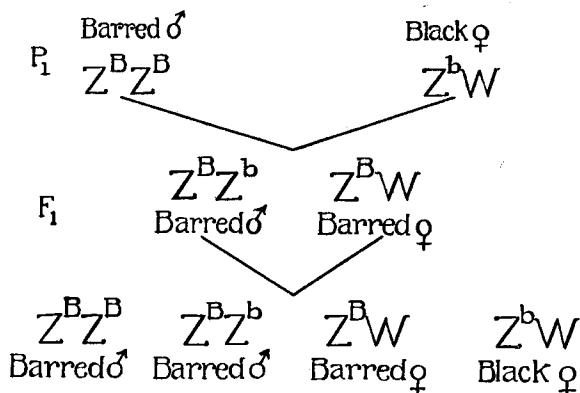


FIG. 77.—Scheme showing the transmission of the sex-linked characters *B* = barred, and *b* = black in the cross shown in Fig. 76.

daughter cell gets both *Z*'s ($8 + 2$). This cell then divides again, the *Z*'s presumably separating so that two second spermatocytes are produced, each with 9 chromosomes ($8 + 1$), including the *Z*. These become the functional sperm. The other spermatocyte, the one without a *Z*, may divide again, but it, or its products, degenerate, and never produce sperm. According to Guyer, there are 17 chromosomes in the female, including one *Z*. Presumably, then, after reduction half of the eggs will contain a *Z* ($8 + 1$), the other half will be without it (8). The egg that carries a *Z* ($8 + 1$), fertilized by a sperm (each sperm carries a *Z* ($8 + 1$)), will make a male with 18 chromo-

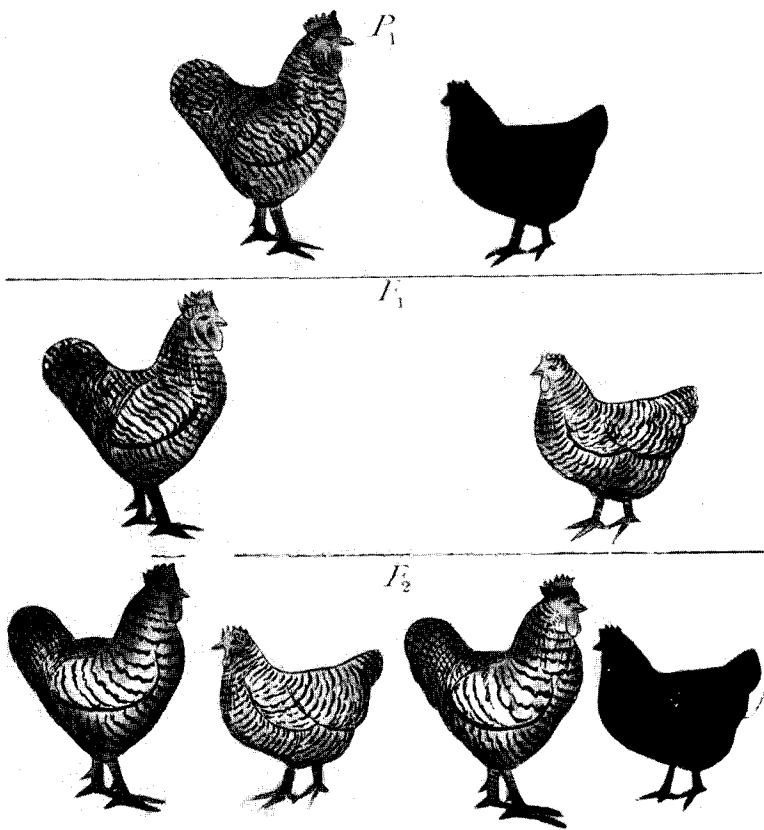


FIG. 76.—Cross between Barred Plymouth Rock male and Black Langshan female.

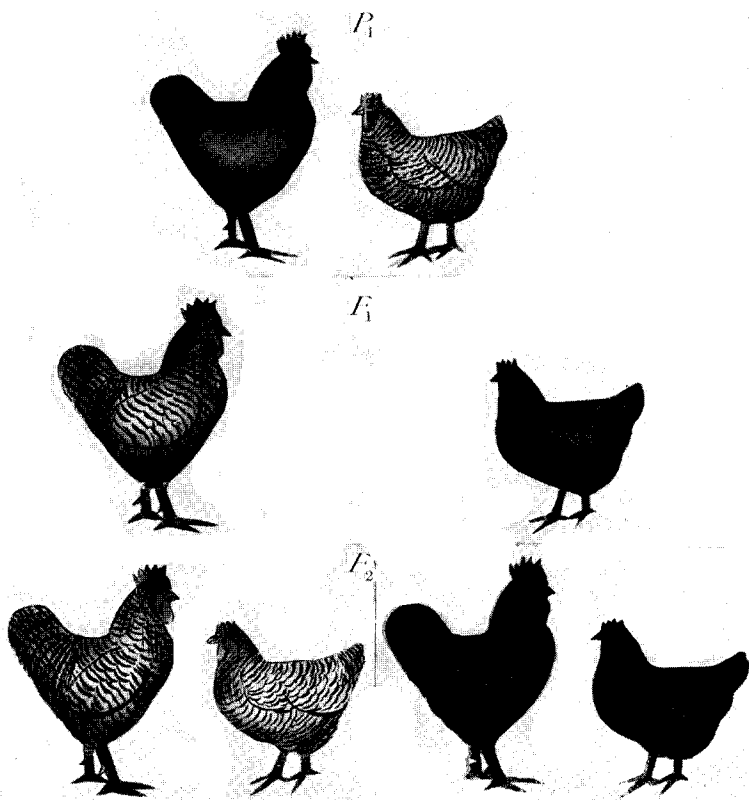


FIG. 78.—Cross between Black Langshan male and Barred Plymouth Rock female.

somes, including two Z 's. The egg that lacks a Z (8), fertilized by a sperm (8 + 1), makes a female with 17 chromosomes, including one Z .

This scheme gives consistent results for sex-linked inheritance in birds. Since the daughter gets her single Z -chromosome from her father, she will show any sex-linked characters carried by his Z -chromosome. If the father carries a sex-linked dominant gene his sons and his daughters will be alike. It should be noticed that while Guyer's scheme gives the same results so far as sex-link-

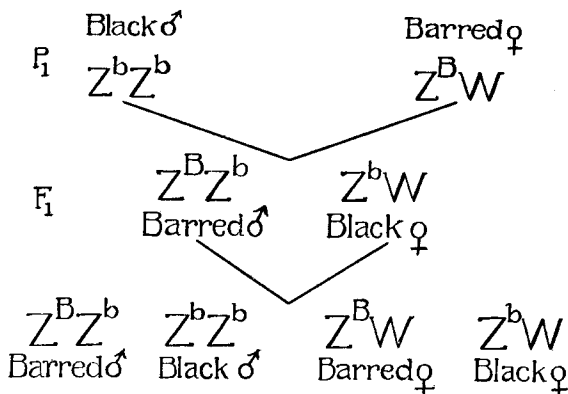


FIG. 79.—Scheme showing the transmission of the sex-linked characters B=barred, and b=black in the cross shown in Fig. 78.

age is concerned, as the one described by Seiler for some moths, the machinery in the male is different in the two cases, while that in the female is presumably the same. In both the female is heterozygous for Z ; in the moth the male is homozygous (ZZ), but in the bird the two Z 's described by Guyer both go to one pole at one of the maturation divisions, and reduce at the other—a procedure not known in any other animal.

In the reciprocal cross (Fig. 78) a black cock is bred to a barred hen. The sons are barred—like their mother—the daughters are black—like their father, criss-cross inheritance. When the barred F_1 cock and the black hen

are inbred, there are four F_2 classes with sex taken into account in the proportion of 1:1:1:1; or ignoring sex, 1 barred to 1 black. The barred and the black races differ by one factor difference (Fig. 79), *viz.*, barred Z^B and its normal recessive allelomorph Z^b . This seems to mean that the Barred Plymouth Rocks is a black race with an additional dominant factor for barring. The Black Langshan is the same black race but without the barring factor.

Until quite recently no cases of crossing over had been observed in forms having the *Abraxas* type of sex-linked inheritance, for, except in one or two cases in poultry, only a single pair of sex-linked genes were known, and two at least must be studied together in order to demonstrate linkage. Goodale has recently studied two sex-linked characters in poultry, and states that crossing over occurs in the male, but whether or not in the female is not stated.

SEX-DETERMINATION AND NATURAL PARTHENOGENESIS

Variations in the ordinary sex-determining mechanism account in some cases for the normal output of males and females produced by parthenogenesis, and determine the exceptional sex-ratios of such species. The honey bee furnishes the best known example. The queen comes from a fertilized egg, and has therefore the double ($2N$) number of chromosomes. Her eggs give off two polar bodies, hence have the reduced, or single number of chromosomes. Any egg that is not fertilized develops parthenogenetically into a male. If there are two X-chromosomes in the bee, as in some of the other insects, the egg is expected to contain only one of them after the extrusion of the polar bodies. Hence, if it develops without doubling its chromosomes, it should give rise to a male. That the male has the single number of chromosomes is also borne out by the evidence from a peculiarity of the first spermatocyte division in which the cytoplasm divides, but the chromosomes do not separate into two

groups. Several stages in the maturation of the spermatozoön of the bee are shown in Fig. 80. In *a*, the spindle for the first spermatocyte division has appeared. A small piece of the cytoplasm cuts off, but the chromosomes do not separate, and they return again (*b* and *c*) to a resting

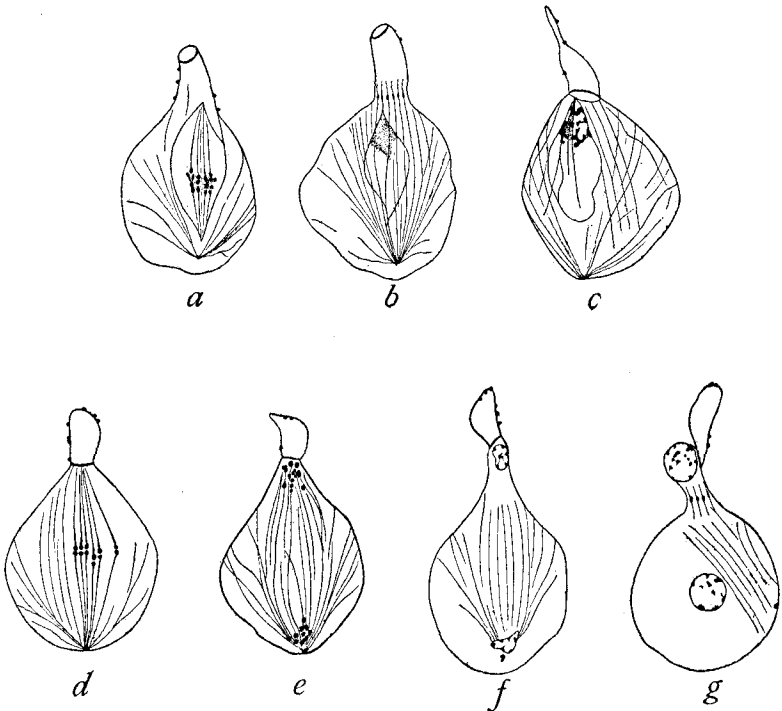


FIG. 80.—First spermatocyte divisions *a-c*, and the second spermatocyte division *d-g* in the bee. (After Meves.)

stage. Another spindle forms (*d*), and the chromosomes separate into two groups, one of which is pinched off as a rudimentary cell that never becomes a spermatozoön. Hence only one, and not four spermatozoöa as in ordinary cases, is formed from each spermatocyte. In the hornet (Fig. 81), the spermatogenesis is similar to that of the bee in that the first division is abortive. It is different

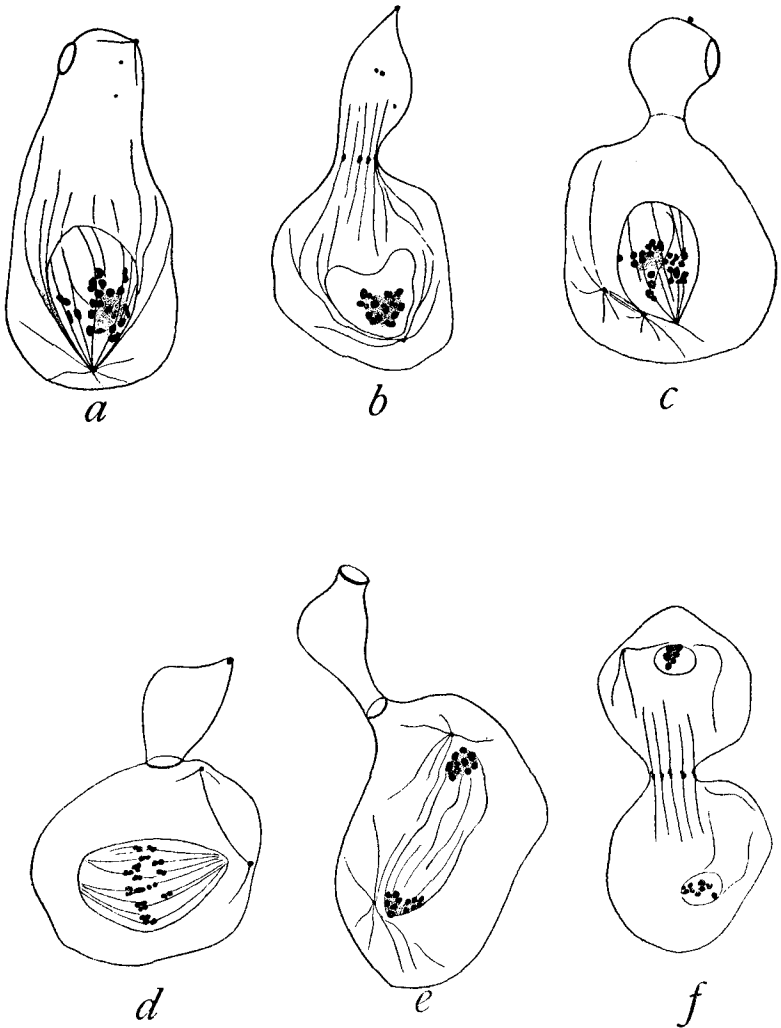


FIG. 81.—First spermatocyte division *a-c*, and the second spermatocyte division *d-f* in the hornet. (After Meves.)

in that the second division produces two functional sperms, both female producing.

Since the male comes from an unfertilized egg, the

Phylloxera caryæcaulis

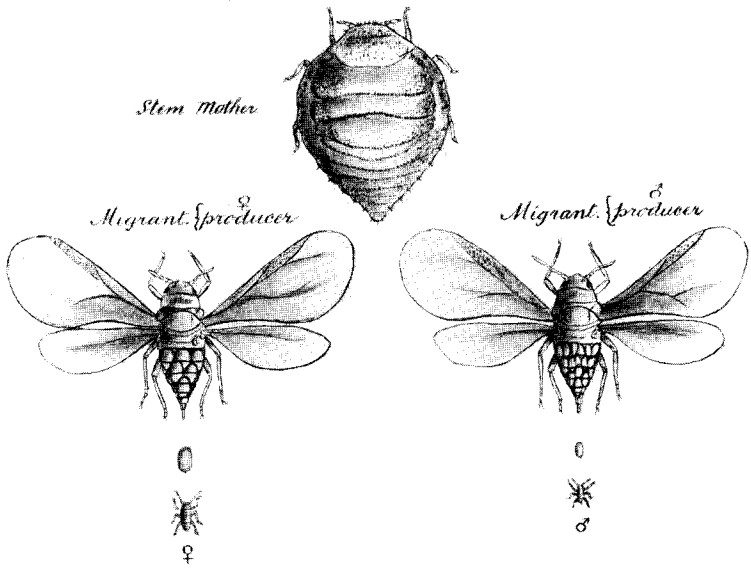


FIG. 82.—Life cycle of *Phylloxera caryæcaulis*.

queen must transmit to him all her characters, thus giving rise to a form of inheritance that has a superficial resemblance to sex-linked inheritance. A queen of a pure race, bred to a male of another race with a dominant factor, produces daughters all showing the dominant character of the father, and sons all showing the recessive character of the mother. Since the son gets his entire chromosome-complex from his mother, he must necessarily be like her, whether the character in question is in the sex-chromosome, or in some other one.

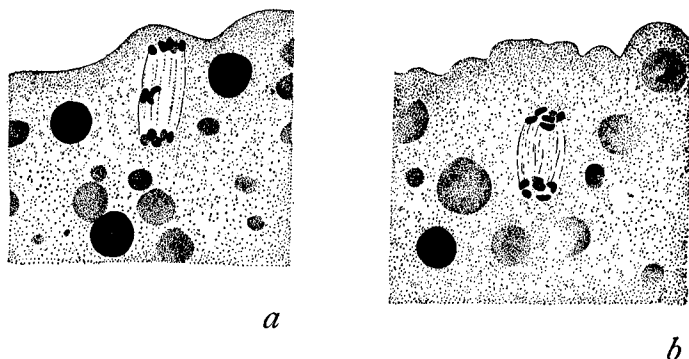


FIG. 83.—Extrusion of the polar body from a male-producing egg with lagging chromosomes on the spindle, *a*; and extrusion of the polar body from a female-producing egg, *b*; in *Phylloxera*.

In the phylloxerans there are two parthenogenetic generations followed by a sexual one (Fig. 82). In the second parthenogenetic generation two whole chromosomes leave certain eggs (Fig. 83) passing into the single polar body which is given off from the egg. Such eggs have two less sex-chromosomes and develop parthenogenetically into males. In other eggs of the same generation all four sex-chromosomes are retained after the polar body is produced. These eggs also develop parthenogenetically, but produce females. Similar changes take place no doubt in the aphids, for the males have been shown to have one less chromosome than the female, although the loss of one

chromosome in the polar body has not yet been observed in the group.

In both phylloxerans and aphids there are two classes of sperm produced in the males as in other insects, one with X, one without it. The latter degenerates, and only the X or female-producing sperm remains functional. A few stages in the spermatogenesis of the bearberry aphid

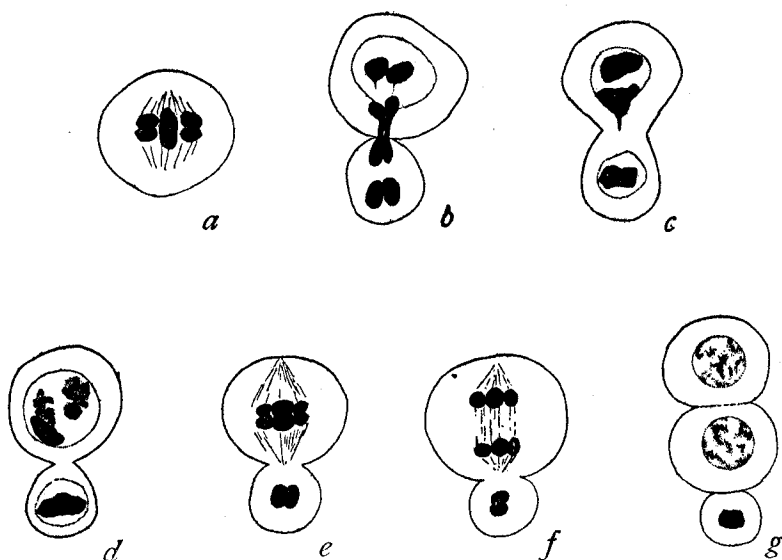


FIG. 84.—First and second spermatocyte division in the bearberry aphid with the formation of one rudimentary cell.

are shown in Fig. 84, *a-g*. In *b*, the chromosomes have divided and moved to opposite poles while the sex-chromosome is drawn out but has not moved yet to either pole. In *c*, the sex-chromosome has been drawn into the larger of the two cells that is produced. In *d*, the division into a larger and a smaller cell is completed. In *e*, preparations for another division are taking place in the larger cell, and in *f* and *g* this is completed. The smaller cell does not divide, and later degenerates. The two spermatozoa from

the two larger cells each contain one X-chromosome and two autosomes. They correspond obviously to the female-producing sperm of other insects. Hence only females arise from fertilized eggs.

The rotifers, especially *Hydatina senta*, are the only animals in which the transition from parthenogenetic to sexual reproduction has so far been gotten under control by regulating the environment, and although the evidence that the environment causes part of its effects by influencing the chromosomal mechanism is not yet established, there is, in my opinion, some indication that such is the case. The common method of reproduction in *Hydatina* is as follows: A parthenogenetic female (Fig. 85, *A*) lays eggs (*D*), each of which, after giving off a single polar body, develops at once (*i.e.*, without fertilization) into a female like the mother. The whole number of chromosomes is retained in the eggs. Several or many generations may be produced in this way. Whitney has shown that if such females are fed on a green alga, *Euglena*, daughters appear (structurally like the others) that produce smaller eggs (*E*). If these eggs develop without fertilization they become males (*C*). Examination of these small eggs show that they give off two polar bodies, and retain a reduced number of chromosomes. This process is the same by which the male bee is produced.

If the female, that produces the small eggs just described from which the males develop, should have been impregnated by a male soon after she hatched, her eggs would then grow larger and surround themselves with a thick-walled coat. They become the winter or resting eggs. Each such egg, after the sperm enters, gives off two polar bodies, reducing in this way the number of its chromosomes. By the addition of the sperm nucleus the full number of chromosomes is recovered.

Whitney has recently shown that there are two classes of spermatozoa produced by the male, large and small;

for, owing to the few sperms produced by each male their actual number can be counted. There are twice as many large as small spermatozoa, if, as may be the case, only the large ones contain chromosomes and are functional,

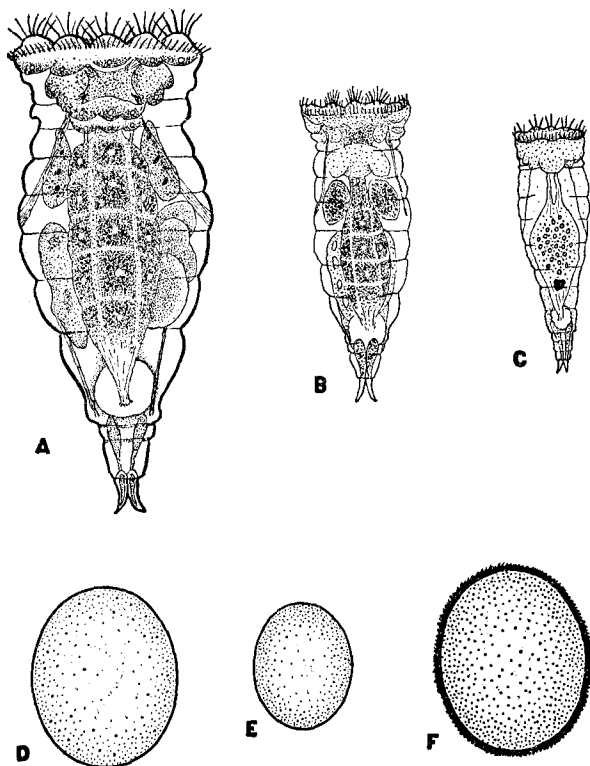


FIG. 85.—*Hydatina senta*, adult female, A; young female soon after hatching, B; adult male, C; parthenogenetic egg, D; male-producing egg, E; resting egg, F. (After Whitney.)

the conditions here would appear to be like those in the hornet, provided there are no chromosomes in the small spermatozoa. This would also explain why all fertilized eggs produce females.

So long as the ordinary parthenogenetic females are fed on the poor diet of *Polytoma*, they continue to produce

parthenogenetic females like themselves (Fig. 86), and this non-sexual process continues indefinitely. If on the contrary, parthenogenetic females are fed abundantly on a rich diet of the green alga *Euglena*, their eggs develop into individuals which, if early fertilized as explained above, become sexual females, *i.e.*, they lay fertilized eggs, but if not fertilized, produce small eggs that, developing parthenogenetically, become males. In other words, the same female becomes either a sexual female, or a female that

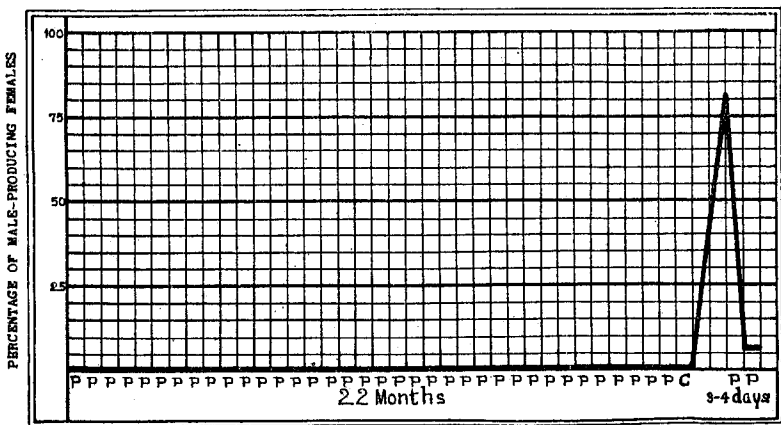


FIG. 86.—Diagram showing how a continuous diet of *Polytoma* (P-P) through twenty-two months yielded only female-producing females, but when the diet was suddenly changed to *Chlamydomonas* (at C), male-producing females appeared at once. (After Whitney.)

gives birth to males. Some recent writers, misunderstanding these relations, have tried to make it appear that the change here is one that is sex-determining, using this expression to all appearances as it is ordinarily employed in other cases, but in fact using the term in such a way as to obscure the one important fact that the results really show, *viz.*, that an environmental change of a specific kind produces a new kind of female that is either a producer of eggs that become males (after or because two polar bodies are extruded), or becomes a sexual female, should she early meet a male.

SEX-DETERMINATION AND ARTIFICIAL PARTHENOGENESIS

Many interesting questions concerning sex-determination might be studied were it as easy for man, as it appears to be for nature, to make eggs develop without fertilization. Only three cases are known in which eggs developing under artificially induced conditions have reached maturity. Delage raised one sea urchin that had been produced artificially to maturity, and determined that it was a male. Tennent has shown that the male is heterozygous for the sex-chromosomes. Hence, if the artificially produced urchin has the half number of chromosomes it should, if like the bee, be a male, but if, as Herlandt has shown, the number of chromosomes may double before development, a female would be expected.

In the frog, Hertwig, and later his pupil Kuschakewitch, found that the number of males is increased up to 100 per cent. if the eggs are detained in the uterus for one to three days before adding sperm to them. Hertwig has attempted to explain the result as due to a relative change in the size of the nucleus that takes place in consequence of the delay, but since the chromosomes are at this time in the metaphase of the second polar spindle, it is not obvious how such an enlargement could be brought about, quite aside from the question as to whether the result imagined would follow even after such a change. I have suggested that these eggs with deferred fertilization may develop parthenogenetically, due either to the egg nucleus alone giving rise to the nuclei of the embryo, or to the sperm alone giving rise to these nuclei, in the latter case, the polar spindle of the egg having been caught at the surface and prevented from taking part in the development. The possibility of the nuclei of the frog arising in one or the other of these ways is shown by the work of Oscar and Gunther Hertwig who have found evidence that after treatment with radium, the sperm-nucleus alone may give rise to the somatic nuclei of the embryo. Packard also

has shown that such kinds of androgenetic embryos may arise in the eggs of *Chætopterus* treated with radium, and by following every stage in the process he has determined also that the embryos have the reduced number of chromosomes.

Other work on the egg of the sea-urchin had seemed to show that while in most cases the egg, that begins to develop parthenogenetically, starts with, and continues to maintain the half number of chromosomes, yet according to a recent observation of Brachet, a parthenogenetic tadpole, eighteen days old, that he produced, had the double number of chromosomes. Whether it may turn out that when the egg nucleus gives rise to the nuclei of the parthenogenetic individual it may sometimes double its number of chromosomes (by failure of the first cytoplasmic division, for example), and that when a sperm gives rise to these nuclei the half number is retained, cannot be stated. Until we have farther information on these points the expectation as to what the sex of parthenogenetically produced frog individuals will be can only be speculative. Loeb has raised seventeen adult, or nearly adult male frogs and three nearly adult female frogs from eggs developing after Bataillon's puncture method of inducing parthenogenesis. One male frog had more than the half number of chromosomes (at least 20 and presumably the whole number, 26?). The number of chromosomes in the females was not determined.

GYNANDROMORPHS AND SEX

In the group of insects especially, it has long been known that individuals occasionally appear that are part male, part female. In the most striking cases the line of division runs down the middle of the body, but there are also antero-posterior gynandromorphs, and individuals with only a quadrant or even a small piece of the body different from the rest in its sex character. Several hypotheses have been advanced to explain these rare com-

binations of the two sexes, and it is probable that gynandromorphs may arise in more than one way, but in *Drosophila* it can be demonstrated that the great majority of gynandromorphs result from dropping out of one of the sex-chromosomes at some early division of the fertilized egg. The demonstration is made possible by using sex-linked characters that are known to be carried by the sex-chromosomes. For example: Yellow body color in *Drosophila* is due to a recessive gene carried by the X-chromosome. Its allelomorph (wild type) lies also, of course, in the normal X-chromosome. If yellow is crossed to wild, and a bilateral gynandromorph should arise, it may be yellow on the male side (as seen in the yellow wings and yellow hairs over half the body) and wild type on the female side (Fig. 87).

Since the male characters arise when only one sex-chromosome is present, it must be the yellow-bearing chromosome in this case that gives the male side. Since the female characters arise when two X's are present, both must be present in the female side, which will here be the wild type, since the gene for wild type dominates the yellow-producing gene. The gynandromorph must have arisen, therefore, at a very early nuclear division in the egg in which one daughter X-chromosome failed to pass into one of the daughter nuclei. The diagram (Fig. 88) shows how such a result might be supposed to have come about.

The diagram indicates that one daughter chromosome X' (bearing the gray gene) has failed to become incorporated in its proper nucleus, which is therefore left with only one X. From this nucleus the nuclei of the male half are produced, while from the XX nucleus the nuclei of the female half arise. That both of these nuclei, the XX and the X nucleus contain other chromosomes derived from both parents has been shown by making one of the original parents homozygous for some recognizable autosomal

Fig. 87 A.

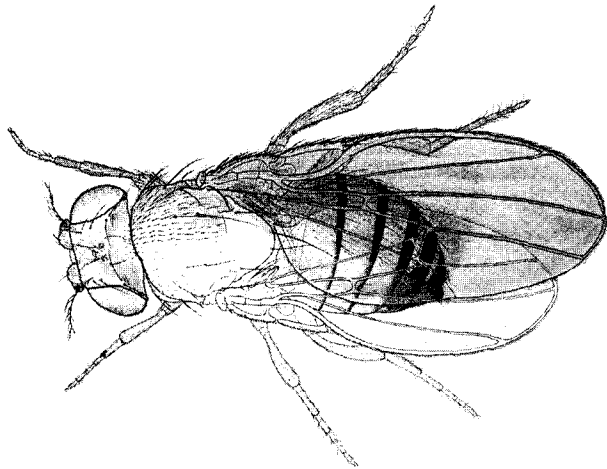


Fig. 87 B.

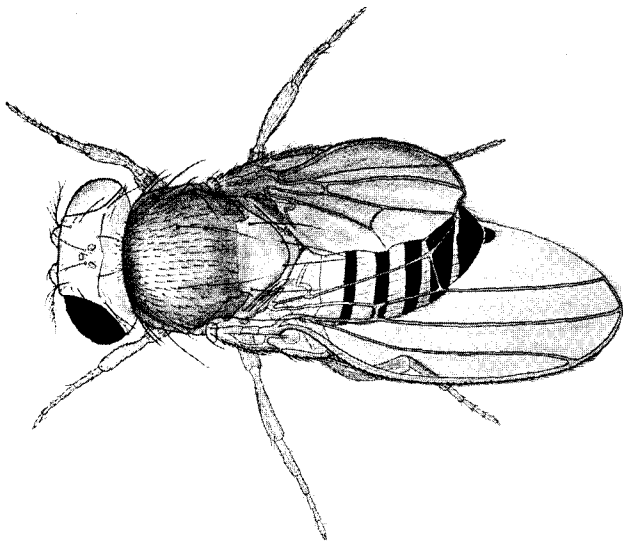


FIG. 87 A.—Gynandromorph. Left side of thorax and abdomen and left wing and legs are yellow in color and male. Right side of thorax and abdomen and wing and legs are gray and female. All of head is gray and female with "white-eosin-compound" eyes. Genitalia are female. The mother of this gynandromorph was a "white-eosin-compound," *i. e.*, she had one X-chromosome with an eosin gene and one with a white gene. The father was yellow white, *i. e.*, his single X-chromosome carried the genes for yellow and for white. Elimination consisted in the loss of one of the maternally derived chromosomes, *viz.*, that one bearing eosin, leaving only the yellow white chromosome to produce the male side of the thorax and abdomen.

FIG. 87 B.—Gynandromorph. Left side is female. Left eye red and wing long, like that of a normal female. Right side, except abdomen, is male with eosin eye and miniature wing. Sex comb on right fore-leg only. The mother of this gynandromorph had one vermilian-bearing X-chromosome; and another X-bearing eosin and miniature genes; the father carried an X-chromosome bearing eosin and miniature.

character. It, or its normal allelomorph, should therefore be present in both nuclei if all the chromosomes of the fertilized egg have divided normally except the X-chromosomes. This, in fact, has been found to be the case (Morgan, Bridges, Sturtevant).

Nearly all of the many hybrid gynandromorphs of *Drosophila* can be explained as above. In a few cases, when the abdomen of the fly was sufficiently female to make mating possible, it has been found that the eggs give the results expected for a female having the sex-linked factors that entered the cross.

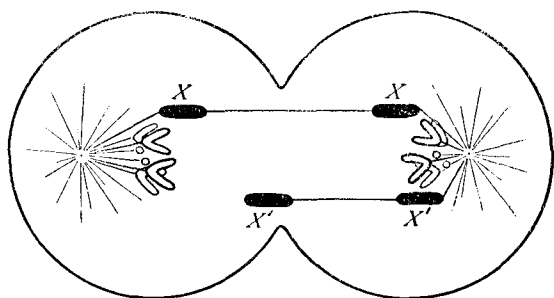


FIG. 88.—Diagram showing elimination of X' at an early cell-division, so that the nucleus to the right gets X and X' and that to the left only X .

In a few cases in *Drosophila* the explanation of chromosomal dislocation will not cover the results. Some of these cases can, however, be accounted for by another hypothesis. Should an egg arise with two nuclei (there are several possible ways for this to occur), one nucleus having one set of factors, the other the other set (the parent being heterozygous), then if each nucleus is separately fertilized a different combination of factors is possible from that possible on the elimination theory. A gynandromorph, described by Toyama, appears to belong to this category. Toyama found two gynandromorphs of the silkworm (Fig. 89) whose mother belonged to a race with banded caterpillars, and whose father belonged to a

race with pale caterpillars. One of these was banded on the left side (which side was also female) and pale on the right side (which was also male). The sex of the two sides was only apparent after the moth had appeared. The banded character of the worm is known to be dominant to the pale character, but neither is sex-linked. The case can be explained, if as the evidence indicates, the mother was

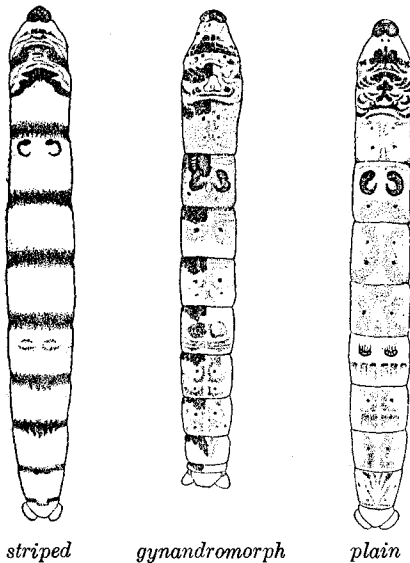


FIG. 89.—Caterpillars of the silkworm moth. A striped one to the left, a plain one to the right, a hybrid gynandromorph in the middle.

heterozygous for a not sex-linked character, banded, and if she produced an egg with two nuclei (Fig. 90). Doncaster has found such eggs in *Abraxas*, and has shown that each nucleus extrudes separately polar bodies, and that each reduced egg nucleus is fertilized by a separate spermatozoön. If as shown in the next diagram one reduced nucleus has a *W*-chromosome, and a factor for banded carried in one of the autosomes, and the other reduced nucleus has a *Z*-chromosome, and in one of the

autosomes a factor for pale, and if a spermatozoön, carrying the factor for pale, fertilizes each nucleus, the two zygotic nuclei will be ZW female and banded, and ZZ male and pale. This gives at least a formal explanation of the results, and helps us to see how such a rare event, the appearance of two gynandromorphs in the same brood, happened to occur at the same time; because, as Doncaster's evidence shows, a double nuclear condition may be characteristic of the eggs of certain females.

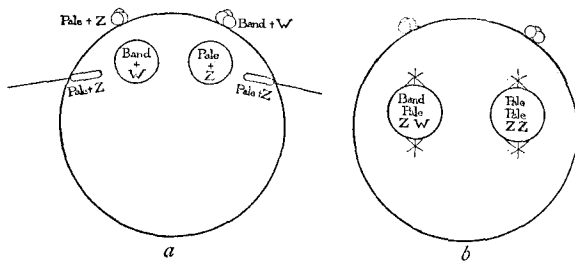


FIG. 90.—Diagram illustrating how a heterozygous egg with two nuclei fertilized by two sperm might produce a gynandromorph like that shown in Fig. 89.

“INTERSEXES” AND SEX GENES

The quantitative relation of one X for male and two X's for female that has been found to hold in many of the groups of animals might seem from a purely *a priori* point of view capable of being modified in such a way that an intermediate condition might be realized, but whether such conditions should be expected to give rise to hermaphrodites or to non-sex-somethings (intermediates)—or to a mosaic of both sexes, or should rather be expected to die could scarcely be foretold. There are three cases in which individuals called “intersexes” have been found, or produced; and since their interpretation has led to a view that has appeared to contradict the ordinary sex-determination scheme, these cases must be briefly referred to here. Goldschmidt has studied very thoroughly “inter-

sexes" that arise when the European and Japanese race of gypsy moths, *Lymantria dispar* and *L. japonica*, are crossed. Riddle has described doves obtained by crossing the white ring dove (*Streptopelia alba*) and the Japanese turtle dove (*Turtur orientalis*) that are intersexual in their mating habits. Olga Kuttner and Banta have found that certain lines of Cladocerans (*Simocephalus*) may produce (parthenogenetically) "intersexual individuals" in the sense that an individual may possess some of the secondary sexual differences of one sex and some of the other.

Some of Goldschmidt's combinations between different races of gypsy moth produce only intersexual females, *i.e.*, individuals that are mostly female, but have also, in spots, male characters. In the most extreme cases they are almost like males, not only in color, but even in the partial production of testes. Other racial combinations give male intersexes, *i.e.*, individuals that are for the most part males, but show, in spots, some of the characteristics of the female. Goldschmidt explains these results by the assumption that the sex factors have different quantitative values in the different races. He represents the female by *FFMm*, and the male by *FFMM*. If the *FF* "factorial set" is represented by 80 units, and the "present" male factor, *M*, by 60 units, then the above formula for the female becomes $80-60 = +20$, and the male formula becomes $80-(60 + 60) = -40$. In the former, female units "dominate," in the latter, the male. Values like these can be arbitrarily set for all the different races. For instance, to the "weak" European race and the "strong" Japanese the following values are assigned:

| Weak European Race | | | Strong Japanese Race | |
|--------------------|-----|--------|----------------------|--------|
| ♀ | FF | Mm | FF | Mm |
| | 80, | 60 | 100, | 80 |
| ♂ | FF | MM | FF | MM |
| | 80, | 60, 60 | 100, | 80, 80 |

If a Japanese female is crossed to a European male, the F_1 female and male may be represented in the following formula:

$$\begin{array}{r} F_1 \text{ ♀ } FF \quad Mm \\ 100, \quad 60 \end{array} \qquad \begin{array}{r} F_1 \text{ ♂ } FF \quad MM \\ 100, 80, \quad 60 \end{array}$$

Both "normal" female and male offspring are expected in equal numbers. The reciprocal cross gives a different result, *viz.*:

$$\begin{array}{r} F_1 \text{ ♂ } FF \quad MM \\ 80 - (80 + 60) \end{array} \qquad \begin{array}{r} F_1 \text{ ♀ } FF \quad MM \\ 80, 80, \quad 60 \end{array}$$

The F_1 female is $FF - M = 0$; and is therefore represented as intersexual. It will be observed that the so-called "female factors" in these formulæ are supposed to be inherited entirely through the mother.

By assigning different values to FF and M in the different races it is possible to express the results in such a way that the sexes obtained by various crosses have different minimal values—those less or more than any assigned value for a given sex are interpreted as intersexes. In the example cited, an exact balance ($=0$) between the conflicting factors produces an individual that is represented as neither male nor female. It is not obvious, however, why it should be made up of parts each of which is strictly comparable to the same part in a male or a female.

While the assignment of arbitrary values to sex factors is a legitimate procedure, it is not a quantitative analysis in the ordinary sense, since the quantities are not referred to some external measure, but are purely arbitrary.

How far an erratic elimination of sex-chromosomes in later stages of cell-division might account for the result cannot be stated, since there are at present no facts to go upon—the chromosome count in somatic cells of the hybrid has not yet been reported, but Goldschmidt thinks

that the mode of development of the embryo precludes this interpretation.

Riddle obtained his intersexual hybrids by causing their mother to produce many more eggs than she would ordinarily produce. This was done by removing the eggs from the nest as soon as they were laid. Towards the end of a series obtained in this way an overworked female produced an excess of males. Some of these males Riddle regards as females that have been changed into males—the completeness of the change being shown in their sexual behavior towards other males, etc. But there is involved in the cross a sex-linked factor that behaves, as R. M. Strong had already shown several years ago, as do sex-linked factors in other birds. It is thus possible to identify the chromosomal make-up of Riddle's intersexual hybrids. His own results show that the hybrids have the expected combination of chromosomes for males. It appears, therefore, that whatever it may be that affects their behavior their sex is determined by their possessing the ordinary chromosome constitution for males.

HERMAPHRODITISM AND SEX

As has been shown, the sex-mechanism, whether $XX-XY$ or $WZ-ZZ$, gives rise to two kinds of individuals—males and females. There are, however, many groups and species of animals where both eggs and sperm are found within the same individuals, and in typical cases there are in such individuals special ducts that are outlets for the male germ-cells and others for the female germ-cells. In these hermaphrodites “sex-chromosomes” are not known to be present, or if present as in *Ascaris nigrovenosa*, they act as sex determinants only in alternate generations.

The usual interpretation of the determination of the sex-cells of hermaphrodites is that their differentiation is determined by the same kind of specific influences that determine, for example, that certain cells of the primitive gut develop into liver cells, others into lung cells, still

others into pancreas cells, etc. There is nothing inconsistent in such a view with the theory that in other cases a different mechanism produces different kinds of germ-cells. Logically, this viewpoint is consistent, but I can sympathize with efforts that are continually being made to find an explanation that makes use of the same kind of process in genetic segregation and in embryonic differentiation. In fact, in 1902, while still under the influence of the then recent advances in the field of experimental embryology (developmental mechanics), I suggested that one might attempt to treat the phenomenon of segregation from the same theoretical standpoint (*viz.*, the realization of alternative states) as was then appealed to for embryonic differentiation. It soon became apparent to me, however, that (1) the two kinds of results depended upon entirely different situations, and therefore need not have a common explanation; (2) that the genetic evidence showed the improbability of explaining segregation and differentiation in the same way; (3) that special tests that I carried out failed to support the supposition of a common explanation; (4) that while no detailed explanation is possible at present for the general phenomena of specific differentiation, yet for Mendelian segregation the reduction division supplies all that the results call for.

SEX RATIOS

The theory of sex-determination has been deduced from the evidence of equality of males and females as well as from the cytological evidence. It remains to explain why in some cases the machine fails to give equality of the two sexes; why, for example, all fertilized eggs of phylloxerans and aphids, or daphnians, or rotifers, or bees, are female; why certain mutant races of flies give twice as many daughters as sons; why other races of flies produce nearly all sons; why the sex ratio in man is about 106 males to 100 females.

It is perhaps needless to point out that if, in a species

in which sex is determined by a chromosome mechanism, it were possible to change the sex by other agencies in spite of the chromosome arrangement, the latter relation would be entirely thrown out of gear and males would transmit sex-linked characters and sex itself like females, and females like males. As no such cases have been found, it is futile to discuss such a possibility.

It has been shown that only the female-producing sperm in phylloxerans and aphids becomes functional, hence it is obvious why all the fertilized eggs develop into females. In daphnians and other crustacea it is not known whether one class of spermatozoa degenerates, but the results are explicable on such a view. In rotifers the production of males only by certain females is due to the eggs developing by parthenogenesis with the haploid number of chromosomes and this explains also the case of the bees, wasps and other hymenoptera. If a queen bee is unfertilized or if her supply of sperm gives out she produces only males. If she contains sperms, then any egg that is fertilized produces a female, and as Petrunkevitch showed several years ago, spermatozoa are to be found in eggs laid in worker cells—such eggs being known to produce workers (♀ ♀). In rotifers, too, the presence of a large and a small class of sperm suggests that only the former is functional.

Certain females of *Drosophila* give a sex ratio of two females to one male. By making such a female heterozygous as to her X-chromosomes (each carrying different factors) it can be determined that the half of the expected sons that die are the ones containing one of these two chromosomes. It is easily possible by means of linked genes to locate a factor in the sex-chromosome (Fig. 91) and to show that whenever it goes to a male the fly dies. All the daughters survive because the lethal factor being recessive does not harm a female whose other chromosome comes from a normal father. The scheme is shown on the next page.

SEX-CHROMOSOMES AND INHERITANCE 199

As many as 20 different lethals have been found in the X-chromosomes of *Drosophila*. Their occurrence in these chromosomes is first noticed by the appearance of such exceptional sex ratios. Lethal factors like these need not be thought of as different in kind from any other mutant factors. They may mean only that the changes that they cause are of such a kind, structural or physiological, that the affected individual cannot develop normally. Some of the lethals may be fatal in

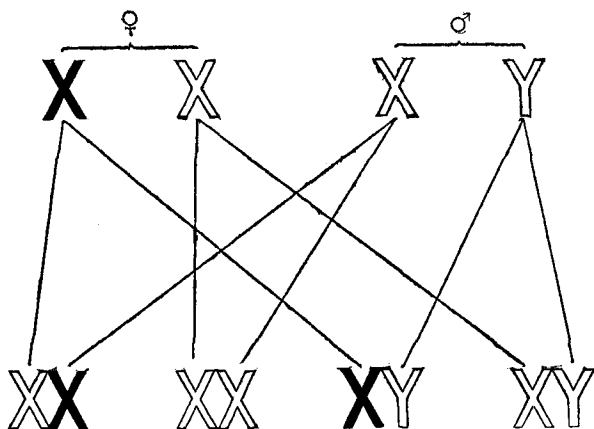


FIG. 91.—Scheme showing the transmission of a lethal sex-linked factor in an X-chromosome the black one in the diagram.

the egg stages, others are known to cause the death of the larvæ, others probably act on the pupæ, and a few even allow an affected male to occasionally come through.

In man and in several other mammals there is at birth a slight excess of males over females. Since male babies die oftener than females, the difference has been said to be an "adaptation," with the implication that it calls for no further explanation. Several possible solutions suggest themselves. The male-producing sperm bearing the sex-chromosome may more frequently develop abnormally than the female-producing sperm. Again, since the spermatozoa must, by their own activity, travel the entire

length of the oviduct to reach the egg as it enters the tube, the greater size or weight of the female-producing sperm may give a slight advantage to the male-producing sperm in the long trip up the tube. This would lead to an excess of males. There are still other possibilities, which if realized, would suffice to slightly change the equality of the output of the machine.

NON-DISJUNCTION

Females of *Drosophila* are occasionally found that give exceptional breeding results which have been explained by Bridges on the view that these females are

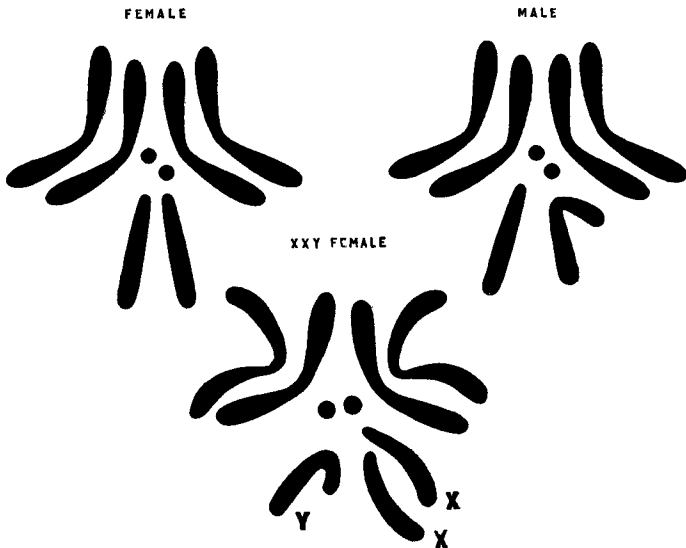


FIG. 92.—Normal female and male groups of chromosomes of the vinegar fly, with the XXY female group below.

XXY individuals (Fig. 92). It has been shown by cytological examination that such females do actually contain an additional Y-chromosome. The four possible ways in which these three chromosomes might be expected to behave at the reduction division when the polar bodies

are given off by the egg are shown in the next diagram (Fig. 93). One X may go out of the egg, and the other X and the Y stay in; or one X may stay in the egg and the other X and the Y go out. In these two cases, X and X may be thought of as members of a pair that conjugate, as in the normal female, and then separate, and chance alone determines whether the Y stays in or passes out. Again Y may go out of the egg and X and X stay in; or X and X

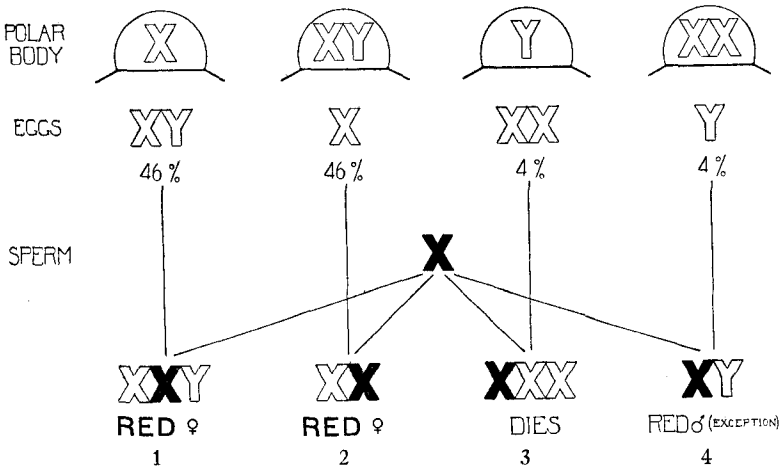


FIG. 93.—Non-disjunction. In the upper part of the figure the four possible modes of elimination of the sex-chromosome from XXY eggs are shown; the results of their fertilization by an X-bearing sperm of the male are shown below.

go out and Y stay in. Here X and Y may be supposed to be members of the conjugating pair, and the free X goes to the same pole as the X that conjugated.

In the diagram, each of these four types of eggs is represented as fertilized by an X-bearing sperm. In order to make the outcome more apparent the original XXY female may be supposed to have had white eyes (clear X's) and the male that fertilized her red eyes (here represented by the black X carrying the gene for red eyes).

Four classes of individuals are expected: (1) Red-eyed females (XXY); (2) red-eyed females (XX); (3) red-eyed

females (XXX) that die, and (4) red-eyed males (XY). The last are exceptional, since white-eyed females normally never produce anything but white-eyed sons. Here the exceptional male is due to an egg without an X, being fertilized by a "female-producing" (or X-bearing) sperm. The three X individuals have never been found, and undoubtedly die, presumably from too many X's. The remaining red females are of two kinds, one normal XX

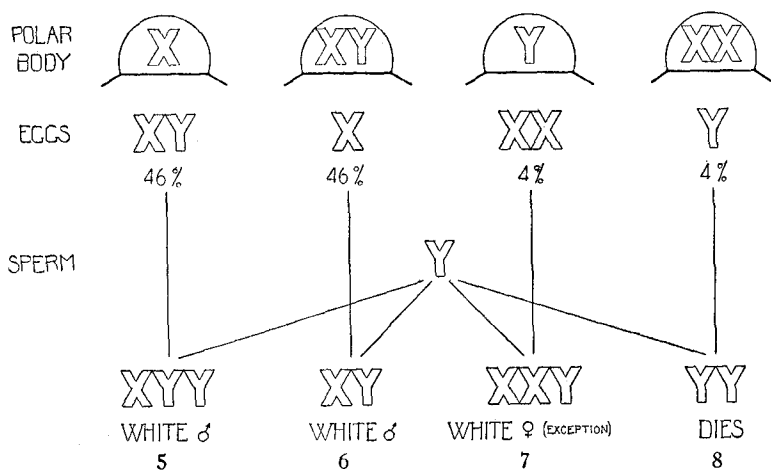


Fig. 94.—Non-disjunction. In the upper part of the figure the four possible modes of elimination of the sex-chromosome from the XXY eggs are shown, and the results of their fertilization by a Y-bearing sperm of the male is shown below.

and the other (XXY), which is expected to repeat the exceptional behavior of her mother. In fact, this is what she does.

In the next diagram (Fig. 94) the fate of the same four kinds of eggs is shown if they are fertilized by a Y-bearing sperm. Four classes of individuals are expected (5) white males (XYY); (6) white males (XY); (7) white females (XXY); and (8) YY individuals. No individuals having the last make-up have ever been found, and there can be no doubt that an individual without at least one X dies. The white-eyed females are exceptional, since white-eyed

mothers by red-eyed fathers have normally only red-eyed daughters. These exceptional white-eyed females (XXY) must repeat the phenomena of non-disjunction, and it has been found that they do so invariably. The white-eyed male XY is normal; the other male should produce some XY sperm and thus transmit both X and Y to some of his daughters. Such daughters as get both X and Y from the entering sperm should show non-disjunction. This has been proven to occur.

An analysis of the data has shown that two of the four types of eggs are more common than the other two. As indicated in both diagrams the types of eggs that result after X and X have united occurs in 92 per cent. of the cases, and since in this type the unmated Y has a random distribution, the XY egg is found in 46 per cent. of cases and the X egg in 46 per cent. The more uncommon type of egg would be expected to result if X and Y united and then separated while the other X had a random distribution.¹ Eight per cent. of such cases occur, giving XX eggs in 4 per cent., and Y eggs in the other 4 per cent. of cases.

These results not only furnish very strong proof of the chromosome theory of sex, but serve also to show how a knowledge of the actual mechanism involved leads to the discovery of how a change in the mechanism gives a new output. The conclusion that females behaving in this way must contain a Y -chromosome was confirmed by the cytological demonstration that showed in them two X 's and a Y .

¹ Since this was written it has been found that after XY synapsis the free X always goes to the same pole as the synapsed X .