THE EFFECT OF HETEROZYGOUS INVERSIONS ON PRIMARY NONDISJUNCTION IN DROSOPHILA MELANOGASTER[1]

CLIFFORD FORBES[2]

Department of Zoology, University of California, Berkeley, California

Received January 15, 1962

BRIDGES (1913, 1916) found in certain crosses exceptional individuals which did not inherit their sex-linked genotypes from their parents in the expected crisscross manner. Instead the males were patroclinous and the females matroclinous. He explained their occurrence by assuming that occasionally the two X chromosomes would fail to disjoin from each other at the reduction division. As a consequence of this failure of segregation both X chromosomes were either retained in the egg or both passed into the polar body. The fertilization of an XX egg with a Y spermatozoon would produce a matroclinous XXY female. The no-X egg when fertilized with an X-bearing sperm would become an X0 patroclinous male. BRIDGES did not find the individuals that were the products of the other possible fertilizations, namely the XXX and 0Y genotypes.

The exceptional XXY F_1 females produce a higher frequency of nondisjunction than do their mothers. BRIDGES (1916) called this phenomenon secondary nondisjunction whereas that from the *P* (parental type) females was called primary nondisjunction. To account for the very rare (1 to 1700) primary exceptions, he postulated that an entanglement caused the synapsed X chromosomes to lag on the meiotic spindle and to separate from each other only with difficulty. To account for the more frequent (4.3%) secondary exceptions he assumed that part of the synapses (16.5%) were XY and that random segregation of the unpaired X chromosomes would produce XX and Y eggs in equal frequency.

Failure of metaphase pairing has been suggested by STURTEVANT and BEADLE (1939) as an alternate hypothesis to explain primary nondisjunction. This failure of metaphase pairing may result from a failure of conjugation at zygotene or from complete separation of formerly paired homologs at diakinesis. If the two unpaired univalents are distributed more or less at random with respect to each other, then they may go to the same or to opposite poles. SANDLER and BRAVER (1954) have shown that in females unpaired chromosomes are lost with a considerable frequency. They favor a hypothesis according to which primary nondisjunction results from the occasional failure of the X chromosomes to pair, with the subsequent loss of one or both of these. Such losses would result in a difference in the recovery of the exceptional male and female classes.

[1] From material submitted to the Graduate School of the University of California in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] Present address: Department of Biological Sciences, University of Idaho, Moscow, Idaho.

SANDLER and NOVITSKI (1956) have reported that the presence of an extra fourth chromosome increases the frequency of primary nondisjunction of X chromosomes. They assume that nonhomologous pairing takes place between the extra fourth chromosome and an X chromosome. The resulting segregation leads to the production of nondisjunctional gametes.

It has been reported (BRIDGES 1916; STURTEVANT and BEADLE 1936) that nondisjunctional gametes are almost always noncrossovers. Therefore in the usual type of primary and secondary nondisjunction the X-chromosomal genotype is the same as that of the maternal parent. BRIDGES rarely found an individual which had received two X chromosomes from its mother but possessed a different X chromosomal genotype. One of the two X chromosomes was similar to one in the maternal parent, but the other was the result of a crossover between the mother's X chromosomes. It would be expected, if crossing-over and nondisjunction were negatively correlated events, that the interchromosomal effect of heterozygous autosomal inversions to increase crossing-over in the X chromosome (STEINBERG 1936) would result in a reduced frequency of primary nondisjunction. However, STURTEVANT (in MORGAN and STURTEVANT 1944) found that the opposite was true. Females heterozygous for one inversion in the autosomes and another in the X chromosomes produced many more primary exceptions than occurred when only the X chromosomes were structurally heterozygous.

COOPER, ZIMMERING and KRIVSHENKO (1955) confirmed STURTEVANT's discovery that the presence of heterozygous autosomal inversions increases the nondisjunction of structurally heterozygous X chromosomes. They reported similar results with several sex-linked and autosomal inversions. In addition, their data showed that the greatest increases occurred when the sex chromosome and both major autosomes were heterozygous for inversions. They obtained 12.0 percent exceptional offspring with such genotypes. The corresponding frequency of nondisjunction calculated with allowance for the loss or very rare survival of XXX or 0Y zygotes was 21.4 percent. The sex ratio of female to male exceptional types was 1:1 in their total data.

COOPER and his associates hypothesized that when two different chromosome pairs are heterozygous for inversions, they may associate not only as homologous pairs but also as nonhomologous complexes. Segregation is assumed to be normal if they pair with their homologous partners. Otherwise the dissociation of the complex would result in randomly directed univalent chromosomes. When both or neither of the X chromosomes go into the egg a "nondisjunctional" exceptional individual may result if the egg is fertilized by the proper spermatozoon. Abnormal segregation of the autosomes (except for the fourth chromosome) would not result in a viable genotype with a normal spermatozoon. In order to test their hypothesis they studied the hatchability of eggs from females heterozygous for various inversions. The hatchability was reduced below the control level when inversions were heterozygous in the X chromosome and in either the second or third chromosome. Similar results were obtained when inversions were present in both major autosomes but with the X chromosome pair structurally homozygous. In agreement with expectation according to their theory, the greatest re-

duction in hatchability resulted when all the major chromosomes were heterozygous for inversions. The decreases were assumed to be greater than the expected losses due to 0Y fertilizations.

COOPER and his associates have attempted to explain the interchromosomal effect of inversions on crossing-over. They suggest that the selective losses of noncrossover gametes as a consequence of nonhomologous pairing may partially account for the interchromosomal effect on crossing-over. REDFIELD (1957) studied the egg mortality and recombination in the X chromosome associated with heterozygous autosomal inversions. She reported losses due to the presence of the heterozygous inversions to be somewhat less in value than those reported earlier by COOPER, ZIMMERING and KRIVSHENKO and not sufficient to explain the interchromosomal effect on crossing-over by the loss of noncrossovers.

ZIMMERING (1958) has compared the crossing-over frequencies in an unrelated chromosome for expected and exceptional offspring from primary nondisjunction. The females were heterozygous for sex-linked and second chromosome inversions. There were no significant differences in crossing-over frequencies between the exceptional and the regular offspring for the Glued Stubble region of the third chromosome.

The finding of nonrandom assortment between autosomes and Y chromosomes by GRELL (1957, 1959) and OKSALA (1958) has been explained by these workers by assuming that nonhomologous chromosome pairing takes place between Y chromosomes and autosomes. A similar finding has been made by FORBES (1960) of nonrandom assortment of second chromosome inversion-translocation genotypes with respect to primary nondisjunction gametes. These findings support the hypotheses of SANDLER and NOVITSKI (1956) and COOPER, ZIMMERING and KRIVSHENKO (1955) that nonhomologous chromosome pairing is the mechanism by which primary nondisjunction is brought about.

Although STURTEVANT (MORGAN and STURTEVANT 1944) and COOPER, ZIMMERING and KRIVSHENKO (1955) have found equality of exceptions when the X chromosome and one pair of autosomes were heterozygous for inversions, there is no reason to believe that this finding should be true for all sex-linked genotypes. Equality of the sexes of the exceptions would not be expected as patroclinous males can arise in two ways from females heterozygous for sex-linked inversions. STURTEVANT and BEADLE (1936) have shown that considerable numbers of patroclinous males, in excess of matroclinous females, were produced from mothers with certain sex-linked inversions. They reported that these exceptional males arose from no-X eggs resulting from four-strand double crossing-over. Patroclinous males should therefore partly be the result of four-strand double crossing-over and partly due to nondisjunction, while matroclinous females should all be due to nondisjunction. Thus one would expect an excess of patroclinous males. In order to explain the absence of this excess, one might assume that in STURTEVANT's work with autosomal inversions, patroclinous males from double crossing-over may not have occurred in a frequency great enough to affect the sex ratio.

In the present investigation the frequencies of female and male exceptions have

been determined for several heterozygous sex-linked inversions and heterozygous autosomal inversions. New findings concerning the sex ratio have been made. In addition an unexpected result has been found when all major chromosome pairs are heterozygous for inversions. This paper reports these findings.

METHODS

Flies were grown in half-pint culture bottles with the usual molasses agar medium enriched with dried yeast. "Tegosept M" (=methylparaben, U.S.P.) was added to inhibit mold growth. A drop of a suspension of living yeast was added before the flies were put into the bottles. To prevent the etherized flies from sticking to the medium, part of a "Kleenex" tissue was put into each bottle. Virgin, etherized females were immediately put into culture bottles with the desired males and were left to deposit eggs for a period of six to seven days. Offspring were classified until all had emerged. The flies were raised in incubators at a temperature of approximately 25 ± ½ °C. In nearly all of the matings, each bottle contained one female together with two or three males.

Three different inversions in the X chromosome were studied. The first of these inversions was *In(1)*dl-49. (For descriptions of this and the other inversions see BRIDGES and BREHME 1944.) The chromosome contained the recessives *y* (yellow) and *v* (vermilion) and the dominant *B* (Bar). The second inversion was *In(1)sc*^{8} with the recessives *y*, *ac* (achaete), and *w*^{a} (apricot). The remaining inversion X chromosome carried two inversions, the shorter one included within the longer. Its genotype is *y*^{2} *sc*$^{8l-8}$ *B* dl-49 *v w*^{a}.

Two autosomal inversion chromosomes were employed. For the second chromosome the *Cy* (Curly) inversion chromosome has *In(2L)Cy* and *In(2R)Cy* in the left and right arms, respectively. For the third chromosomes the LVM balancer possesses In(3L + 3R)P (Payne).

When BRIDGES (1913) reported nondisjunction, he recognized the exceptional females and males by their being matroclinous and patroclinous, respectively, in phenotype for sex-linked characters. In the present work an improved method of detecting nondisjunction that gives particularly reliable evidence concerning the origin of each exceptional female makes use of tester males from a stock with marked Y chromosomes. This stock was derived from translocations between the X and Y chromosomes. The Y chromosome is in two parts. The shorter arm, Y^{S}, is attached to the proximal part of the X chromosome. The longer arm, Y^{L}, remains free but contains the centromere for the Y chromosome segment. This free Y chromosome segment carries a small part of the X chromosome containing the locus of yellow with the wild-type allele of yellow. The X chromosome in these males has yellow and white apart from the attached short arm of the Y chromosome. The *P* females to be tested for the occurrence of nondisjunction were homozygous for yellow. With all of the X chromosomes containing yellow, the presence of the Y chromosome segment, Y^{L}, makes an individual containing it not-yellow. Exceptional females can be identified by the presence of the Y chromosome as shown by their not-yellow phenotype. They can also be recognized by their retention of matroclinous phenotypes such as vermilion.

This technique has certain advantages. These are:

1. The possibility of contamination by not-virgin females is eliminated. All "matroclinous" females that are the result of an unknown mating will be yellow. The exceptional females produced as a result of nondisjunction were not-yellow because of their Y chromosome.

2. The presence of an unknown Y chromosome within a *P* female, which produces secondary nondisjunction, can be detected by progeny testing regular F_1 males. To be fertile males must receive both arms of the Y chromosome. The sons of the *y w* males with the marked Y chromosome will be sterile since they receive only one part of the complete Y of their fathers. If the mother had contained an unknown Y chromosome, some of the F_1 males would receive it and be fertile. A check on the desired absence of secondary nondisjunction was initially done by testing all the F_1 males in each culture by collecting eggs from the cultures on small petri dishes. Later the presence of larvae in the culture bottles after all of that generation had been classified was used as an indicator of secondary nondisjunction. Cultures showing evidence of secondary nondisjunction were discarded.

RESULTS

Nondisjunction with In(1)*dl-49*: Females heterozygous for *y* dl-49 *v B* and y^2 *cv v f* in the first chromosome and for four autosomal genotypes were prepared from one and the same mating. Females to be tested for the production of exceptional offspring were mated individually to two or three $y\ w \cdot Y^S / y^+ \cdot Y^L$ males. The parents remained in the bottles for six to seven days. The exceptional offspring from these crosses were not-yellow, vermilion, Bar females and yellow, white males.

Table 1 contains data on the frequencies of female and male exceptions with

TABLE 1

Exceptional offspring from In(1)*dl-49. Females with four autosomal genotypes*

Genotype of females				Exceptions				Expected		
				Females	Percent	Males	Percent	Females	Males	Total
y dl-49 *v B* / y^2 *cv v f*	+ / +	+ / +	Expt. 1	1		2		1096	1055	2154
			Expt. 2	3		1		1045	1069	2118
			Total	4	.09	3	.07	2141	2124	4272
y dl-49 *v B* / y^2 *cv v f*	*Cy* / +	+ / +	Expt. 1	28		17		731	700	1476
			Expt. 2	18		35		787	714	1554
			Total	46*	1.52	52	1.72	1518	1414	3030
y dl-49 *v B* / y^2 *cv v f*	+ / +	*P* / +	Expt. 1	31		54		1117	1124	2326
			Expt. 2	33		49		864	845	1791
			Total	64†	1.55	103	2.50	1981	1969	4117
y dl-49 *v B* / y^2 *cv v f*	*Cy* / +	*P* / +	Expt. 1	1		27		1385	1253	2666
			Expt. 2	0		21		1357	1224	2602
			Total	1	.02	48	.91	2742	2477	5268

* Experiments 1 and 2 are significantly different with an unexplained deficiency of males in Expt. 1.
† There is a significant excess of male exceptions. Chi-square = 9.1; P = less than .01 with one degree of freedom.

*In(1)*dl-49. There are two sets of data as the work was repeated under the same conditions. When the autosomes were structurally homozygous there were four female and three male exceptions, that is, .16 percent of 4272 progeny.

There were considerable increases in the frequency of exceptional offspring when one inversion was present in heterozygous form in either major autosome. When Curly was heterozygous in the second chromosome, there occurred in the first set of data 28 female and 17 male exceptions in 1476 progeny. Thus there were fewer exceptional males than females. In the second set, 18 female and 35 male exceptions were present among 1554 progeny. The data do not constitute a homogenous sample (P = .02–.01).

The Payne inversions when heterozygous in the third chromosome were associated also with a large increase of exceptions over the frequency from females with homozygous autosomes. There were from the combined data, 64 female and 103 male exceptions among 4117 progeny. The excess of male over female exceptions is significantly different from a 1:1 expectation.

The genotypic combination of the Curly and Payne inversions was accompanied by unexpected results. It had been expected that the *P* females with two heterozygous autosomal inversions would produce more nondisjunction as reported for a double inversion experiment (which also involved the presence of a translocation) by COOPER, ZIMMERING and KRIVSHENKO (1955) rather than fewer than the *P* females with one heterozygous autosomal inversion. However, in the first experiment there were one female and 27 male exceptions among 2666 progeny. When this experiment was repeated, no more exceptional females were found, but there were 21 more male exceptions among the 2602 progeny. These data total one female and 48 male exceptions among 5268 progeny.

These data are from experiments with a single inversion which reduces crossing-over considerably. Next a long inversion, *In(1)sc*^{s}, that permits more crossing-over to take place will be considered.

Results with In(1)sc^{s}: The data for this inversion are presented in two parts. The first part was derived from a limited exploratory experiment which made use of mass matings. The second part was derived from experiments conducted with single females mated to two males apiece. The crosses used in the two sets of experiments were similar but the genotypes differ somewhat. The genotype of the X chromosome with normal gene order in the first cross was *y w*, while second was *y*^{2} *cv v f*. The male genotypes were *y v f*·Y^{L}/*y*$^{+}$·Y^{s} and *y w*·Y^{s}/*y*$^{+}$·Y^{L}, respectively.

Table 2 contains the results with *In(1)sc*^{s} and the four autosomal genotypes. When no heterozygous inversions were present in the autosomes, there were one female and 38 male exceptions among 2547 offspring. When one heterozygous inversion was present in the autosomes there were fewer exceptional females than there were with *In(1)*dl-49 and a greater frequency of patroclinous males in excess of exceptional females. When Curly was heterozygous there were four female and 82 male exceptional offspring among 2705 progeny. When Payne was heterozygous there were four female and 80 male exceptions among 1736 progeny. Some possible reasons for such a result will be considered later

TABLE 2

Exceptional offspring from In(1)sc^{8}. *Females with four autosomal genotypes*

Genotype of females				Exceptions				Expected		
				Females	Percent	Males	Percent	Females	Males	Total
y ac sc^{8} w^{a} / *y w*	+ / +	+ / +	Expt. 1	0		12		363	331	706
y ac sc^{8} w^{a} / *y^{2} cv v f*	+ / +	+ / +	Expt. 2	1		26		898	916	1841
			Total	1	.04	38	1.49	1261	1247	2547
y ac sc^{8} w^{a} / *y w*	*Cy* / +	+ / +	Expt. 1	1		26		429	317	773
y ac sc^{8} w^{a} / *y^{2} cv v f*	*Cy* / +	+ / +	Expt. 2	3		56		979	894	1932
				4	.15	82	3.03	1408	1211	2705
y ac sc^{8} w^{a} / *y^{2} cv v f*	+ / +	*P* / +		4	.23	80	4.61	801	851	1736
y ac sc^{8} w^{a} / *y^{2} cv v f*	*Cy* / +	*P* / +		0		88	6.31	637	669	1394

after data for inversions that suppress crossing-over almost completely have been considered. When both autosomal inversions were present together, there were no female exceptions. There were 88 patroclinous males in a total of 1394 individuals.

Results with Ins(1)sc^{S1-8}, *dl-49*: The chromosome possessing more than one sex-linked inversion was *sc^{S1-8}*, dl-49. This genotype contained the recessive markers *y^{2} v w^{a}* and the dominant *B*. The not-inverted chromosome used with the *sc^{S1-8}*, dl-49 inversions was *y^{2} cv v f*. Three different methods were used in making the crosses. In Experiment 1, females to be tested for nondisjunction were mass mated to *y w*·Y^{S}/*y*$^{+}$·Y^{L} males. The exceptional females were not-yellow, vermilion, Bar. The exceptional males were yellow, white. In the second experiment two females and several white males were the parents of each individual culture. The exceptional females were matroclinous, and therefore were yellow, vermilion, Bar. The exceptional males were white. In Experiment 3 the genotypes of the parents were the same as in Experiment 1 but only one female and two males were placed in each culture.

Table 3 contains the results with *sc^{S1-8}*, dl-49 and the four autosomal genotypes. Females heterozygous for the sex-linked inversions but with homozygous autosomes produced ten female and 20 male exceptions among 8617 progeny. When the *P* females contained Curly in addition to their sex-linked genotype, there were 77 female and 67 male exceptions among 3878 total progeny. When Payne was present these females produced, among 5708 offspring, 125 and 129 female and male exceptions, respectively. The exceptions produced with this sex-linked genotype and one autosomal inversion have a 1:1 sex ratio similar to the earlier reported results by STURTEVANT (MORGAN and STURTEVANT 1944) and by COOPER, ZIMMERING and KRIVSHENKO (1955).

TABLE 3

Exceptional offspring from Ins(1)sc^{S1-8}, *dl-49. Females with four autosomal genotypes*

Genotype of females				Exceptions Females	Percent	Males	Percent	Expected Females	Males	Total
y^2 *B v* w^a* / y^2 *cv v f*	+ / +	+ / +	Expt. 1	5		11		2383	2048	4447
			Expt. 2	2		2		777	617	1398
			Expt. 3	3		7		1434	1328	2772
				10	.12	20	.23	4594	3993	8617
y^2 *B v* w^a / y^2 *cv v f*	*Cy* / +	+ / +	Expt. 2	17		15		646	518	1196
			Expt. 3	60		52		1376	1194	2682
				77	1.99	67	1.73	2022	1712	3878
y^2 *B v* w^a / y^2 *cv v f*	+ / +	*P* / +	Expt. 2	33		30		640	542	1245
			Expt. 3	92		99		2155	2117	4463
				125	2.19	129	2.26	2795	2659	5708
y^2 *B v* w^a / y^2 *cv v f*	*Cy* / +	*P* / +	Expt. 1	4		53		1876	1610	3543
			Expt. 2	0		23		905	643	1571
			Expt. 3	1		21		1219	1232	2473
				5	.07	97	1.28	4000	3485	7587

* One exceptional female was presumed to be an equational exception. Unfortunately no progeny test was carried out. Its phenotype was not-yellow w^a v^2 *f*.

Females heterozygous for the sc^{S1-8}, dl-49 inversion chromosome and in addition heterozygous for Curly and Payne inversions produced five exceptional females and 97 exceptional males among 7587 total. These results are of the same nature as those obtained with the other sex-linked inversions. There was a low frequency of female exceptions and a great equality of the sex ratio of the exceptional offspring when the P female carried inversions in both autosomes. These results have been obtained with three different sex-linked inversions.

DISCUSSION

The increase in the frequency of primary nondisjunction associated with the addition of an autosomal inversion to a genotype containing heterozygous sex-linked inversions can be explained with the assumption of nonhomologous pairing between that autosome and an X chromosome after the hypothesis suggested by COOPER *et al.* (1955). The results with two heterozygous autosomal inversions and heterozygous *Ins(1)*dl-49 B^{M1}, which COOPER, ZIMMERING and KRIVSHENKO list among their data, do not coincide with the results found with the several sex-linked inversions used in the present study. They report a high number of exceptions (141 female and 161 male exceptions among 2518 offspring) in contrast to the low values reported herein.

There was the possibility that the different sex-linked inversions might account for the differences. In order to test this possibility a limited cross was carried out with *Ins(1)*dl-49 B^{M1} / + and heterozygous inversions in the second and third chromosomes. The autosomal inversions were *In(2L + 2R)Cy* and *In(3LR)* Ubx^{130} (Ultrabithorax^{130}). There were three exceptional males and no exceptional

females among the 625 progeny. This value is similar to that reported in the major part of the data of the present work. It can be assumed the differences in sex-linked inversions did not cause the high nondisjunction.

The two autosomal inversions that COOPER, ZIMMERING and KRIVSHENKO employed were heterozygous for a translocation. Accordingly crosses with *Ins(1)*dl-49 B^{M1} and an autosomal inversion translocation heterozygote were carried out. The females were *In(1)*dl-49 B^{M1} / + *In(2L + 2R)Cy* / T(2;3)*Xa* (Xasta). There were 122 exceptional females and 117 exceptional males in a total of 1416 progeny. The percent of nondisjunction with allowances for genotypes which do not survive, was 28.9 (These experiments have been reported elsewhere, see FORBES 1960.) Thus it is likely that the translocation was responsible for the high frequency of nondisjunction reported by COOPER, ZIMMERING and KRIVSHENKO (1955). COOPER (personal communication) has also found combinations of autosomal inversions which have low frequencies for primary nondisjunction.

There yet remains the necessity of an explanation for the low frequencies of primary nondisjunction when all the major chromosome pairs are heterozygous for inversions. Possibly the simplest mechanism to bring out such results would be the existence of nonhomologous chromosome pairing between second and third chromosomes heterozygous for inversions. Such associations and subsequent segregation would not lead to X chromosome nondisjunction. If the unpaired second chromosome would pair with an unpaired third rather than with an X chromosome such a result would likely result. Further research is necessary on this item.

A distinction should be made between the origins of male and female exceptions. In certain crosses male exceptions are significantly in excess of female exceptions. The origins of exceptional females and males are not the same. All exceptional females come from eggs whose pronuclei received two X chromosomes whereas the exceptional males arise as a consequence of one or the other of two different processes. One of these mechanisms, nondisjunction of the sex chromosomes, will result in pronuclei without any X chromosomes and therefore will lead to the production of patroclinous males. The other mechanism leading to the production of no-X eggs and possible patroclinous males is four-strand double crossing-over within heterozygous inversions. In view of the twofold origin of exceptional males, the frequency of exceptional females is a more reliable index of nondisjunction.

With inversions not involving the entire X chromosome, such as *In(1)*dl-49, there may be another way in which patroclinous males can arise. Second anaphase bridges may result from certain three-strand double crossovers when one crossover takes place within the heterozygous inversion and a second occurs between the limits of the inversions and the centromere. If second anaphase bridges were to result in no-X eggs, then patroclinous males might result from crossing-over with only one crossover actually within the inversion. Additional research will be necessary to clarify this possibility.

The frequencies of female exceptions differ considerably between the different sex-linked inversions when one autosomal inversion is present. These can be arranged in order from the highest to the lowest frequency of female exceptions.

The sequence is sc^{s1-s}, dl-49, next dl-49, and then sc^{s}. These same inversions show an inverse relationship in the production of patroclinous males in excess of matroclinous females. The inversion, sc^{s}, associated with the highest excess of male over female exceptions, has the lowest frequency of female exceptions. The sc^{s1-s}, dl-49 inversions have no significant excess of male over female exceptions and the highest frequency of female exceptions. The results with *In(1)*dl-49 are intermediate. If the excess frequency of patroclinous males indicates the frequency of four-strand double crossing-over and the frequency of crossing-over in general, and if the frequency of exceptional females is indicative of the nondisjunction frequency; then the negative correlation may be stated as being between crossing-over and nondisjunction. It is likely that the two variables are dependent upon a third factor, namely, structural heterozygosity of the X chromosomes concerned.

No evidence for a difference in the frequency of primary nondisjunction (i.e. female exceptions) was found for the Curly or Payne inversions. For males there were significantly more exceptions with *In(1)*dl-49 and *In(1)*sc^{s} with Payne than with Curly. For sc^{s1-s}, dl-49 there were more exceptional males with Payne than with Curly, but the difference was not significant.

SUMMARY

The frequencies of primary nondisjunction have been studied in females of *Drosophila melanogaster* heterozygous for one or the other of several sex-linked inversions and also heterozygous for autosomal inversions.

Nondisjunction of structurally heterozygous X chromosomes was increased by the presence of one heterozygous autosomal inversion. The amount of the increase was found to be dependent upon the particular X chromosome inversion employed. The frequencies of nondisjunction with one autosomal inversion were highest with the sex-linked inversion sc^{s1-s}, dl-49, intermediate with *In(1)*dl-49, and lowest with *In(1)*sc^{s}. Male exceptions in excess of female were most frequent with *In(1)*sc^{s}, intermediate with *In(1)*dl-49, and absent with *Ins(1)*sc^{s1-s}dl-49. The excesses of exceptional males are believed to have resulted from four-strand double crossing-over within the heterozygous inversions.

When both major autosomes were heterozygous for inversions, the frequencies of nondisjunction were much lower than in the corresponding experiments with only one autosomal inversion. The number of female exceptions was lower, but not significantly so, than in the controls without autosomal inversions. With two autosomal inversions, all sex-linked inversions tested produced many times more male than female exceptions.

The observed results are in accord with the assumption of nonhomologous pairing leading to primary nondisjunction provided additional assumptions are made. Nonhomologous chromosome pairing would be assumed to occur between autosomes rather than X chromosomes and autosomes when all the major chromosomes are heterozygous for inversions.

ACKNOWLEDGMENT

The author wishes to thank DR. CURT STERN for guidance and advice during the research and in the preparation of the manuscript.

LITERATURE CITED

BRIDGES, C. B., 1913 Non-disjunction of the sex chromosomes of Drosophila. J. Exptl. Zool. **15**: 587–606.

1916 Non-disjunction as proof of the chromosome theory of heredity. Genetics **1**: 1–52, 107–163.

BRIDGES, C. B., and K. S. BREHME, 1944 *The Mutants of Drosophila melanogaster*. Carnegie Inst. Wash. Publ. **552**.

COOPER, K. W., S. ZIMMERING, and J. KRIVSHENKO, 1955 Interchromosomal effects and segregation. Proc. Natl. Acad. Sci. U.S. **41**: 911–914.

FORBES, C., 1960 Nonrandom assortment in primary nondisjunction in *Drosophila melanogaster*. Proc. Natl. Acad. Sci. U.S. **46**: 222–225.

GRELL, R. F., 1957 Non random assortment of non-homologous chromosomes. Genetics **42**: 374.

1959 Non random assortment of non-homologous chromosomes in *Drosophila melanogaster*. Genetics **44**: 421–435.

MORGAN. T. H., and A. H. STURTEVANT, 1944 Maintenance of a Drosophila stock center, in connection with investigations on the constitution of the germinal material in relation to heredity. Carnegie Inst. Wash. Yearbook **43**: 164–165.

OKSALA, T., 1958 Chromosome pairing, crossing over and segregation in meiosis in *Drosophila melanogaster* females. Cold Spring Harbor Symp. Quant. Biol. **23**: 197–210.

REDFIELD, H., 1957 Egg mortality and interchromosomal effects on recombination. Genetics **42**: 712–728.

SANDLER, L., and G. BRAVER, 1954 The meiotic loss of unpaired chromosomes in *Drosophila melanogaster*. Genetics **39**: 365–377.

SANDLER, L., and E. NOVITSKI, 1956 Evidence for a genetic homology between chromosomes I and IV in *Drosophila melanogaster* with a proposed explanation for the crowding effect in triploids. Genetics **41**: 189–193.

STEINBERG, A. G., 1936 The effect of inversions in the autosomes on crossing over in the X chromosome of *Drosophila melanogaster*. Genetics **21**: 615–624.

STURTEVANT, A. H., and G. W. BEADLE, 1936 The relations of inversions in the X chromosome of *Drosophila melanogaster* to crossing over and disjunction. Genetics **21**: 554–604.

1939 *An Introduction to Genetics*. W. B. Saunders, Philadelphia and London.

ZIMMERING, S., 1958 A simultaneous measure of interchromosomal effects on autosomal crossing over and sex chromosome nondisjunction in Drosophila. Genetics **43**: 354–361.