SEX CHROMOSOME MEIOTIC DRIVE IN *DROSOPHILA MELANOGASTER* MALES

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Manuscript received December 14, 1982
Revised copy accepted November 10, 1983

ABSTRACT

In *Drosophila melanogaster* males, deficiency for *X* heterochromatin causes high *X-Y* nondisjunction and skewed sex chromosome segregation ratios (meiotic drive). *Y* and *XY* classes are recovered poorly because of sperm dysfunction. In this study it was found that *X* heterochromatic deficiencies disrupt recovery not only of the *Y* chromosome but also of the *X* and autosomes, that both heterochromatic and euchromatic regions of chromosomes are affected and that the "sensitivity" of a chromosome to meiotic drive is a function of its length. Two models to explain these results are considered. One is a competitive model that proposes that all chromosomes must compete for a scarce chromosome-binding material in Xh^- males. The failure to observe competitive interactions among chromosome recovery probabilities rules out this model. The second is a pairing model which holds that normal spermiogenesis requires *X-Y* pairing at special heterochromatic pairing sites. Unsaturated pairing sites become gametic lethals. This model fails to account for autosomal sensitivity to meiotic drive. It is also contradicted by evidence that saturation of *Y*-pairing sites fails to suppress meiotic drive in Xh^- males and that extra *X*-pairing sites in an otherwise normal male do not induce drive. It is argued that meiotic drive results from separation of *X* euchromatin from *X* heterochromatin.

IN *Drosophila melanogaster* males, deficiency for the proximal, heterochromatic portion of the *X* chromosome causes meiotic *X-Y* nondisjunction and distorted sex chromosome recovery ratios. Four classes of sperm—*X*, *Y*, *XY*, and nullo-*XY*—are produced, but reciprocal meiotic products are not recovered equally. More *X* than *Y* and far more nullo-*XY* than *XY* sperm are recovered (GERSHENSON 1933; SANDLER and BRAVER 1954). Cytological analysis reveals frequent pairing failure at metaphase I and nondisjunction at anaphase I. Reciprocal meiotic products are equally frequent at the secondary spermatocyte stage, so there is no chromosome loss at meiosis I (PEACOCK 1965). The absence of micronuclei implies that chromosomes are not lost in later stages either (R. W. HARDY, unpublished observations). Electron microscopy reveals abnormalities in spermiogenesis, the most common being a failure of individualization of syncytial spermatids (PEACOCK, MIKLOS and GOODCHILD 1975).

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The implication is that the distorted segregation ratios result from preferential breakdown or dysfunction of *Y* and *XY* sperm. Note that it is the normal chromosome, the *Y*, that is recovered poorly. The term "meiotic drive" is frequently used to describe cases in which an altered gene or chromosome results in meiotic or gametic elimination of the homolog (SANDLER and NOVITSKI 1957; ZIMMERING, SANDLER and NICOLLETTI 1970).

Other examples of sex chromosome meiotic drive involving sperm dysfunction in Drosophila are known. Sperm dysfunction was first invoked to explain the meiotic behavior of *X* chromosomes deficient for the euchromatin. In males carrying one of these heterochromatic "free *X* duplications" and an attached-*XY* chromosome, no chromosome loss occurs, but the free duplication is recovered in more than 50% of the progeny (LINDSLEY and SANDLER 1958). Selective sperm elimination also occurs in males carrying a translocation ($T(1;4)B^S$) between the *X* and the tiny fourth chromosome. Disjunction is regular in these males (*Y* from X^P4^D and 4^PX^D from *4*), but the longer member of each bivalent (the *Y* and 4^PX^D) is recovered poorly (NOVITSKI and SANDLER 1957).

In all three cases—*X* heterochromatically deficient (Xh^-) males, $T(1;4)B^S$ males and attached-*XY*/*Dp* males—it is the longer member of an homologous pair that is recovered poorly. A plausible explanation for these inequalities is that the severity of selection against sperm in a meiotic drive genotype is proportional to the amount of sex chromatin (or all chromatin) in the sperm. In each of these cases, the most chromatin-rich sperm suffer the strongest selection; the other classes are presumably selected against as well but not as strongly because they contain less chromatin.

An alternative explanation (suggested by BAKER and CARPENTER 1972) is that each susceptible chromosome carries one or more discrete "response genes" that cause sperm death when acted on by a meiotic drive genotype. This would be analogous to the Segregation distorter (*SD*) system in which *SD*/+ males undergo selective elimination of sperm carrying the wild-type homolog. Sensitivity in the *SD* system is encoded by a single heterochromatic region called Responder (*Rsp*) (SANDLER and CARPENTER 1972; HARTL and HIRAIZUMI 1976). Perhaps the *Y* carries a responder-like gene that makes it sensitive to sex chromosome meiotic drive. These hypotheses are susceptible to experimental test as they make different predictions about the segregation of drive sensitivity in a variety of rearranged genotypes. Several experiments designed to characterize drive sensitivity and test the two hypotheses are described.

Another question concerns the role of pairing sites or "collochores" which are found at several sites in *X* heterochromatin and on both arms of the *Y* chromosome (COOPER 1964). These collochores function as *X-Y* attachment sites during first meiosis. In the absence of most of the *X* heterochromatin, pairing occurs irregularly, causing frequent nondisjunction. Several investigators have suggested that decreased *X-Y* pairing is also responsible for meiotic drive (BAKER and CARPENTER 1972; PEACOCK and MIKLOS 1973). The reason for this suggestion is the high correlation between the frequency of nondisjunction and the severity of meiotic drive. Changes in the temperature at which

Xh^- males are raised (ZIMMERING 1963) or in the genetic background (PEACOCK and MIKLOS 1973) produce correlated changes in nondisjunction and drive. EMS-induced *X*-linked meiotic mutants that cause elevated *X-Y* nondisjunction invariably cause distorted recovery ratios as well. As with the Xh^- males, the degree of distortion is correlated with the frequency of nondisjunction (BAKER and CARPENTER 1972). PEACOCK and MIKLOS (1973) suggested that the pairing sites of the *X* and *Y* chromosomes act as gametic lethals if they do not interact with their homologous counterparts during meiosis. This hypothesis accounts for the depressed *Y*:*X* ratio because the pairing site shortage on the deleted *X* would leave excess, unreacted sites on the *Y* even when pairing occurs. It would also explain the very poor recovery of *XY* sperm because they come from spermatocytes in which pairing fails altogether. Two experiments designed to test the importance of "saturation" of *X-Y*-pairing sites are described.

MATERIALS AND METHODS

Chromosomes: The chromosomes used in this study are all described by LINDSLEY and GRELL (1968). Brief descriptions are included here to facilitate reading the paper.

$Xh^- = In(1)sc^{4L}sc^{8R}$: an *X* chromosome deficient for approximately 90% of the heterochromatin. It is a product of recombination between $In(1)sc^4$ and $In(1)sc^8$. It is marked with *y* and w^a and is deficient for *bb*.

$In(1)sc^{8L}sc^{4R}$: an *X* chromosome duplicated for approximately 90% of the basal heterochromatin. It is the reciprocal product of recombination between $In(1)sc^4$ and $In(1)sc^8$. This chromosome is also deficient for scute, an essential gene near the tip of the *X* and is, therefore, inviable in males unless they carry a scute duplication. It is marked with y^{31d}.

$In(1)sc^{51L}sc^{4R}$: another heterochromatically duplicated *X* derived by recombination. It is not deficient for any essential loci. It is marked with y^{c4}.

Dp(1;f)3: a free *X* duplication consisting of all of the heterochromatin and a few euchromatic bands from the tip and from the proximal region. It was derived as an *X-ray*-induced deletion of most of the *X* euchromatin. It is marked with y^+ and is bb^+.

Dp(1;f)1144 and *Dp(1;f)165*: two very small free *X* duplications (about the size of chromosome *4*) consisting of an *X* centromere and tip and a small piece of centromeric heterochromatin. Both are marked with y^+ and are bb^-.

B^SY: a *Y* chromosome marked with the B^S (Bar-Stone) duplication.

$Y^Lbb^+ = Y^Ly^{3M}$: derived from an exchange between the base of the short arm of the *Y* and the heterochromatic tip of $In(1)sc^{51}$. It is marked with y^{3M}.

$Y^Lbb^- = Y^Ly^+B2$: derived from a similar exchange between the short arm of the *Y* and $In(1)sc^8$ that must have been distal to Xbb^+ and proximal to Ybb^+. It is marked with y^+.

Y^S and $Y^S.Y^S$: spontaneous *Y* fragments consisting of one and two, respectively, short arms of the *Y*. Both are bb^+ but are otherwise unmarked.

$T(2;3)bw^{V4}$: A dominant brown-variegated translocation broken in *3L* in the heterochromatin and at the tip of *2R* near brown. The result is that the entire left arm of the third chromosome is moved to the tip of *2R*.

Dp(2;f)f29: A free duplication consisting of a substantial portion of second chromosome heterochromatin and very little euchromatin. It is marked with y^+ from the *X*. It was constructed and kindly supplied by J. BRITTNACHER.

Crosses: Crosses were made in vials on medium containing cornmeal, molasses, yeast, carrageenin and propionic acid. Each vial contained one male and one or two females. Crosses were incubated at 25°. Parents were transferred to fresh food on day 5 and discarded on day 12. Progeny were counted on days 12, 15, 17, 20 and 22. Fertility tests were made by crossing single males with two or three virgin females in vials.

Data analysis: Since the purpose of most of the crosses is to measure the effect of the presence of particular chromosomes on sperm viability in drive genotypes, the most generally useful parameter is the recovery probability (R) of a chromosome. It is defined as the probability of survival of a sperm as a consequence of carrying the chromosome. For example, if X-bearing sperm survive 75% as well as otherwise identical non-X sperm, then $R_X = 0.75$. The formulas for calculating Rs depend upon the cross and will be detailed at the appropriate places in RESULTS. In some crosses, the data supply more than one independent estimate of R. In those cases, the method of maximum likelihood is used to estimate R. For each R value, a 95% confidence interval was calculated by minimum χ^2 iteration.

RESULTS

Sensitivity to meiotic drive

Y *sensitivity*: If the poor recovery of the Y chromosome in Xh^- males is due to a unique Y response locus, it must map to one or the other arm of the submetacentric Y chromosome. When the two arms are attached to separate centromeres, sensitivity should segregate with one of them. To determine which arm, males carrying the Y fragments Y^S and Y^L were crossed to normal females (Table 1, lines 1 and 2). Two different Y^L chromosomes were tested, one with (Y^Lbb^+) and one without (Y^Lbb^-) the *rDNA* which is located at the base of Y^S adjacent to the centromere. Since these Y fragments all have a Y centromere, a sensitivity locus near the centromere on either side might be expected to segregate with all of the fragments. In both crosses, Y^S and Y^L segregate regularly from each other as can be seen from the absence of Xh^- and Y^SY^L progeny. The relative recovery of Y^L and Y^S in lines 1 and 2 provides information on the location of the putative response gene. In both experiments, the recovery of Y^L is depressed relative to Y^S, implying that Y^L is more sensitive than Y^S. The recovery depression in line 1 is not due to zygotic lethality of the Y^L chromosome. In a cross involving normal $X/Y^S/Y^L$ males, Y^Lbb^+ was recovered in 2390 of 4842 progeny.

Chromosome recoveries can be compared by means of the parameter R, defined as the viability ratio of otherwise identical sperm with and without the chromosome in question. For crosses 1 and 2, Table 1, there are three R values: R_{YL}, R_{YS} and R_X. One segregation parameter—P, the probability of Xh^- segregating to the Y^s pole—is also required. The relative probabilities of recovering XY^L, XY^S, Y^L and Y^S sperm, respectively, are $1/2(1 - P)R_{YL}R_X$, $1/2PR_{YS}R_X$, $1/2PR_{YL}$ and $1/2(1 - P)R_{YS}$. This model assumes that each chromosome affects sperm viability independently so that recovery probabilities can be multiplied. This assumption is tested and confirmed. If the numbers in each class are A, B, C and D, respectively, then $P = \sqrt{BC/AD}/(1 + \sqrt{BC/AD})$, $R_X = \sqrt{AB/CD}$ and $R_{YL}/R_{YS} = \sqrt{AC/BD}$. Note that the crosses permit calculation of R_X because otherwise identical sperm with and without Xh^- are generated. However, R_{YL} and R_{YS} cannot be calculated because all non-Y^L sperm carry Y^S and vice versa. The data permit only an estimate of the ratio of R_{YL} to R_{YS}. This ratio is 0.442 in line 1 indicating that Y^L is recovered less than half as well as Y^S. The magnitude of the discrepancy is less in line 2 but still significantly different from 1. This result implies that, if a single Y response locus exists, it must be on the long arm. However, the result could also be explained

TABLE 1

Recovery of Y *chromosome fragments from* Xh^- *males*

Experiment No.	Paternal genotype	Sperm genotype								P	R_{Y1}/R_{Y2}	R_X
		X	XY	XL^L	XY^S	Y	Y^L	Y^S	Y^SY^L			
1	$Xh^-/Y^Lbb^+/Y^S$	0		699	1703		1698	3560	0[a]	0.519	0.442 (±0.022)	0.444 (±0.022)
	$Xh^-/Y^Lbb^-/Y^S$	0		1320	1851		1961	2818	0	0.499	0.704 (±0.031)	0.665 (±0.030)
2	$Xh^-/B^SY/Y^Lbb^+$	0	51	73		121	145			0.522	0.764 (±0.158)	0.461 (±0.100)
	$Xh^-/B^SY/Y^S$	0	103		553	319		1396		0.525	0.206 (±0.023)	0.358 (±0.034)
	$Xh^-/Y^Lbb^+/Y^S$	0		236	611		592	1423		0.509	0.401 (±0.033)	0.414 (±0.034)
3	$Xh^-/Y^Lbb^+/Y^S$	0		423	1092		1106	2137		0.536	0.448 (±0.029)	0.442 (±0.028)
	$Xh^-/Y^Lbb^+/Y^S.Y^S$	0		592	1008		1582	2561		0.506	0.602 (±0.032)	0.384 (±0.022)

Males of the indicated genotypes were crossed to *y w bb* females. The males in experiment 2 were derived as brothers. Those in experiments 1 and 3 were half-brothers. R_{Y1}/R_{Y2} is the ratio of the recovery probability of the larger *Y* chromosome divided by that of the smaller. Thus, in lines 1, 2, 5, 6 and 7, it is R_{YL}/R_{YS}. In line 3, it is R_Y/R_{YL}, and in line 4 it is R_Y/R_{YS}.

[a] One hundred and twenty-eight white male progeny were tested for fertility. All were sterile.

by postulating that all Y chromatin is sensitive to Xh^- induced drive, the degree of sensitivity being a function of length.

To decide between these alternatives, it is necessary to know whether the short arm is sensitive at all. Two experiments designed to measure short arm sensitivity were carried out. In the first, males of the genotypes $Xh^-/Y^L/Y^S$, $Xh^-/B^SY/Y^S$ and $Xh^-/B^SY/Y^L$ were generated as brothers from a cross of $Xh^-/Xh^-/B^SY$ females by $y\ w/Y^S/Y^L$ males and were crossed to chromosomally normal $y\ w\ bb$ females. $Xh^-/B^SY/Y^S$ males were distinguished from their rare Xh^-/B^SY brothers by screening their progeny for the bobbed phenotype. The non-Bar offspring of the former males are bb^+, whereas those of the latter males are bb. If Y^L carries a specific response locus, then the recovery ratio of an intact Y to Y^L should be 1:1. The additional short arm material in the intact Y should not contribute to its sensitivity. The recovery of B^SY relative to Y^Lbb^+ is 0.764, which is significantly different from 1 (line 3). In this cross, as in all others in Table 1, P is defined as the probability of Xh^- segregating with the smaller element (in this case, Y^L). Lines 4 and 5 of Table 1 permit an indirect comparison of Y^L and Y as each is compared to a common standard (Y^S). Again, the Y appears considerably more sensitive than Y^L as $R_Y/R_{YS} = 0.206$ and $R_{YL}/R_{YS} = 0.401$. The depressed recovery of B^SY in these experiments is not a consequence of zygotic inviability. When $y\ pn/y\ pn/B^SY$ females were crossed to Xh^-, $y\ w^a/y^+Y$ males, 2127 y daughters (XX), 2187 $y\ B$ daughters (XXY), 755 ypn sons (XO) and 748 $y\ pn\ B$ sons (XY) were recovered.

The second experiment compares recovery of Y^S with $Y^S.Y^S$, a chromosome duplicated for the short arm. If the short arm lacks sensitivity, then there should be no difference between these chromosomes. $Xh^-/Y^L/Y^S.Y^S$ and $Xh^-/Y^L/Y^S$ males were generated as half-brothers and were crossed to normal females. The R_{YL}/R_{YS} ratio is 0.448 (Table 1, line 6), whereas the $R_{YL}/R_{YS.YS}$ ratio is 0.602 (Table 1, line 7). These results are significantly different and imply that short arm material is sensitive to Xh^- induced meiotic drive. Thus, there is no single Y response locus. Either all Y chromatin is sensitive to drive, the degree of sensitivity being a function of length, or there are several discrete, dispersed response loci. The results do not permit a decision between the two alternatives.

X *chromosome sensitivity*: Is Y chromatin unique in its sensitivity to Xh^- induced drive? Or is the X also affected? The crosses in Table 1 also supply an answer to this question. In each cross, the two Y chromosomes disjoin regularly from each other. The result is production of otherwise identical sperm classes with and without the X. If the X is insensitive to its own recovery disruption, the X and non-X classes should be recovered in equal frequencies. This is not the case. Xh^- recovery ranges from 0.384 to 0.665, in all cases significantly different from one. X recovery is seriously disrupted by the presence of the heterochromatic deficiency. This recovery depression cannot be due to dominant zygotic lethality. In a cross of $Xh^-/In(1)\Delta 49$ females to $y\ w/B^SY$ males, Xh^- was recovered in 269 of 518 B^+ daughters.

A similar deficiency of females was reported for $Xh^-/Y/Y$ males by SANDLER and BRAVER (1954). COOPER'S (1964) cytological analysis of these males re-

vealed that the two *Y*s pair regularly and Xh^- is always a univalent at first meiosis. Yet, half of the secondary spermatocytes carry Xh^-, which indicates that meiotic loss is not occurring. The implication is that *X* sperm are eliminated more frequently than otherwise identical non-*X* sperm.

For the crosses in Table 1, it is possible to test for independence of R_X and R_{Y1}/R_{Y2}. To do so, we must assume random *X* disjunction ($P = 0.5$). Since $P = \sqrt{BC/AD}/(1 + \sqrt{BC/AD})$, we have $0.5 + 0.5\sqrt{BC/AD} = \sqrt{BC/AD}$ or $\sqrt{BC/AD} = 1$. This implies that $BC = AD$. If a 2×2 table is constructed with Y^L and Y^S on one axis and Xh^- and *O* on the other it will be seen that *BC* and *AD* are cross products. To test for equality of cross products, contingency tests were performed on the seven crosses in Table 1. Five of the 7 generated nonsignificant χ^2 values (1 d.f.). This implies not only that Xh^- disjoins randomly in those five crosses, but also that each chromosome affects sperm viability independently, since independence was assumed in calculating the expected values. This observtion agrees with that of NOVITSKI and SANDLER (1957) who found that chromosome recovery probabilities could be multiplied to obtain sperm viabilities in the $T(1;4)B^S$ system. In the two exceptional cases (lines 1 and 6) the observed numbers are significantly different from the expected values with *P* set to 0.5. This means either that Xh^- shows a weak tendency to segregate to the Y^S pole ($P_1 = 0.519$ and $P_6 = 0.536$) or that Xh^- and Y^L interact slightly in their effects on viability. There is no way to tell which assumption is violated. In either case, this is a minor effect and has no bearing on the issue of chromosomal sensitivity to drive. If *R* values are calculated on the assumption of random Xh^- disjunction, they come out only trivially different from the reported ones.

What part(s) of the *X* is sensitive? Since the Xh^- chromosome used in these studies is deficient for 90% of the heterochromatin, euchromatic sensitivity is implied. To test the sensitivity of *X* heterochromatin, males carrying Xh^-, a *Y* and a free *X* duplication that carries all of the heterochromatin but very little euchromatin, *Dp(1;f)3*, were crossed to normal females. Once again, the heterochromatic elements, the *Y* and *Dp*, disjoined regularly from each other. This is evident from the absence of *YDp* and *X* offspring in Table 2, line 2. Also, as in the crosses in Table 1, Xh^- disjoins approximately at random ($P = 0.540$) relative to the *Y* and *Dp*. Recovery of both the *Y* and Xh^- chromosomes is depressed, as shown by the low R_X (0.338) and R_Y/R_{DP} (0.260) values (see also Haemer 1978 for similar results).

The relative frequencies of *XY, XDp, Y* and *Dp* sperm (approximately 1:2:2:4) in Table 2, line 2, are what one would expect from the operation of meiotic drive on sperm classes initially equal in frequency but containing different amounts of chromatin. *XY* sperm have the most chromatin and *Dp* sperm the least with *XDp* and *Y* sperm inbetween. But are the four classes initially equal in frequency? The 1:2:2:4 frequencies could be explained by a completely different mechanism. Suppose that *XY:Dp* disjunctions are twice as frequent as *XDp:Y* disjunctions so that the initial frequencies are 2:1:1:2. If meiotic drive acts to eliminate three-fourths of the *XY* sperm but does not affect the other classes, the observed ratios would result. The two mechanisms can be easily

TABLE 2

Recovery of X *chromosomes from* Xh^- *males*

Paternal genotype	Sperm genotype								P	R_Y/R_{Dp}	R_X	R_Y	R_{Dp}
	X	*XY*	*XDp*	*XYDp*	*O*	*Y*	*Dp*	*YDp*					
Xh^-/B^sY	1113	152			1287	688			0.664		0.437 (±0.040)	0.270 (±0.025)	
$Xh^-/B^sY/Dp(1;f)3$	1	149	672	0	0	516	1694	1	0.540	0.260 (±0.024)	0.338 (±0.030)		
$Xh^-/B^sY/Dp(1;f)1144$	958	241	849	157	1120	653	1198	602					0.94 (±0.049)
$Xh^-/B^sY/Dp(1;f)164$	858	97	695	44	1215	344	1450	279					0.98 (±0.055)

Males of the indicated genotypes were crossed to *y w*/*y w* females. The males in lines 1 and 2 were derived as brothers.

distinguished by cytological analysis as they lead to very different predictions (1:1:1:1 *vs.* 2:1:1:2) about the frequencies of the four classes of secondary spermatocytes.

To this end, testes from $Xh^-/Y/Dp(1;f)3$ males were squashed in acetic orcein and examined under phase optics. Metaphase I nuclei ($n = 27$) always exhibited two autosomal bivalents, a sex bivalent and a univalent Xh^-. This agrees with the observation of COOPER (1964) who reported univalent behavior of Xh^- in $Xh^-/Y/Y$ males. Half of the secondary spermatocytes in $Xh^-/Y/Dp$ males (40 of 86) carried an *X* which shows that the unpaired *X* was not lost in the first meiosis. The four classes of secondary spermatocytes were equal in frequency (21 *XDp*, 23 *Y*, 19 *XY* and 23 *Dp*), which argues that the *X* did not segregate preferentially with the *Y* or free duplication. The numbers are small, however, and are not inconsistent with the slight disjunctional bias suggested by the genetic data. The unequal recoveries must reflect selective elimination of at least three of the four classes of sperm.

What about recovery of the free duplication? Since the *Y* and *Dp* disjoined regularly from each other, we can tell only that *Dp* recovery exceeded *Y* recovery. To tell whether the *Dp* is affected at all, we must compare the results of the $Xh^-/B^SY/Dp$ cross with those from the sibling Xh^-/B^SY controls. For the control data, *P* is defined as the probability of *X-Y* disjunction. The relative probabilities of *X*, *Y*, nullo-*XY* and *XY* sperm are, respectively, $1/2\ PR_X$, $1/2\ PR_Y$, $1/2\ (1 - P)$ and $1/2\ (1 - P)\ R_XR_Y$. If the observed numbers in each class are *A*, *B*, *C* and *D*, respectively, then $R_X = \sqrt{AD/BC}$, $R_Y = \sqrt{BD/AC}$ and $P = \sqrt{AB/CD}/(1 + \sqrt{AB/CD})$. Both R_X and R_Y can be calculated because otherwise identical sperm with and without both chromsomes are generated. Since the males in lines 1 and 2 are siblings, the differences between R_X in the two experiments (0.437 in line 1 and 0.338 in line 2) must reflect an enhancement of the level of meiotic drive by the free duplication. The same enhancement should be evident in the R_Y values. R_{Y2} cannot be measured independently of R_{Dp} in the second cross. But if we assume that $R_{DP} = 1$ (the duplication is insensitive to drive), then R_{Y2}/R_{Dp} (which can be measured) becomes R_{Y2}, and we can ask whether R_{Y2}/R_{Y1} (like R_{X2}/R_{X1}) is less than 1. It is not. R_{Y2}/R_{Y1} could be made to be less than 1 only by letting R_{Dp} be less than 1. This implies that the Dp is sensitive to drive. This argument is based on the untestable assumption that the free duplication alters only the level of meiotic drive and not the relative sensitivities of Xh^- and B^SY. The assumption is untestable because R_Y cannot be measured in the *Dp* cross. To argue that the *Dp* is insensitive to drive ($R_{Dp} = 1$), one would have to assume that it acts to increase the sensitivity of Xh^- while leaving that of the *Y* unchanged. This seems unlikely, but it cannot be strictly ruled out. The most likely interpretation of these data is that both the heterochromatin and euchromatin of the *X* are affected by meiotic drive.

An alternative explanation is that a unique *X* chromosome response function resides either in the centromeric or the telomeric region of the *X* as both Xh^- and $Dp(1;f)3$ have *X* centromeres and telomeres. To test this hypothesis, the sensitivities of two small free *X* duplications, $Dp(1;f)1144$ and $Dp(1;f)165$, were

assessed. Both chromsomes are comparable in size to the dot-like fourth chromosome and carry an *X* centromere, an *X* telomere and very little else. If a unique *X* response locus resides in either region, these chromosomes should be as sensitive as the large free duplication. However, if drive sensitivity is a function of size, both chromosomes should be nearly insensitive. The data (Table 2, lines 3 and 4) support the latter prediction. In both crosses, the small free duplication disjoins randomly from the other sex chromosomes permitting a comparison of otherwise identical sperm classes with and without the free duplication. Duplication- and nonduplication-bearing sperm were recovered approximately equally in both crosses. Thus, there cannot be a special response locus in the centromeric or telomeric regions of the *X*.

The *X* chromosome and the *Y* chromosome data are consistent with the idea that the recovery of a sperm class is inversely proportional to its sex chromatin content.

Autosomal sensitivity: Is the meiotic effect of Xh^- restricted to sex chromosomes, or are autosomes affected as well? In the crosses described, autosomal sensitivity would go undetected because the autosomal content of all sperm classes is the same. To detect an effect on autosomes it is necessary to generate sperm containing different amounts of autosomal chromatin. This has been accomplished by two different methods. One makes use of a reciprocal but asymmetric translocation between the second and third chromosomes, and the other involves a free second chromosome duplication.

T(2;3)bw^{V4} is broken in the proximal heterochromatin of *3L* and at the tip of *2R* near the brown locus. The result is that *3L* is moved to the tip of *2R*. Males or females heterozygous for this translocation and for normal homologs generate four classes of gametes: (1) normal gametes with four autosomal arms (4AN), (2) translocation gametes with four autosomal arms (4AT), (3) *2L·2R3L;3* gametes with five autosome arms (5A) and (4) *2;3R* gametes with three autosome arms (3A). Adjacent II segregations, which would produce *2;2L·2R3L* and *3;3R* gametes, do not occur in this system (GLASS 1933). When males and females heterozygous for *T(2;3)bw*^{V4} are crossed, aneuploid gametes can generate viable zygotes if they combine with reciprocal aneuploid types of the other sex.

When normal *X* males and females heterozygous for *T(2;3)bw*^{V4} are crossed, deficiency and duplication sperm classes should be recovered in equal frequencies. The females also carried the second chromosome balancer, *SM1*, to prevent unequal segregation from asymmetric dyads. Two hundred and thirteen 5A and 245 3A sperm (not significantly different from one to one) were recovered (Table 3). The 1925:952 ratio of 4AN to 4AT sperm reflects the recessive lethality of the translocation. If autosomes are unaffected by Xh^- induced drive, the results for Xh^- males should resemble the normal *X* controls. If autosomes are affected by Xh^- induced drive, then in Xh^- males, recovery of the 3A class should exceed that of the 5A class, and the ratios 4A:3A and 5A:4A should be lower than in the normal *X* control. The results, presented in Table 3, demonstrate that autosomes are sensitive to Xh^- induced drive. The 5A:3A ratio (calculated without the nullo-*XY* data because of the viability

TABLE 3

Sperm recovery frequencies from Xh^-; $T(2;3)bw^{V4}$ *males*

Paternal genotype	Sperm sex chromosome genotype	Sperm autosomal genotype				
		3A	4AN	4AT	5A	Sums
Xh^-/y^+Y	Xh^-	158 (158)	595 (604)	315 (310)	42 (37)	1110
	Xh^-/Y	14 (14)	50 (52)	27 (27)	5 (3)	96
	O	124	499	38	2	663
	Y	85 (85)	334 (323)	161 (166)	13 (20)	593
	Sums	257	979	503	60	1799
X/y^+Y	X	122	913	488	110	1633
	Y	123	1012	464	103	1702
	Sums	245	1925	952	213	3335

Xh^-/y^+Y; $T(2;3)bw^{V4}/Sb$ males and sibling X/y^+Y; $T(2;3)bw^{V4}/Sb$ controls were crossed to y/y $T(2;3)bw^{V4}/SM1$ females. For the experimental data, sums and expected values (parentheses) are calculated without the nullo-X; nullo-Y flies because of the viability problems discussed in the text.

problem discussed later) is only about one to four (60:257) in the Xh^- cross. The 5A:4A and 4A:3A ratios also change in the expected direction (decrease) in Xh^- *vs.* controls. Relative to the euploid class, Xh^- increases the viability of 3A sperm and decreases the viability of 5A sperm. This implies that in Xh^- males, the probability of recovery of a sperm is inversely proportional to its autosomal content.

The recovery probability of an autosome arm can be calculated as follows. The initial proportions of 3A, 4AN, 4AT and 5A (a, b, c and d, respectively) sperm are assumed to be the same in Xh^-/Y and X/Y males. Sperm viability in X/Y controls is assumed to be perfect. Sperm viability in Xh^-/Y is assumed to be inversely proportional to the number of autosome arms and can be expressed as 1, R_A, R_A and R_A^2 for 3A, 4AN, 4AT and 5A sperm, respectively. The contribution of sex chromosomes to sperm inviability can be neglected and the data summed across sex chromosome classes because the effect of sex chromosomes on sperm viability is the same in each autosomal class demonstrated later. a, b, c and d (the predrive frequencies) are estimated from the XY controls. The maximum likelihood estimate of R_A is 0.501. When this value is used to calculate expected numbers for the four classes, they agree closely with the real numbers (Table 3, Sums), $\chi^2 = 0.95$ with 2 d.f. The fact that a single estimate of the recovery probability of an autosomal arm fits all of the data implies that autosomal recovery probabilities are multiplicative. The effect of adding an autosome arm on sperm viability is the same whether one starts with three or four autosome arms.

Multiplicative viability effects also appear when the relationship between autosomal and sex chromosome recovery probabilities is analyzed. With the exception of the nullo-X,nullo-Y class, the frequencies of the various autosomal classes are the same in each sex chromosome genotype. For example, the same 5A:3A ratio is found in XY, X and Y sperm classes. To demonstrate this point, expected numbers in each class were calculated assuming complete independ-

ence of autosomal and sex chromosomal recovery. The calculated numbers (in parentheses in Table 3) agree closely with the real ones, implying that autosomal and sex chromosomal recovery probabilities are independent. This means that the same value of R_A (0.501) applies to *X*, *Y*, and *XY* sperm and that the same values for R_X (0.430) and R_Y (0.239) (calculated using only the 3A and 4AN data) apply to 3A, 4A and 5A sperm.

The nullo-*X*,nullo-*Y* data differ from the data for the other classes in that there is a marked deficiency in recovery of both the euploid *2L·2R3L;3R* and the aneuploid *2L·2R3L;3* sperm classes. The few flies derived from these sperm that did survive were late hatching, thin-bristled, and tended to get stuck in the food, a phenotype that suggests Minute. A plausible explanation is partial dominant lethality of the paternally transmitted *2L·2R3L* due to variegation for a Minute locus near the breakpoint. There is a strong Minute at 58D just a few bands proximal to the breakpoint. Variegation is implied by the fact that *2L·2R3L* recovery is poor only in the *XO* males and also by the fact that the *3L* breakpoint of the translocation is heterochromatic. To test this explanation, *XO* zygotes carrying a paternal *2L·2R3L* element were generated by a different route. *In(1)sc*^{4L}*sc*^{8R}*,y; T(2;3)bw*^{V4}*/SM1;+* females were crossed to *y/y*$^{+}$*Y; T(2;3)bw*^{V4}*/+;Sb* males. *X* chromosome four-strand double exchanges in the female generate nullo-*X* eggs which, when fertilized by *X* sperm, give rise to *XO* males, one-third of which should carry a paternal *2L·2R3L* chromosome. Of 55 *XO* males recovered in this cross, none carried a paternal *2L·2R3L* chromosome, whereas 31 carried a maternal *2L·2R3L* chromosome. Thus, it is the zygotic *XO* genotype, rather than the nullo-*X*,nullo-*Y* sperm genotype, that is responsible for the poor recovery. This strongly implies variegation. It is interesting that the same chromosome that shows poor recovery when transmitted from the father shows approximately normal recovery when transmitted from the mother, judging from the fact that the *XY*:*O* ratio in 3A and 4AN classes is normal (compare with Table 2, line 1). This is an apparent example of a parental source effect on variegation (discussed by SPOFFORD 1976).

Two of the nullo-*XY* classes, the 3A and 4AN classes, do not carry a paternally transmitted *2L.2R3L* chromosome and so have normal viability. It is possible to compare the recovery of these two classes to determine if they, like the other classes, obey the chromatin quantity rule and if the effect of adding an autosome arm is the same for those two classes as for the rest. The estimate of R_A for these two classes is 0.512 which is very close to the 0.501 figure obtained for the rest of the data. Thus, the effect of adding an autosome arm is the same in nullo-*XY* sperm as in *X*, *Y* or *XY* sperm. These results imply that the level of meiotic drive is the same in both disjunctional and nondisjunctional meiocytes.

The results from this experiment permit a comparison of the sensitivities of autosomes and sex chromosomes. If recovery probabilities are inversely proportional to length, then an autosome arm and an *X* should be about equally sensitive. They are: $R_X = 0.430 \pm 0.057$ and $R_A = 0.501 \pm 0.045$. Since the *X* is missing most of the heterochromatin, we might expect it to be slightly

less sensitive than an autosome arm. However, the autosome arm is not full length either. The experiment actually measures the sensitivity of *3L* from a break somewhere in the heterochromatin to the tip minus the tip of *2R*. This might well be considerably smaller than a full autosome arm. The *Y* chromosome, which is approximately the same size as a normal *X*, turns out to be somewhat more sensitive than either Xh^- or the partly deficient autosome arm. This is consistent with the fact that the *Y* is not deficient for anything and is in fact duplicated for part of the *X*. Thus, the data are approximately consistent with the inverse chromatin quantity rule.

This experiment tests the effect of deficiency for *X* heterochromatin on recovery of a whole autosomal arm (*3L*) including euchromatin and some heterochromatin. What effect does Xh^- have on autosomal heterochromatin alone? To answer this question, use was made of a free second chromosome duplication [*Dp(2;f)f29*] consisting of most of the second chromosome heterochromatin but very little euchromatin (J. BRITTNACHER, personal communication). Males carrying this free duplication in addition to two normal second chromosomes and either Xh^- or a normal *X* were crossed to normal females. Recovery of the free duplication is depressed in the Xh^- cross relative to the control (Table 4). Sperm carrying the free duplication are recovered 83% (±5.7%) as well as non-*Dp* sperm. From the translocation cross, it was found that sperm carrying an additional autosome arm were recovered only 50% (±4.5%) as well as sperm without it. These results are consistent with the idea that the effect of a chromosome on sperm viability is proportional to length. The euchromatic-heterochromatic content of a chromosome does not seem to matter.

Possible mechanisms

Material shortage: The demonstration that the probability of recovery of a sperm class from an Xh^- male is inversely proportional to its chromatin content suggests that chromosomes may be competing for a scarce resource. Suppose that an *X* heterochromatic locus is involved in production or distribution of an essential chromosome-processing material and that deficiency for that locus leads to a shortage of the material. Suppose further that binding sites for the material are equally spaced along a chromosome and that all sites must be occupied for a chromosome to be fit for spermiogenesis. Under shortage conditions, some chromosomes would garner enough of the material and some would not. Those that do not would become sperm lethals. The longer a chromosome, the lower the likelihood of garnering enough of the material and the higher the likelihood of becoming a sperm lethal. The more chromatin a sperm carries, the less likely it is to be free of a lethal chromosome.

This model has at least two testable consequences. One is that chromosome recoveries should be nonindependent whether binding occurs before or after anaphase I. If binding occurs before anaphase I, chromosomes compete directly. In the small fraction of spermatocytes in which the *2L.2R3L* and *3L.3R* chromosomes garner enough, less remains for the sex chromosomes than in the other spermatocytes. So, although the sex chromosomes assort independ-

TABLE 4

Recovery of Dp(2;f)f29 *from* Xh$^-$ *males*

Paternal genotype	*Dp*	non-*Dp*	R_{Dp}
Xh$^-$*/Y; +/+/Dp(2;f)f29*	1313	1803	0.831 (±0.057)
X/Y; +/+/Dp(2;f)f29	975	1113	

Males of the indicated genotypes were crossed to *y w/y w* females.

ently of the autosomes, recovered 5A sperm will be less likely to carry an *X* or a *Y* than will non-5A sperm. If binding occurs after anaphase I, direct competition is reduced, but a threshold effect should be in evidence. Sperm classes with chromatin quantities greater than the threshold should have very poor viability, and those with chromatin quantities less than the threshold should have good viability. The viability differences would be greater than predicted under the independence model. The second prediction is that addition of extra chromatin to the genome should exacerbate the shortage and lead to higher drive levels.

The first prediction can be tested in experiments that monitor recovery of both sex chromosomes and autosomes. In males of genotype *Xh*$^-$*/Y;T(2;3)bw*^{V4}*/Sb*, sex chromosome recovery ratios should depend on autosomal genotype and vice versa. This is not the case. As noted before, autosomal and sex chromosome recovery probabilities are independent.

An experiment that tests the second prediction has already been described. Males of the genotypes *Xh*$^-$*/Y*^{S}*/Y*^{L}, *Xh*$^-$*/Y*^{S}*/Y*, and *Xh*$^-$*/Y*^{L}*/Y* (ranging from least to most chromatin) were generated as brothers and crossed to normal females. The severity of drive can be gauged by comparing recovery of the independently assorting *X* in the three genotypes (Table 1). *Y* recovery ratios are uninformative because they are dependent on length of *Y* fragments. *X* recovery is the same in all three experiments. This suggests that the degree of meiotic drive does not depend on the amount of material in the genome.

In a second test of the same idea, sibling males of the genotypes *Xh*$^-$*/Y/Dp(1;f)3* and *Xh*$^-$*/Y/Y* were crossed to normal females. A *Y* chromosome is considerably longer than *Dp(1;f)3* so these two genotypes differ substantially in chromatin content. The results in Table 5 indicate that they do not differ in drive level. In two replicates, *X* chromosome recovery is the same in all crosses (except in one case in which the difference is in the wrong direction).

In a third test of this idea, males with four sex chromosomes (*Xh*$^-$*/Y/Y*^{S}*/Dp(1;f)3*) were compared to their siblings with three sex chromosomes (*Xh*$^-$*/Y*^{S}*/Y* and *Xh*$^-$*/Y/Dp(1;f)3*, Table 6). *X* recovery is compared by means of the sex ratio (females to males) instead of R_X because not all of the progeny classes are distinguishable in the four-sex chromosome cross, preventing calculation of R_X. The ratio of females to males does not differ in pairwise contingency tests between the four-sex chromosome cross and each of the controls. Thus, the amount of sex chromatin in a genotype does not affect the level of meiotic drive.

TABLE 5

Comparison of sibling $Xh^-/Y/Y$ and $Xh^-/Y/Dp$ *males* × *y w bb females*

Experiment	Paternal genotype	Sperm classes							Recovery ratios		
		XB^SY	XY	XDp	B^SY	Y	Dp	P	R_{Y1}/R_{Y2}	R_Y/R_{Dp}	R_X
1	$Xh^-/Y/B^SY$	117	115		260	188		0.538	1.19 (±0.147)		0.525 (±0.082)
	$Xh^-/Y/Dp(1;f)3$		499	1377		1360	2474	0.552		0.446 (±0.027)	0.452 (±0.027)
2	$Xh^-/Y/B^SY$	210	262		447	661		0.479	0.736 (±0.071)		0.432 (±0.046)
	$Xh^-/Y/Dp(1;f)3$		230	555		655	1244	0.530		0.467 (±0.040)	0.396 (±0.034)
	$Xh^-/B^SY/Dp(1;f)3$	46		218	179		663	0.531		0.239 (±0.037)	0.291 (±0.043)

The males in experiment 1 were siblings, as were those in experiment 2. R_{Y1}/R_{Y2} is the recovery ratio of B^SY to the unmarked Y.

TABLE 6

The effect of extra heterochromatin on X *chromosome recovery from* Xh^- *males*

Paternal genotype	Progeny sex ratio	*N*
$Xh^-/Y^S/B^SY/$	0.31	353
Dp(1;f)3	0.26	2991
$Xh^-/Y^S/B^SY$	0.34	1709
$Xh^-/B^SY/Dp(1;f)3$		

Males of the indicated genotypes were brothers and were crossed to *y w bb* females.

Pairing-dysfunction model: Two tests of the idea that unsaturated pairing sites are responsible for meiotic drive were carried out. The first is based on the following argument. If nondisjunction and meiotic drive in Xh^- males are both consequences of the absence of *X* heterochromatic pairing sites, then addition of a chromosome carrying the *X*-pairing sites to an Xh^-/Y genome should suppress both defects. *Dp(1;f)3* is an *X* chromosome with all of the heterochromatin (*i.e.*, all of the pairing sites) and very little else. In $Xh^-/Y/Dp(1;f)3$ males, the *Y* and free duplication should pair and disjoin regularly and should be recovered equally. In fact the *Y* does disjoin regularly from the free duplication (Tables 2 and 5), but its recovery remains poor. In most crosses the *Y* is recovered less than half as often as the free duplication. Thus, addition of extra *X*-pairing sites suppresses one defect (nondisjunction) but not the other (meiotic drive).

The *Dp* does affect the level of meiotic drive, however. R_X declines from 0.437 in Xh^-/B^SY males to 0.338 in sibling $Xh^-/B^SY/Dp$ males (Table 2). Evidently, the weak Xh^-:*Y* pairing that occurs in Xh^-/Y males reduces drive relative to $Xh^-/B^SY/Dp$ males where Xh^- is a univalent. This implies that *X-Y* pairing is important for spermiogenesis but not because pairing sites have to be saturated. Evidently, the *X* euchromatin must participate in pairing. The reason for this requirement is not obvious.

If unreacted pairing sites are responsible for the skewed segregation ratios in deficiency-*X* males, then other genotypes sharing this pairing site asymmetry but not deficient for *X* heterochromatin should also exhibit aberrant segregation. For example, an *X* with double the normal dose of heterochromatin might complete meiosis with unreacted pairing sites which would act as gametic lethals. Thus, recovery of *X* chromosomes duplicated for heterochromatin provides a second test of the pairing-dysfunction model. Two such chromosomes, $In(1)sc^{8L}sc^{4R}$ and $In(1)sc^{S1L}sc^{4R}$, were tested over B^SY (Table 7). $In(1)sc^8sc^4$ is a dominant semilethal because of the scute region deficiency. The lethality is covered by the scute allele of *Dp(1;f)3*. The sex ratio in line 1 is, therefore, calculated as *XDp* females divided by B^SY males. $In(1)sc^{S1L}sc^{4R}$ is not scute deficient so no viability problems arise. In both cases, *X* recovery is normal, indicating that extra pairing sites do not become gametic lethals.

The pairing-dysfunction model also fails to account for the poor recovery of autosomes in Xh^- males in which no pairing site asymmetries can be invoked.

TABLE 7

Recovery of heterochromatically duplicated X *chromosomes*

Paternal genotype	Sperm genotypes						Sex ratio (females to males)
	X	*XY*	*XDp*	*Y*	*Dp*	*YDp*	
In(1)sc^{8L}*sc*^{4R}/*B*^{S}*Y/Dp(1;f)3*	257	126	974	1081	1090	861	0.90[a]
In(1)sc^{51L}*sc*^{4R}/*B*^{S}*Y*	2153	0		1903			1.07

Males of the indicated genotypes were crossed to *y w/y w* females.

[a] In calculating the sex ratio in line 1, only the *XDp* and *Y* classes were used because of the viability problems discussed in the text.

Clearly, any successful model must account for the depressed recovery of paired as well as unpaired chromosomes from deficiency-*X* males.

DISCUSSION

The deficiency of *Y* relative to *X* and of *XY* relative to nullo-*XY* classes in the offspring of *Xh*$^{-}$ males reflects selection against developing sperm in proportion to their chromatin content. The evidence for this claim is that recovery of *Y* chromosome fragments (*Y*^{S}, *Y*^{S}.*Y*^{S}, *Y*^{L}*bb*$^{-}$ and *Y*^{L}*bb*$^{+}$), *X* chromosome fragments (*Xh*$^{-}$, *Dp(1;f)3*, *Dp(1;f)164* and *Dp(1;f)1144*) and autosomal *fragments* (*3L* and *Dp(2;f)f29*) are all disrupted, the degree of disruption being inversely proportional to size. The discrimination in these experiments is not very fine, so that it is not possible to distinguish between continuous sensitivity and multiple discrete sensitivity sites. It is possible, however, to rule out the notion that a chromosome contains a unique response locus. It is clear that both arms of the *Y* and the euchromatic portion of the *X* are sensitive. It is likely that the *X* heterochromatin is also sensitive.

In trying to explain these observations, it is tempting to think in terms of shortage of an essential chromatin-binding material. However, shortage models generally imply competition among chromosomes. The data exhibit no such effect; the probability of recovery of one chromosome is independent of that of a second.

Not all shortage models need imply competition. If the shortage is of something that cannot be sequestered, such as time, no competition would result. More time for one chromosome need not mean less for another. Although the idea that *X* heterochromatic deficiencies might disrupt a meiotic timer, leading to a shortage of time for an essential chromosome processing step, is consistent with the data, it is difficult to test directly.

Another possibility is that deficiency for *X* heterochromatin leads to production of a toxin that interacts with sperm chromatin. The more chromatin in a sperm the higher the probability of a lethal interaction. The failure to detect a titration effect would imply either that a single "hit" suffices to kill a sperm or that the toxin is present in sufficient excess that one interaction does not affect the probability of another.

It is important to note that there is no direct evidence that sperm dysfunc-

tion is due to improperly processed or damaged chromosomes. It could be that *X* heterochromatic deficiencies disrupt some other aspect of sperm development in such a way as to render their viability sensitive to the amount of perfectly normal chromatin they contain. This would also explain the failure to detect viability interactions among chromosomes. No simple way to distinguish among these alternatives suggests itself.

The role of *X-Y* pairing in spermatogenesis remains obscure. Contrary to the suggestion by PEACOCK and MIKLOS (1973), saturation of sex chromosome-pairing sites does not prevent sperm dysfunction. In $Xh^{-}/Y/Dp(1;f)3$ males, the *Y* and *Dp* pair regularly. Since both chromosomes have full doses of pairing sites, no sperm dysfunction should occur. However, the *Y* is recovered less than half as frequently as the *Dp*. Although this experiment rules out saturation of pairing sites as an important variable, it does not eliminate *X-Y* mispairing as a cause of sperm dysfunction. The considerable evidence for correlation between nondisjunction and meiotic drive implies an important role for *X-Y* pairing in spermatogenesis. Plausible pairing models that are consistent with the data can be suggested. For example, suppose that an important regulatory event in spermatogenesis, such as activation of one or more essential *X*-linked spermatogenesis genes, depends upon pairing of the *Y* with both the euchromatic and heterochromatic portions of the *X*. Separation of the heterochromatin from the euchromatin would disrupt this interaction because the euchromatin has no pairing sites of its own.

Indeed, there is considerable evidence for the importance of *X* chromosome continuity in spermatogenesis. The occurrence of sperm dysfunction in $Xh^{-}/Y/Dp(1;f)3$ males is one piece of evidence. *X;4* translocations with proximal euchromatic *X* breaks also exhibit skewed segregation ratios. Despite regular bivalent pairing and disjunction, the longer member of each bivalent (the *Y* and $4^{P}X^{D}$) exhibits depressed recovery (NOVITSKI and SANDLER 1957; ZIMMERING 1960). Chromosome recovery probabilities in these males are consistent with the inverse chromatin quantity rule. Translocations involving the *X* can have even more serious effects on spermatogenesis. Unlike autosome-autosome translocations which are generally fertile, translocations involving the *X* and one of the major autosomes (the second or third chromosomes) cause complete male sterility. The sterility is dominant in the sense that a duplication covering the *X* breakpoint does not restore fertility. The only exceptions are translocations with terminal breaks in both chromosomes and some (but not all) translocations with *X* heterochromatic breaks (LIFSCHYTZ and LINDLSEY 1972).

Further evidence for the importance of *X* chromosome continuity comes from studies of interactions between *X* heterochromatic deficiencies and other chromosomal rearrangements. Xh^{-} males carrying the $Ymal^{+}$ chromosome (a *Y* duplicated for a substantial piece of proximal *X*) are sterile. This sterility cannot be suppressed by addition of a free *X* duplication (RAHMAN and LINDSLEY 1981). Xh^{-} males heterozygous for otherwise fertile *Y*-autosome translocations are sterile even in the presence of another *Y* chromosome or a free *X* duplication (LINDSLEY and TOKUYASU 1980).

The reason for the importance of *X* chromosome continuity in spermato-

genesis remains a mystery. Whether or not it has to do with *X-Y* pairing will have to await further experimentation. From the present study, it can be concluded only that separation of *X* heterochromatin from *X* euchromatin causes sperm dysfunction and that the probability of dysfunction depends on the amount of chromatin a sperm contains.

Finally, the evolutionary implications of these results merit brief consideration. It has been suggested (BAKER and CARPENTER 1972) that meiotic drive evolved in male Drosophila to permit selective elimination of the aneuploid products of nondisjunction at the gamete stage. Any mechanism that lowers the probability of formation of a functional aneuploid gamete might be favored by selection. It is clear, however, that the meiotic drive system triggered by *X* heterochromatic deficiencies does not selectively eliminate aneuploid sperm. It acts against all sperm in proportion to their chromatin content. Although it is true that *XY* sperm receive particularly rough treatment because of their unusually high chromatin content, *XY* sperm give rise to *XXY* females which are quite viable and fertile. Although their fertility is somewhat poorer than that of *XX* females, fitness is affected far more drastically by the nullo-*XY* sperm which give rise to sterile *XO* males. Meiotic drive actually favors nullo-*XY* sperm because they have less chromatin than *X* or *Y* sperm and, thus, exacerbates the consequences of *X-Y* nondisjunction and lowers fitness. It seems unlikely, then, that meiotic drive is an evolved mechansim. Rather, it must be a pathological consequence of breakdown in some aspect of sperm development.

The author gratefully acknowledges the guidance and support of L. G. ROBBINS. Thanks are also due to L. G. ROBBINS, T. FRIEDMAN, E. SWANSON, D. L. LINDSLEY and A. T. C. CARPENTER for comments on the manuscript. This work was submitted in partial fulfillment of the requirements for the Doctor of Philosophy, Zoology Department and Genetics Program, Michigan State University. It was supported by National Science Foundation grant PCM 79-01824 to L. G. ROBBINS.

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