THE MEIOTIC BEHAVIOR OF GROSSLY DELETED X CHROMOSOMES IN DROSOPHILA MELANOGASTER[1]

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IT HAS been known for many years that the proximal heterochromatin of the X chromosome functions in disjunction. In the early paper of MULLER and PAINTER (1932), in which they demonstrate that the proximal half of the X is genetically inert, the only function that they can attribute to this region other than that directly assignable to the normal allele of *bb* is the control of disjunction of the X chromosome from the Y chromosome at spermatogenesis. It was the purpose of this investigation to examine in more detail the role of the proximal heterochromatin of the X chromosome in sex chromosome disjunction. The experiments to be reported were suggested by a paper by GERSHENSON (1940) and are in part a repetition, and in part an extension, of his work. GERSHENSON's approach was essentially to fractionate the proximal heterochromatin in a series of free X chromosome duplications, and to examine the influence of these duplications on the disjunction of normal homologs. Because his extensive investigations are published in Ukranian[5] and are thus largely unavailable to English-speaking geneticists, they will be reviewed briefly here.

It is possible, by irradiation of a normal X chromosome, to induce the loss (as an interstitial deletion) of a major portion of the euchromatin with or without sections of the adjoining proximal heterochromatin. The resulting deleted chromosome [Del(1)] consists of the centromere of the X chromosome and some or all of the proximal X heterochromatin plus a portion of the euchromatic tip marked with y^+. The deleted chromosome may also carry a portion of the proximal euchromatin; the amount of euchromatin carried by such a chromosome can be so small as to have a negligible effect on viability when hyperploid in either sex. Such chromosomes are carried as free duplications [Dp(1;f)] marked with y^+. GERSHENSON measured a series of these duplications cytologically and studied their effect on disjunction of X from X in females and of X from Y in males. He

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reports that the duplications fell into three cytologically well-defined classes: about 0.5 times, 0.25 times, and 0.1 times the length of a normal X. He was able to rule out a significant contribution of the euchromatic portion of the duplications to the measurable differences in length, and consequently he ascribes the difference between the long and intermediate duplications to *Block A* (0.25 times the length of a normal X) and that between the intermediate and the short duplications to *Block B* (0.15 times the length of a normal X). On the basis of the disjunction in +/+/ Dp and +/dl–49/Dp females, the duplications could be divided into four classes characterized by relatively high, intermediate, low, and negligible frequencies of secondary nondisjunction. The correlation between these classes and cytological length was good, but not exact. GERSHENSON argued that the amount of secondary nondisjunction is a measure of the interference by the duplication with normal disjunction of the X chromosomes and consequently of the pairing affinity of the duplication for the X chromosome. Proceeding from this premise he concluded that the high nondisjunction duplications carried a pairing site (presumably equivalent to the collochores of COOPER 1941, 1951) that the intermediate, low, and negligible nondisjunction duplications lacked; similarly, that the intermediate nondisjunction duplications contained a pairing site that the low and negligible nondisjunction duplications lacked; and finally, that the low nondisjunction duplications contained a site that the negligible class lacked. It was also possible to infer three pairing sites on the basis of disjunction in X/Y/Dp males. The correlation among the four classes of duplications defined by nondisjunction in females and the four defined by nondisjunction in males was not perfect: it indicated, in fact, that there are two pairing sites in the proximal X heterochromatin that function both in males and in females, one that functions in females only, and one that functions in males only. The designation and location of these pairing sites are diagrammed in Figure 1.

GERSHENSON further took those duplications causing maximal nondisjunction as demonstrating 100 percent of the potential effect of the proximal heterochromatin; then by observing the effect of removing the pairing sites one at a time (proceeding from the most distal, proximally), he was able to estimate the rela-

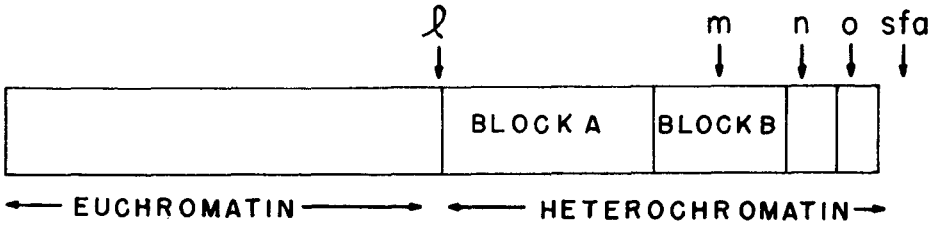

FIGURE 1.—A map of pairing sites in the proximal X chromosome heterochromatin as inferred by GERSHENSON (1940) from measurements of the rates of secondary nondisjunction induced in males and females by heterochromatic X chromosome deletions and by cytological measurements of these deletions in oogonia (figure modified from FIGURE 48 in GERSHENSON 1940).

tive effect, and inferentially the relative pairing affinity, of each pairing locus in both males and females. These estimates are tabulated in Table 1.

We undertook these experiments to check several points that are not clear from GERSHENSON's paper. If, as he postulates, a high rate of secondary nondisjunction effected by a duplication is indicative of a high pairing affinity between the duplication and its normal homologs, it can be further postulated that such a high pairing affinity would evoke a low incidence of primary nondisjunction, i.e., a reciprocal relation might exist between the incidence of primary and secondary nondisjunction. It is well established that reciprocal products of primary nondisjunction are not recovered with equal frequencies. This has been attributed by SANDLER and BRAVER (1954) to the meiotic loss of unpaired homologs. The possible role of meiotic loss of unpaired duplications in GERSHENSON's experiments is not easy to assess. Consequently, the effect of a newly derived series of duplications on secondary nondisjunction in +/dl–49/Dp females, and on primary nondisjunction in attached-X/Dp females and in $Y^sX \cdot Y^L$/Dp males was determined.

TABLE 1

The average relative synaptic activity of different groups of genes of the inert region of the X chromosome in females and males of Drosophila melanogaster

Group of genes	Synaptic activity in females (%)	Synaptic activity in males (%)
l	70.2	18.3
m	0.0	13.1
n	13.5	69.6
o	16.3	0.0

The synaptic activity of the entire inert region of the X chromosome is assumed to be 100 percent (Table 48 of GERSHENSON 1940).

In general, the duplications studied in +/dl–49/Dp females fell into groups in much the same way as did those studied by GERSHENSON. Also, the predicted reciprocal relation between the incidence of primary and secondary nondisjunction is fully realized. It was further determined that meiotic loss of the duplications does occur, but that in general it is not a major factor to be considered in the interpretation of the nondisjunction data. Finally, an entirely unexpected phenomenon was encountered in the results from some of the $Y^sX \cdot Y^L$/Dp males. In these cases the incidence of the $Y^sX \cdot Y^L$ chromosome (=XY) among the progeny of XY/Dp males is reduced to much below 50 percent (as low as 16 percent in one case). It can be shown that this reduced recovery is not the result of meiotic loss of the XY chromosome, nor can it be attributed to zygote mortality; it must be, therefore, that functional gametes bearing reciprocal products of meiosis do not function equally in fertilization (see also NOVITSKI and I. SANDLER 1957).

Origin and characterization of duplications

The thirteen duplications used in this study were derived by DR. A. WELTMAN in the following manner: Canton-S males were X-irradiated with approximately

4500r and crossed to $\underline{y\ v\ car}$/Y females. Non-y daughters were collected and were presumed to contain a duplication of the type described in the introduction. Each was crossed to $Y^sX \cdot Y^L$, *In(1)EN*, y *B*/0 males. The y^+ *B* males recovered in the following generation were crossed, where possible, to exceptional (y^+) sisters and otherwise to regular (y) sisters. This mating scheme automatically eliminates any duplication that is lethal or sterile in XY/Dp males (this, incidentally, included all duplications carrying car^+). Furthermore, any duplication that contained the normal allele of *pn* (0.8) was arbitrarily considered to carry excessive distal euchromatin and was discarded. Each of the remaining duplications was tested for the presence of the normal alleles of *ac*, *sc*, and *su-w*^{a} distally and of *su-f* and *bb* proximally. The results of these tests are summarized in Table 2.

TABLE 2

Genetic constitution of deletions

	Loci carried						
	Distally		Proximally		Translocation with		
Deletions	*sc*	*su-w*^{a}	*su-f*	*bb*	II	III	IV
Dp(1;f)3	+	—	+	+	—	—	—
Dp(1;f)10	+	?	—	—	—	—	—
Dp(1;f)12	+	+	+	+	—	—	—
Dp(1;f)18	+	+	—	+	—	—	—
T(1;?)42	+	?	—	+	*	*	*
T(1;3)51	+	+	—	+	—	+	—
Dp(1;f)52	+	—	+	+	—	—	—
Dp(1;f)122	+	—	—	+	—	—	—
T(1;3)142	+	+	+	+	—	+	—
Dp(1;f)164	—	—	—	—	—	—	—
Dp(1;f)167	+	+	+	+	—	—	—
T(1;4)174	+	—	—	—	—	?	+
Dp(1;f)179	+	+	—	—	—	—	—

For general discussion, see text.

* This deletion was lost before translocation tests could be performed. The fact that the primary exceptional females from XY/Del(1)142♂ × $\underline{y\ w}$/0 ♀ had outstretched wings (probably viable hyperploids) suggests that this duplication is also associated with an X autosome translocation.

Each duplication used in these studies was also tested for linkage between y^+ and the autosomes. Two of the duplications showed linkage with chromosome 3 and a third was linked with chromosome 4. In the two T(1;3)'s, bb^+, as well as y^+, was linked to chromosome 3. These then are peculiar translocations in that they carry the tip and the centric region of the X chromosome, but not the intervening euchromatic region from pn^+ through car^+. They may be described as "deletional translocations." The X chromosome was apparently broken distally and proximally and the third chromosome broken once; the tip of the X was then attached to the centric portion of chromosome 3 and the acentric portion of the third was attached to the centromere of the X. The interstitial portion of the X was lost as an acentric. That these translocations are of the cytological constitu-

tion expected from the above events has been confirmed in polytene preparations. Is it possible that the T(1;4) is also a deletional translocation in which X centromere portion either is not marked with bb^+ or has been lost. It might be noted that there are no bona fide cases of what ABRAHAMSON *et al.* (1956) have termed "half-translocations" among the aberrations reported here; this is, of course, to be expected, since meiosis has not intervened between irradiation and sampling. These aberrations will henceforth be referred to generically as deletions [Del(1)] of which there are two structural types—deletional translocations (e.g., T(1;3)142) and free duplications (e.g., Dp(1;f)118).

RESULTS

Disjunction in females

The data from crosses of females of constitution *y v f*/Del and *y v*/*In(1)*dl-49, *y* fa^n/Del with $Y^sX{:}Y^L$, *In (1)EN*, *y B*/0 males are presented in Tables 3 and 4. A comparison of the frequencies of nondisjunction in the two situations reveals a remarkably good inverse correlation. The deletions arranged in order of decreasing frequency of secondary nondisjunction in X/*In(1)*dl-49/Del females (see Table 5) correspond reasonably well with an arrangement in order of increasing primary nondisjunction in attached-X females; furthermore, if the known and suspected translocations are eliminated from this list, the inverse relation becomes nearly exact. It can be seen from Table 5 that the frequencies of nondisjunction do not form a continuous distribution; however, such a small sample of duplications cannot be considered to demonstrate a discontinuous dis-

TABLE 3

Progeny of y v f/*Del* ♀ × $Y^SX{\cdot}Y^L$, y B/*0* ♂

	Constitution of egg nucleus and phenotype of progeny				Primary nondisjunction
	XX	Del	XX/Del	0	$\left[\frac{\text{XX/Del} + 0}{\text{total}}\right]$
Deletion	*y v f* ♀	*B* ♂	*v f* ♀	*y B* ♂	
0	830	..	..	795	...
Dp(1;f)3	1137	1004	43	22	0.03
Dp(1;f)10	866	324	246	726	0.45
Dp(1;f)12	1447	1214	78	35	0.04
Dp(1;f)18	1391	1000	46	64	0.04
T(1;?)42	221	181	16	5	0.05
T(1;3)51	599	583	234	192	0.26
Dp(1;f)52	863	709	38	18	0.03
Dp(1;f)122	1390	1262	93	78	0.06
T(1;3)142	666	592	310	350	0.34
Dp(1;f)164	706	491	349	320	0.36
Dp(1;f)167	1265	1061	41	39	0.03
T(1;4)174	275	213	266	211	0.49
Dp(1;f)179	1070	730	213	228	0.20

TABLE 4

Progeny of y v/In(1)*dl-49*, y fa^n/*Del* ♀ × *YSX·YL*, y B/*0* ♂

Deletion	Constitution of egg nucleus and phenotype of progeny: X, *y B* ♀	X, *y* ♂	X/Del, *B* ♀	X/Del, + ♂	X/X, *y* ♀	Del, *B* ♂	Secondary nondisjunction: 2(X/X + Del)/total + X/X + Del
Dp(1;f)3	1261	1270	1136	1344	287	255	0.178
Dp(1;f)10	1900	2058	522	622	4	4	0.003
Dp(1;f)12	848	921	795	925	213	202	0.192
Dp(1;f)18	1243	1479	1233	1398	237	185	0.136
T(1;?)42	629	767	541	672	1109	974	0.615
T(1;3)51	1385	1692	1351	1615	58	57	0.037
Dp(1;f)52	1072	1288	1115	1198	191	162	0.131
Dp(1;f)122	1464	1831	1395	1710	189	140	0.093
T(1;3)142	1643	1913	1477	1661	43	41	0.024
Dp(1;f)164	1737	1983	1482	1815	3	4	0.002
Dp(1;f)167	701	771	717	576	165	109	0.165
T(1;4)174	744	697	746	673	1	1	0.001
Dp(1;f)179	957	1140	911	976	19	14	0.016

TABLE 5

Summary of disjunctional behavior of deletions separated according to structure and arranged in order of decreasing secondary nondisjunction in females

Deletion	Behavior in females: Primary nondisjunction	Secondary nondisjunction	Secondary nondisjunction (GERSHENSON, 1940)*	X/Del: X/Del + X	Proximal constitution: *su-f*+	*bb*+	Behavior in males: Primary nondisjunction	XY + XY/Del: Total
Dp(1;f)12	0.04	0.193	....	0.493	+	+	<0.001	0.474
Dp(1;f)3	0.03	0.178	....	0.495	+	+	0.001	0.445
Dp(1;f)167	0.03	0.163	....	0.506	+	+	<0.001	0.279
Dp(1;f)52	0.03	0.131	....	0.495	+	+	<0.001	0.474
Dp(1;f)18	0.04	0.136	....	0.492	—	+	<0.001	0.453
Dp(1;f)122	0.06	0.093	0.086(6) 0.032(5)	0.485	—	+	<0.001	0.476
Dp(1;f)179	0.20	0.016	0.017(6)	0.474	—	—	0.001	0.246
Dp(1;f)164	0.36	0.002	0.001(2)	0.470	—	—	0.485	0.460
Dp(1;f)10	0.45	0.003	....	0.224	—	—	0.613	0.361
T(1;?)42	0.05	0.616	....	0.465	—	+	0.037	0.336
T(1;3)51	0.26	0.037	....	0.491	—	+	0.002	0.335
T(1;3)142	0.34	0.024	....	0.469	+	+	0.040	0.159
T(1;4)174	0.49	0.001	....	0.496	—	—	0.482	0.423

* Frequencies of secondary nondisjunction in females characteristic of GERSHENSON's four classes of duplications. Each frequency is the average of the number of duplications indicated in parentheses.

tribution. The classes of deletions indicated by the incidence of secondary nondisjunction in GERSHENSON's crosses (*y sc/In(1)*dl-49, *y w lz*/Del × *y v f B*/Y) correspond quite well with those indicated by the present experiments except that his observed frequencies of nondisjunction are generally lower than those being reported here (see also Table 5). This might be simply because the rates of nondisjunction are inherently different owing to differences in genetic background, or it might be that the deletions showing the highest rate of secondary nondisjunction in these experiments have no counterpart in GERSHENSON's experiments; i.e., they may possess an additional pairing site. The latter possibility is not unreasonable because these deletions would be retained only rarely by the methods available to GERSHENSON, which relied on the recovery of a primary exception (attached-X/Y/Del), from the attached-X female in which the deletion was originally recovered, for establishment of a line. Table 3 demonstrates that such reliance would definitely result in the recovery of a biased sample of deletions characterized by higher average primary nondisjunction from an attached-X chromosome. In these experiments the XY chromosome obviates this difficulty.

On the basis of their disjunction from the attached-X chromosome (Tables 3 and 5), the duplications (exclusive of the translocations) do not form a continuous distribution, and the discontinuities in this classification coincide with those based on the secondary nondisjunction data.

An examination of the constitution of the duplications showing these different behaviors reveals no correlation between euchromatic content (*sc*, *su-w^a*, *su-f*) and disjunctional behavior. All those duplications characterized by low nondisjunction from the attached-X and high secondary nondisjunction of +/dl-49 carry the *bb$^+$* region of the X chromosome. Duplications associated with high nondisjunction from the attached-X and normal disjunction of + from dl-49, on the other hand, do not carry *bb$^+$*. These observations are similar to those of GERSHENSON.

As stated in the introductory portion of this report, one of the purposes of these studies was the examination of the behavior of the deletions with respect to the phenomenon of meiotic loss. One simple index of meiotic loss of a deletion is the depression, below 50 percent, of its recovery. It will be realized that such a depression may also have its origin in a decrease in viability, owing to hyperploidy. Although the deletions studied here were selected for minimal euchromatic content, there is no possibility of a clear distinction between meiotic loss and inviability as the cause of depressed recovery of deletion bearing individuals, but in these cases arguments can be brought to bear that render unlikely a significant influence of inviability. In the first place, the effect of duplication on the viability of a hyperploid individual should be correlated with the genetic content of the duplication such that inviability is associated with certain factors carried in the duplication. In these experiments there is no obvious relation between the recovery of a particular deletion and its genetic (i.e., euchromatic) content. Secondly, gen-

eral experience suggests that the effect of X chromosome hyperploidy on viability would be greater in males than in females. In only one of the cases examined among the present series of deletions [Dp(1;f)167], is there any evidence of a greater discrepancy in recovery of the deletion in males than in females. In this case the ratio of X to X/Del ova recovered from +/dl-49/Del females is 701:717 among females and 771:576 among males. It is probably a reasonable approximation to say that, except for Dp(1;f)167, the discrepancies observed in the deletion-bearing classes are not attributable to inviability.

Among the exceptional progeny from crosses of attached-X/Del females, any discrepancy in recovery of the deletion owing to events transpiring in the female is obscured by the unequal production of XY and 0 sperm caused by meiotic loss of the XY chromosome in the male. However, +/dl-49/Del females produce X and X/Del ova as reciprocal products of regular disjunction, and by analogy with the known behavior of the Y chromosome during regular disjunction in X/X/Y females (SANDLER and BRAVER 1954), meiotic loss of the deletion should occur. The ratio in which X and X/Del ova are recovered is unaffected by whether they are fertilized by an XY- or a 0-bearing sperm. Consequently, the recovery of the deletion among the regular progeny of X/X/Del females was selected as a measure of loss of the deletion. Except for Dp(1;f)167, where only regular females are used because of the suspected inviability of X/Del males, both sexes are lumped for these comparisons. It is found that there is a correspondence between recovery of the deletion and its disjunctional behavior. Deletions characterized by low primary nondisjunction and high secondary nondisjunction are recovered in close to 50 percent of the gametes, whereas those characterized by high primary and low secondary nondisjunction are recovered in less than 50 percent of the gametes.

It is of interest to compare the effects of X heterochromatin with the effect of the Y chromosome on disjunction in females. The normal segregation of a Y from an attached X is a common observation and is comparable to the segregation of Dps(1;f)3, 12, 18, 52, 122, and 167 from attached X chromosomes. The effect of a Y chromosome on the disjunction of *In(1)*dl-49 from a normal X has been calculated from the data of STURTEVANT and BEADLE (1936) in the same manner as was done in Table 4. The frequency of secondary nondisjunction observed by STURTEVANT and BEADLE was 0.61. This value is much greater than that for any of the deletions studied either in the present paper or by GERSHENSON with the exception of Del(1)42 (0.62), which is thought to be associated with a translocation. This observation agrees very well with the predictions from COOPER's theory (1948) of secondary nondisjunction in female *Drosophila melanogaster*, which states that nondisjunction of two X's from a Y is the result of non random segregation from an X-Y-X trivalent in which each X pairs with a different arm of the Y. Such a trivalent cannot be formed when the extra element is one armed; consequently, a bivalent (one X plus the extra element) and univalent (the other X) are formed, with the chromosomes of the bivalent separating normally and the univalent proceeding at random, as originally postulated by BRIDGES (1916) to

explain secondary nondisjunction. Both models utilize an X/X bivalent with the extra element univalent to explain regular disjunction. BRIDGES' model predicts a maximum rate of secondary nondisjunction of 50 percent, which is not exceeded by any of the duplications studied, but which is exceeded when T(1;?)42 or the Y is the extra element. The reason for the high frequency of secondary nondisjunction observed in the presence of T(1;?)42 is difficult to explain. To be consistent with COOPER's theory, the element that is homologous to the X's should be two armed. Since T(1;?)42 carries a normal allele of *bb*, we concluded that it carried the centric region of the X chromosome; the possibility exists, however, that T(1;?)42 is a T(X;Y) and that the bb^+ allele was derived from the Y. Unfortunately, this line have been lost and this possibility cannot be checked. However, it is difficult to understand how segregants from such a translocation could yield the aneuploid-looking exceptions from XY/Del(1)42 males by which this deletion was originally judged to be a translocation.

Disjunction in males

Primary nondisjunction of the deletions from an XY chromosome was measured in the following mating: $Y^SX{\cdot}Y^L$, *In(1)EN*, *y B*/Del ♂ × *y w*/0 ♀; the data are presented in Table 6. When the relative frequencies of primary nondisjunction of the deletions are examined in Table 5, it is evident that a correlation exists between the behavior of the different deletions in males and in females. The single discontinuity in the distribution of frequencies of nondisjunction divides the duplications into a group that separates almost perfectly from the XY chromosome and a group that appears to separate randomly from it.

TABLE 6

Progeny of y w/0 ♀ × $Y^SX{\cdot}Y^L$, y B/*Del* ♂

	Constitution of sperm nucleus and phenotype of progeny				Primary nondisjunction	Recovery of XY
	XY	Del	XY/Del	0	$\frac{XY/Del+0}{Total}$	$\frac{XY+XY/Del}{Total}$
Deletion	*y B* ♂	*w* ♀	*B* ♂	*y w* ♀		
0	816	..	..	945	....	0.463
Dp(1;f)3	2296	2854	0	7	0.001	0.446
Dp(1;f)10	1179	467	357	2246	0.613	0.361
Dp(1;f)12	2502	2769	0	2	<0.001	0.475
Dp(1;f)18	2663	3208	0	2	<0.001	0.453
T(1;?)42	564	1055	0	62	0.037	0.336
T(1;3)51	682	1352	1	3	0.002	0.335
Dp(1;f)52	2653	2940	0	2	<0.001	0.474
Dp(1;f)122	2103	2318	0	1	<0.001	0.476
T(1;3)142	197	1016	4	47	0.040	0.159
Dp(1;f)164	1231	1513	1219	1368	0.485	0.460
Dp(1;f)167	1299	3349	0	3	<0.001	0.279
T(1;4)174	967	1302	886	1226	0.482	0.423
Dp(1;f)179	592	1814	0	3	0.001	0.246

With one exception, there is no evidence of loss of the deletions in XY/Del males; in fact, there are generally more deletion-bearing progeny recovered than not. In Dp(1;f)10, however, only 19.4 percent of the progeny carry the duplication; this compares well with 22.4 percent, which is the recovery of Dp(1;f)10 among the progeny of X/X/Dp females. The striking feature about the data from XY/Del males, however, is that in every line the XY chromosome is recovered in fewer than half of the progeny. In some cases the deficiency of XY bearing classes is severe, and it is quite likely that this apparent loss of the XY obscures any loss of the deletions that might be occurring. Table 4 shows that whereas there has been a correlation between the behaviors measured with respect to the different lines up to this point, there is no logical seriation of the apparent loss of XY. Deletions with high and low synaptic activity show both high and low recovery of XY. These departures from expected ratios were originally considered to be the result of meiotic loss of the XY chromosome. The observations were not, however, in accord with the ideas of SANDLER and BRAVER on meiotic loss of *In(1)sc^{4L}, sc^{8R}* in *In(1)sc^{4L}, sc^{8R}/sc^{8}*·Y males in three respects. In the first place, loss of the XY was not correlated with the disjunction of this chromosome from its homolog; situations with nearly perfect disjunction (Dp(1;f)179) or nearly random disjunction (Dp(1;f)10) showed a grossly deficient recovery of XY. In the second place, high loss of the XY chromosome was not accompanied by the recovery of gametes from which it had been lost; that is to say, the virtual absence of a nullo XY, nullo Dp class from Dp(1;f)167 is incompatible with the loss of XY during meiosis as an explanation of the deficiency of this chromosome among the progeny. Finally, it is impossible to account for recovery of the deletion in more than half of the progeny (as high as 80 percent in one case) by invoking the phenomenon of meiotic chromosome loss. We concluded, therefore, that the discrepancy must be the result of gametic loss, either before or after fertilization. The latter should be detectable by the failure of an appreciable proportion of the zygotes formed to develop into adults. Consequently, the proportion of eggs fertilized by XY/Del males (from lines characterized by low XY recovery) that developed into adult flies was determined. If the observed discrepancy were the consequence of zygote mortality, then the addition of the dead eggs to the deficient class should at least eliminate the discrepancy. It is evident from Table 7 that this is not the case. It is therefore concluded that sperm bearing reciprocal meiotic classes do not participate equally in fertilization. This conclusion is similar to one arrived at by NOVITSKI and I. SANDLER (1957) in a different situation and will be discussed more thoroughly later. It will be noticed that three of nine duplications show the marked reduction of the XY class, and three of the four translocations show it. The significance of this escapes us at the moment. Those deletions associated with a more nearly normal recovery of the XY chromosome (0.423–0.476) apparently have the same effect as the absence of a homolog on the recovery of XY. SANDLER and BRAVER's tests of XY/0 males showed a 47.3 percent recovery of XY as opposed to 51.0 percent recovery from XY/FR-2 males. In the present experiments, 46.2 percent XY were recovered from XY/0 males. Thus it

TABLE 7

Percentage eclosion from crosses of $Y^{S}X{\cdot}Y^{L}$/Del ♂ × y/y ♀

Deletion	No. of eggs	Constitution of sperm nucleus and phenotype of progeny: XY *y B* ♀	Del + ♂	XY/Del *B* ♀	0 *y* ♂	Eclosion: total adults / total eggs	Recovery of XY: XY+XY/Del / total adults
0	357	172	...	...	171	0.961	0.501
Dp(1;f)12	1792	583	982	0	1	0.874	0.372
Dp(1;f)18	2737	1249	1286	0	1	0.927	0.493
T(1;3)51	592	88	204	0	0	0.493	0.301
T(1;3)142	731	70	273	0	2	0.472	0.203
Dp(1;f)167	2449	888	1279	0	0	0.885	0.410
Dp(1;f)179	1140	292	797	0	3	0.958	0.267

appears that the recovery of the XY chromosome from these XY/Del males is the same as from XY/0 males even though most of the deletions do behave as homologs of the XY chromosome by the criterion of perfect disjunction.

The reduced recovery of XY-bearing sperm might be a consequence of some peculiarity of the structural relations within the XY-Dp bivalent. If so, rearrangement of the heterochromatin within the XY might result in other bivalent structures, and therefore affect this particular phenomenon. To test this idea, we investigated the effect of certain of the duplications on the recovery of $XY^{L}{\cdot}Y^{S}$ (PARKER 1954), in which the distribution of the heterochromatic elements is quite different from that in $Y^{S}X{\cdot}Y^{L}$. The data from these tests, presented in Table 8, are apparently not different from those given in Table 6. In other words, there is no apparent effect of the distribution of the heterochromatin within the XY chromosome on its meiotic behavior in combination with a duplication. It should be pointed out, however, that the heterochromatin of these two chromosomes is probably the same, and derived from the Y chromosome for a considerable distance on either side of the centromere.

TABLE 8

Progeny of $XY^{L}{\cdot}Y^{S}$, y^{2} su-w^{a} w^{a}/*Del* ♂ × y w/0 ♀

Deletion	Constitution of sperm nucleus and phenotype of progeny: XY y^{2} *su-w*^{a} *w*^{a} ♂	Del *w* ♀	XY/Del (*su-w*^{a})*w*^{a} ♂	0 *y w* ♀	Recovery of XY: XY+XY/Del / total
0	3733	....	..	4367	0.461
Dp(1;f)18	2526	3613	1	23	0.410
T(1;?)42	83	190	0	25	0.279
T(1;3)51	650	1279	2	14	0.335
Dp(1;f)122	2139	3275	4	6	0.395
T(1;3)142	339	1732	9	117	0.158
Dp(1;f)179	1420	2722	5	28	0.341

Some data gathered in the process of testing the deletions for linkage with autosomes provide additional information on the observed unequal recovery of homologs. XY, *y B*/0; *Cy*/+; *Cx, D*/+ males were crossed to attached-X/Del females, and *B* sons (XY/Del) of three types (*Cy; Cx,D;* and *Cy;Cx,D*) were selected from the progeny and crossed to *y* females to test for linkage between y^+ and *Cy* and/or *D*. The data from combinations, some of which have previously given reduced recovery of the XY, are presented in Table 9. It can be seen that in the presence of *Cy* the recovery of XY from XY/Dp(1;f)179 and XY/T(1;3)51, but not from XY/T(1;3)142, becomes more nearly normal. Furthermore, Dp(1;f)167 fails to affect the recovery of the XY in the presence of *Cy* and/or *D*, whereas in the original tests its effect was considerable. These and other data suggest very strongly that the recovery of XY is influenced by the autosomal constitution. A further indication of this possibility is that whereas Dp(1;f)112 did not give a particularly low recovery of XY in the original experiments, it gave only 37.3 percent recovery in the egg count data presented in Table 7; also, statistical examination of the original data indicates culture-to-culture heterogeneity in the recovery of the XY chromosome (in some lines at least), giving in some cases normal recovery and in others a characteristically lowered recovery of XY.

The effect of some of the deletions on the recovery of the X and the Y chromosomes from X/Y/Del males has been measured. Although these data are preliminary, they are sufficient to show that recovery of Y-bearing classes may be

TABLE 9

The effect of the autosomal constitution of the parental male on the results of crosses of $Y^{S}X{\cdot}Y^{L}$/Del ♂ × y/y ♀

Deletion	Autosomal constitution of parental male	Constitution of sperm nucleus and phenotype of progeny			
		XY	Del	XY/Del	0
		y B ♀	+ ♂	*B* ♀	*y* ♂
T(1;3)51	*Cy*/+	155	186	0	2
	Cx, D/+	86	239	1	0
	Cy/+; *Cx,D*/+	87	124	1	0
Dp(1;f)52	*Cy*/+	147	168	0	0
	Cx,D/+	46	44	0	0
	Cy/+; *Cx,D*/+	59	62	0	0
Dp(1;f)122	*Cy*/+	296	264	0	0
	Cx,D/+	87	92	0	0
	Cy/+; *Cx,D*/+	191	184	0	0
T(1;3)142	*Cy*/+	63	292	1	4
	Cy/+; *Cx,D*/+	88	248	0	1
Dp(1;f)167	*Cy*/+	115	115	0	0
	Cx,D/+	112	102	0	0
	Cy/+; *Cx, D*/+	65	42	0	0
Dp(1;f)179	*Cy*/+	317	251	1	0
	Cx,D/+	31	114	0	0

Data from a selected sample of deletions.

reduced. For example, among the progeny of X/Y/T(1;3)51, 51.8 percent carry the X, 48.6 percent carry the translocation and 29.9 percent carry the Y; among the progeny of X/Y/Dp(1;f)167 males, 50.9 percent carry the X, 45.3 percent carry the duplication and 31.4 percent carry the Y. It will be noticed that in neither of these cases is any chromosome recovered in appreciably more than half of the progeny; consequently, it seems unlikely that the reduced recovery of the Y chromosome from X/Y/Del males results from impaired function of Y-bearing sperm. The data, however, can be explained by meiotic loss of the Y chromosome.

DISCUSSION

The progeny of males carrying an attached XY chromosome and certain free heterochromatic duplications derived from the X chromosome is sometimes characterized by a high incidence of duplication bearing individuals and a correspondingly low incidence of XY bearing individuals (Table 6). That this inequality in the recovery of homologs is not associated with zygote mortality can be easily demonstrated by egg counts (Table 7). We have concluded from these observations that homologous chromosomes are not recovered in *functional sperm* in the same proportion that exists in the cells of the parental male (i.e., 1:1). If a premeiotic phenomenon were the basis of the observations, then the aberrant proportions of XY to Del recovered in the mature sperm would have to exist in the primary spermatocytes. To shift the proportion of homologs in favor of the deletions, one might postulate the existence of some proportion of spermatocytes of genotype XY/Del/Del, Del/0 or Del/Del. The first of these, however, would exhibit normal recovery of the XY, and the second and third would be nullo X and would probably not survive. Consequently, it seems likely that the shift in ratio occurs between the onset of meiosis and fertilization. Generally speaking, there are two hypotheses that might be advanced to account for the observed unequal recovery of homologs: One is that the four spermatids give rise to uniformly functional sperm, but that chromosome behavior during meiosis is abnormal, such that one homolog becomes included in less than half (e.g., meiotic loss) or more than half (defined as meiotic gain) of the spermatids; the other is that each homolog is included in half the products of the meiotic divisions, but that these products—secondary spermatocytes or spermatids—produce sperm that do not function uniformly in fertilization (defined as gamete dysfunction).

Meiotic loss is visualized as the exclusion of a chromosome from both daughter nuclei of a meiotic division, which exclusion does not affect the ability of either nucleus to develop into a functional gamete, and has been correlated with univalence of the lost chromosome (SANDLER and BRAVER 1954). Exclusion could be the consequence of such factors as disintegration of the chromosome, failure of the chromosome to replicate, failure of the chromosome to become included on the spindle, or lagging. The reasons that meiotic loss cannot account for the observations described in the preceding paragraph are enumerated in the section on results. As an example of meiotic gain, the phenomenon of sex ratio in *Drosophila pseudoobscura* (GERSHENSON 1928) comes to mind. STURTEVANT and DOBZHAN-

SKY (1936) showed that in males of this and related species, which carry a certain sex-linked gene, there is commonly an extra replication of the X chromosome in the primary spermatocyte, such that four rather than two chromatids are apportioned among the four spermatids. In these spermatocytes there is a simultaneous failure to congress and subsequent disintegration of the Y chromosome (meiotic loss) with the result that nearly 100 percent of the sperm carry the X but not the Y chromosome.

For gamete dysfunction to be detectable, alternative gametic types must function unequally in fertilization. Thus if one gametic type functions in fewer, another must function in more than its share of fertilizations; consequently, the chromosomes in the complement of the latter gametic type will be recovered preferentially among the resultant zygotes. Unless this is a null complement, e.g., nullo X, nullo Y, some chromosomes will be recovered in more than half of the progeny. This provides a nearly absolute distinction between meiotic loss and gamete dysfunction as explanations of any case of unequal recovery of homologs. Meiotic loss can never result in the recovery of a homolog in more than half the zygotes, whereas, with the one exception just mentioned, gamete dysfunction must result in the recovery of a homolog in more than half the zygotes. Phenomena that can be described as meiotic gain are similar to gamete dysfunction by this criterion.

NOVITSKI and I. SANDLER (1957) published observations very similar to those presented here on the genetic behavior of $T(1:4)B^s$ during spermatogenesis. $T(1;4)B^s$ is a reciprocal translocation in which the X chromosome is broken immediately to the left of *B* and the fourth chromosome is broken distal to *ci*. They have shown that the part of the X with the fourth centromere ($=X^D$) regularly separates from the fourth chromosome, whereas the proximal portion of the X, with the tip of chromosome 4 appended ($=B^s$), regularly separates from the Y chromosome. Homologs are not, however, recovered equally frequently from either bivalent, and egg counts have shown that these inequalities cannot be explained by zygote mortality. Furthermore, the probability that a particular homolog (e.g., chromosome 4) will be recovered from one bivalent multiplied by the probability that a particular homolog (e.g., the Y chromosome) will be recovered from the other bivalent is exactly equal to the probability that they will be recovered together (Y;4). The independence in the recovery of homologs from the two bivalents, as demonstrated by this algebraic cross check, places certain limitations on the possible explanations of the observed inequalities, both for the case of $T(1;4)B^s$, and, by extrapolation, in the cases of XY/Del also. It says, in fact, that the frequency with which a homolog is recovered is independent of the genotype of the gamete in which it is recovered, thus rendering phenomena such as gamete mortality or preferential fertilization unlikely explanations of the observations. NOVITSKI and SANDLER have pointed out that the observation that gametes with perfectly normal complements (i.e., Y and 4) are recovered with reduced frequencies is also incompatible with this type of explanation. The data presented in the present report demonstrate that the same gametic type is re-

covered with a reduced frequency in some crosses but not in others, and that it is in fact the nondeletion-bearing class (i.e., XY); this provides additional evidence that the recovery of a homolog is independent of the gametic genotype.

To account for their observations, NOVITSKI and SANDLER have suggested that some of the products of spermatogenesis are regularly nonfunctional and that there is, in addition, non randomness in the orientation of the particular bivalents of a T(1;4)B^s heterozygote at first meiotic metaphase that results in the unequal inclusion of homologous chromosomes in the functional gametic nuclei, thus allowing detection of the initial asymmetry in the production of functional sperm. Independent orientation of the bivalents of T(1;4)B^s at first meiotic metaphase provides an explanation of the precise algebraic cross check mentioned in the preceding paragraph. Their hypothesis has the virtue of saying that gamete dysfunction is an attribute of the products of normal spermatogenesis, and the genotype of the male affects only the distribution of homologs to those products. As they recognize, however, it does require postulation of two independent phenomena; (1) regular dysfunction of some of the products of spermatogenesis and (2) preferential orientation of a bivalent at the first meiotic metaphase, neither of which has been demonstrated to occur in Drosophila; it might be noted, however, that orientation of asymmetric dyads does occur in the secondary oocytes of Drosophila (NOVITSKI 1951) and that, as with every case reported here, it is always the smaller element that becomes included in the functional gamete nucleus.

It seems quite likely that the phenomenon that occurs independently in the two bivalents of T(1;4)B^s males is occurring in certain of the XY/Del bivalents described in the present communication. Observation of the grossly unequal recovery of the XY versus the deletion seems to depend on some peculiarity in the nature of the bivalent (perhaps the inequality in the mass of the homologs suggested by NOVITSKI and SANDLER) and on the autosomal constitution. It may in fact be that if the autosomal requirements were understood, a wide variety of bivalents might be made to exhibit unequal recovery of homologs. The notion of gamete dysfunction provides alternative explanations of the results, including the algebraic cross check, under consideration. Most of them require that the genotype determine that specific meiotic products be nonfunctional rather than which homologs become included in meiotic products that are nonfunctional independent of the genotype. For example, one could postulate a strictly meiotic phenomenon in which, when the two chromosomes of a bivalent separate at the first division, one of them, with a probability related to events transpiring in the primary spermatocyte, in some way induces an abortive second meiotic division, or interferes with spermiogenesis, such that that particular product is recovered in fewer than half, whereas its homolog is recovered in more than half, of the functional sperm. It may be further postulated that such a phenomenon operates independently on two bivalents in a primary spermatocyte. Such a description fits aspects of a case described in Nicotiana by CAMERON and MOAV (1957). They found that the presence, in the microsporocytes of diploid *Nicotiana tabacum*, of

a particular alien chromosome derived from *Nicotiana plumbaginifolia* results in the early abortion of all microspores that do *not* carry the alien chromosome but do carry a full complement of *N. tabacum* chromosomes. These results resemble those obtained from XY/Del males in that the class of gametes that do not receive the abnormal element are recovered with reduced frequency. Finally, a model based on meiotic gain will account for the non random recovery of homologs; a phenomenon similar to that of sex ratio in *D. pseudoobscura* could be the basis of the behavior of XY/Del bivalents, and operating independently in two bivalents, could yield results similar to those observed in $T(1;4)B^s$ males. This is, of course, not an exhaustive list of alternatives to the hypothesis of NOVITSKI and SANDLER, nor has any of these alternatives a particular virtue that makes it preferable to their hypothesis. They are presented to illustrate the fact that the data presented are consistent with several models.

One final point should be made. It seems reasonably clear from the arguments presented by NOVITSKI and I. SANDLER and from the arguments presented here that the unequal recovery of homologs from males of certain constitutions is not caused by a reduced fitness of mature gametes, and does, therefore, appear to be related to the meiotic mechanics in these males. If this is indeed the case, then this phenomenon, whatever its mechanical basis, would be classified as an instance of meiotic drive (DUNN 1953; SANDLER and NOVITSKI 1957)—that is, this represents a case in which gene frequency could be drastically influenced by some meiotic phenomenon.

SUMMARY

The disjunction of a series of X chromosome deletions (constructed by deleting, with X irradiation, all but a negligible amount of the euchromatin of the X and a variable amount of the proximal heterochromatin) was studied in X/X/Del females, attached-X/ Del females, and attached-XY/Del males. With one interesting exception, the data agree with the notions of GERSHENSON (1940) which are outlined in the introduction of this paper. The exception was found in the results from matings of males carrying the attached XY chromosome and certain of the deletions. Among their progeny the deletion is recovered in considerably more than half of the individuals whereas the XY is recovered in considerably less than half. The following points have been established: (1) Egg counts have shown that this is not zygote mortality. (2) The fact that the deletions are recovered in excess of 50 percent of the progeny eliminates meiotic chromosome loss as the explanation of the discrepancy. (3) Evidence is presented indicating an autosomal influence on this phenomenon. Finally, it has not yet been possible to determine the physical basis of these results. However, it appears that whatever the physical basis, this phenomenon could cause meiotic drive in a population.

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