MEIOTIC BEHAVIOR OF TANDEM METACENTRIC COMPOUND X CHROMOSOMES IN DROSOPHILA MELANOGASTER[1,2]

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Received September 15, 1964

A tandem metacentric compound X chromosome is composed of two X chromosomes attached to a medially located centromere and arranged in tandem sequence so that the synaptic configuration is a spiral (NOVITSKI 1954). An approximation to the tandem metacentric has been achieved by the construction of an attached-X heterozygous for *In(1)y*^{4} (SIDOROV, SOKOLOV and TROFIMOV 1936; STURTEVANT and BEADLE 1936; NOVITSKI and SANDLER 1956). Bona fide tandem metacentrics have also been synthesized (e.g., NOVITSKI and LINDSLEY 1950) and their meiotic behavior investigated (NOVITSKI 1951, 1955; NOVITSKI and SANDLER 1956).

The anaphase II bridges produced by exchange between the arms of a tandem metacentric are generally lethal (STURTEVANT and BEADLE 1936; NOVITSKI 1951), but NOVITSKI in 1955 postulated an exception to this generality. He noted that two structurally distinct types of second-anaphase bridges were generated by tandem metacentrics—each composed of two separating sister centromeres, one connected by a single chromatid and the other connected by two chromatids of equal length. NOVITSKI suggested that, although the single bridges are lethal, the double bridges are excluded from the daughter nuclei at anaphase II, producing nullo-X eggs that are recovered when fertilized by X-bearing sperm.

The evidence favoring this hypothesis is as follows: in crosses in which the female parent carries a tandem metacentric compound X and a marked Y chromosome, one-half of the egg nuclei will receive the marked Y and thus produce, when fertilized by X-bearing sperm, *regular patroclinous males* that differ from their father by the presence of the marker on the Y. Nullo-X eggs that result, for example, from the exclusion of second-anaphase bridges from the presumptive egg nucleus will, when fertilized by X-bearing sperm, produce a class of *exceptional patroclinous males* that are distinguishable from the regular patroclinous male class by the absence of the marker carried by the maternal Y chromosome. Thus use of the marked Y enables identification of nullo-X eggs that should have received an X-chromosome centromere. NOVITSKI (1955) observed, in crosses of this sort, frequencies of exceptional patroclinous males of 0.044 and 0.049, which dropped to 0.005 when the tandem metacentric was made heterozygous for *In(1)dl-49*. He argued that since double bridges come only from the double

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[1] Supported by Grant RG-9965 from the Public Health Service.

[2] Research sponsored by the U. S. Atomic Energy Commission under contract with the Union Carbide Corporation.

exchange, which is much reduced in *In(1)dl-49* heterozygotes while single exchange and hence single bridges are less reduced, it is reasonable to suppose that the exceptional patroclinous male class measures the incidence of double bridges.

If NOVITSKI's hypothesis is correct, then the exceptional patroclinous male class provides an estimate of the frequency of double exchange tetrads, E_2, in the tandem metacentric compound, since double second-anaphase bridges result from one half the four-strand double exchanges. Therefore, in NOVITSKI's experiments, E_2 was 35 to 39 percent. (These figures should perhaps be reduced somewhat because a fraction of the exceptional patroclinous males result from nondisjunction of the marked Y from the compound.)

Homozygosis data from tandem metacentrics heterozygous for markers also yield estimates of E_2. Although, in the experiments just described, the compound chromosome was completely homozygous, in his earlier studies, NOVITSKI (1951) used females carrying the same tandem metacentric heterozygous for *cv* and *v*, but no marked Y, so that homozygosis but not the incidence of exceptional patroclinous males was determined. Appropriate computations (see *Analysis of results*) for these cases yield estimates of E_2 of 10 to 14 percent. Thus the estimates of E_2 derived in these two ways from different experiments do not agree.

Because estimates of E_2 for tandem metacentrics derived from different classes of flies scored in different experiments do not agree, we have investigated the meiotic behavior of adequately marked tandem metacentrics in females with a marked Y to measure both homozygosis and the incidence of exceptional patroclinous males. When homozygosis can be accurately measured and E_2 reliably estimated, the exceptional patroclinous males observed are not adequately explained by the supposition that they are derived from the double bridges formed at anaphase II. They are accounted for, however, by the hypothesis that they result from loss of the ring X chromosomes generated by exchange between the arms of the tandem metacentric. In other respects, our data corroborate and extend the observations and conclusions embodied in the works of STURTEVANT and BEADLE (1936), NOVITSKI (1951, 1955), and NOVITSKI and SANDLER (1956).

Origin of tandem metacentric compounds: Two types of tandem metacentric compound X chromosomes (TMX) were used in these experiments. One was synthesized as follows: females heterozygous for a normal X chromosome marked with *y*, *cv*, *v*, and *sd* and an inverted chromosome carrying the left end of *In(1)sc*^{4} and the right end of *In(1)EN* with Y^L appended as a second arm and marked with *y*, *sc*^{4}, *sn*, and *g* ($X \cdot L^L$, *In(1)sc*^{4L}, *EN*^{R}, *y sc*^{4} *sn g/y cv v sd*) were irradiated with 2000r and crossed to $Y^S X \cdot Y^L$, *In(1)EN, v f B/0* males. The genotype of the irradiated female and the compound-generating exchange are shown in Figure 1A. This event gives rise to a *y* non-*B* female. Some of these matroclinous exceptions were simply nondisjunctional; some were stable compounds that behaved as though they were attached-X's; and others were tandem metacentrics, which will be symbolized TMX, *y* or simply TMX. Six independently formed TMX lines of the type shown in Figure 1A were established and tested. All the lines behaved alike superficially, and consequently the data have been summed for analysis. In retrospect it would have been more prudent to gather

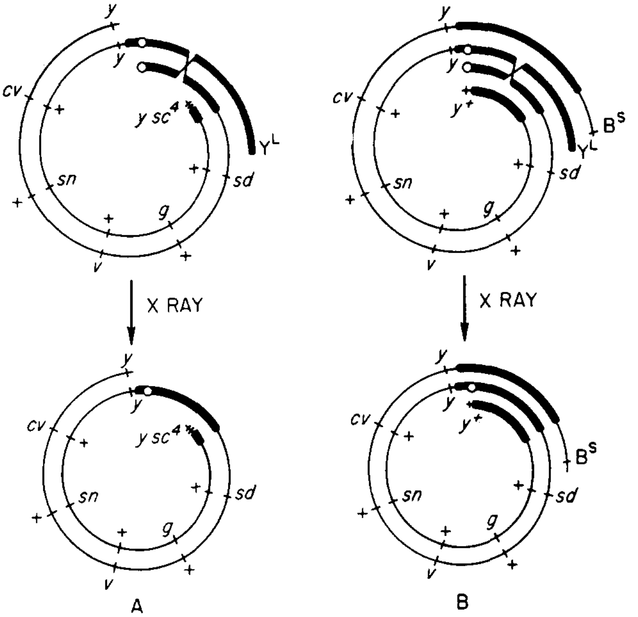
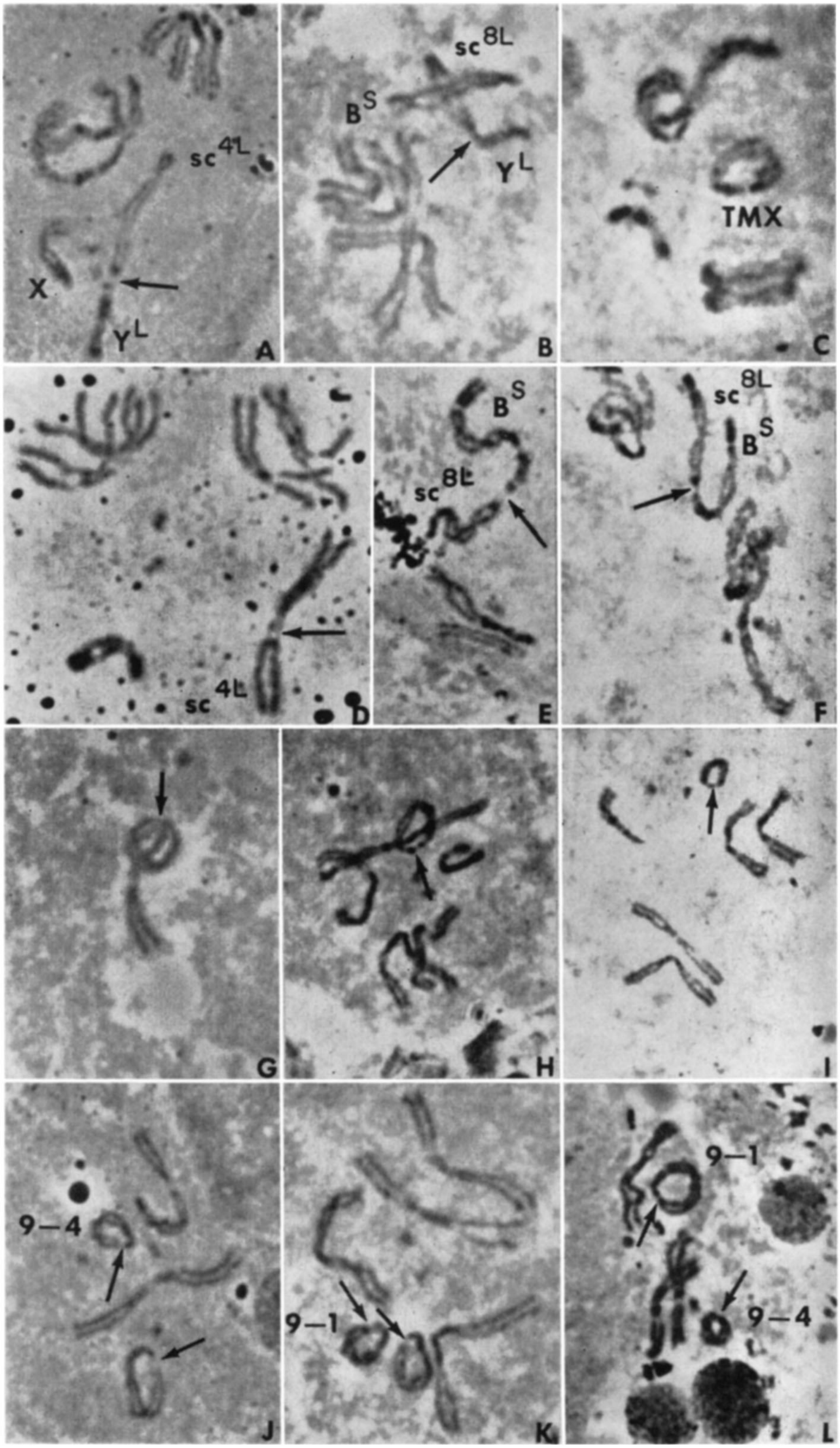


FIGURE 1.—The origin and distribution of markers in the tandem metacentric compound X chromosomes used in this investigation. (Only two of the four strands shown.) Heavy lines represent heterochromatin; light lines euchromatin.

more data from fewer lines, because our investigations have demonstrated that tandem metacentrics of independent origin display subtle differences in behavior.

A similar approach was used to synthesize the second type of tandem metacentric (TMXB^S) shown in Figure 1B, which was made for the purpose of generating tandem compound ring X chromosomes (SANDLER and LINDSLEY unpublished) but which was examined as a tandem metacentric in these experiments. In this case, however, the irradiated female was heterozygous for Dp(1;1)B^S TAG, *B^S y cv v sd* [a normal X chromosome with a duplication for the proximal portion of the X chromosome from T(1;4) B^S appended terminally (see LINDSLEY and SANDLER 1963] and X·L^L, *In(1)sc*^{8L}, *EN*^{R}, *sn g* (Figure 1B); they were crossed to *y*/Y males and *y*$^+$ *B*^{S} daughters selected for further testing. From a number of such TMXB^S chromosomes, two (TMXB^S 9–1 and TMXB^S 9–4) were selected for further study. Since the two seem to differ slightly, they will be treated separately.

Cytology of tandem metacentric compounds: In mitotic figures, TMX chromosomes are two-armed chromosomes superficially resembling the large autosomes; they have, however, several distinguishing features. One is that in early prophase the autosomes tend to pair, leaving the TMX without a partner; in rare instances the TMX gives evidence of assuming its spiral synaptic configuration (Figure 2C). Another distinguishing feature is that, whereas the ends of the autosomal arms are free of heterochromatin, one arm of TMX, *y* has the small distal heterochromatic segment from *In(1)sc*^{4} (Figure 2D) and TMXB^S carries on one arm


sc^{4L}
X
Y^{L}
A
sc^{8L}
B^{S}
Y^{L}
B
TMX
C
sc^{4L}
D
B^{S}
sc^{8L}
E
sc^{8L}
B^{S}
F
G
H
I
9–4
J
9–1
K
9–1
9–4
L

the large heterochromatic segment of *In(1)sc*^{8} and on the other a large heterochromatic segment as well as the euchromatic duplication derived from Dp(1;1)*B*^{S} TAG (Figures 2E, F).

Figures 2A and B show mitotic figures from females of the type used to produce TMX and TMXB^S, respectively. The centromeric heterochromatin of the free X chromosomes used to generate TMX is identical with that of the X's used to generate TMXB^S. As described, however, the distal ends of the chromosomes are different: the inverted X is *In(1)sc*^{4} in TMX and *In(1)sc*^{8} in TMXB^S; the uninverted X is normal in TMX and carries the *B*^{S} duplication in TMXB^S.

As indicated in Figure 1, the exchange that leads to the formation of the TMX's produced in this study occurs between the proximal heterochromatin of the X in normal sequence and the Y^L arm of the X in inverted sequence. Since the point of exchange need not be identical for TMX's of independent origin, the structure of the heterochromatin at the base of the arm in normal sequence is indeterminate, but the structure of the remainder of the TMX is identical for different TMX's from females of the same genotype. A comparison of the proximal heterochromatin of the uninverted arm of TMX, *y*, TMXB^S 9–1, and TMXB^S 9–4 (Figure 2D-F) reveals that the heterochromatic content of the base of the X in normal sequence is more extensive in TMX and TMXB^S 9–1 than in TMXB^S 9–4. As expected, the proximal heterochromatin of the inverted arm is the same for all three compounds. These observations can be confirmed in the single-ring derivatives of these tandem metacentrics (Figure 2G-I). These differences were confirmed by comparing pairs of single-ring derivatives of different tandem metacentrics in cells heterozygous for the two rings (Figure 2J-L). A possible scheme for the origin of the three tandem metacentrics, constructed from the information in Figure 2, is presented in Figure 3. The difference in pericentric heterochromatic content between TMXB^S 9–1 and TMXB^S 9–4 results in striking differences in the behavior of the tandem rings produced (SANDLER and LINDSLEY unpublished).

In salivary gland preparations the configurations are as expected. The arms of TMX's synapse to form a spiral, but this configuration is generally indistinguishable from that of a cell heterozygous for a closed X or a long X-chromosome inversion. In TMXB^S the *B*^{S} duplication is evident (Figure 4).

Expected behavior of tandem metacentric compound: The products of no, single, and double exchange in a tandem metacentric compound X are shown in Figure 5. Discussion of these products requires that certain definitions be established. There are two types of single exchange: one occurs between homologous chromatids attached to the same centromere (Exchange A, Figure 5) and will be referred to as *reciprocal*; the other occurs between homologous chromatids at-

FIGURE 2.—Mitotic cytology of tandem metacentric compound chromosomes. **A**. X·Y^L, *In(1)sc*^{4L}.*EN*^{R}, *y sc*^{4} *sn g/y cv v sd* female of the type that produced TMX. **B**. X·Y^L,*In(1) sc*^{8L}.*EN*^{R}. *sn g*/Dp(1;1)B^S TAG, *B*^{S} *y cv v sd* female of the type that produced TMXB^S. **C**. TMX, *y* female showing spiral synapsis of arms of TMX. **D**. TMX, *y*. **E**. TMXB^S 9–1. **F**. TMXB^S 9–4. **G**. X^c derivative of TMX, *y*. **H**. X^c 9–1. **I**. X^c 9–4. **J**. X^c/X^c 9–1. **K**. X^c/X^c 9–4. **L**. X^c 9–1/X^c 9–4. (Arrows represent centromere positions.)

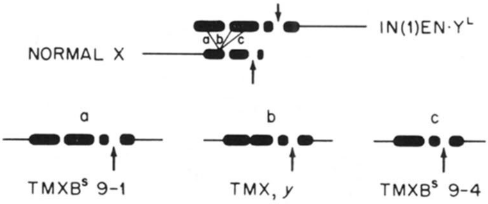


FIGURE 3.—Hypothetical heterochromatic exchanges that would account for the observed pericentric heterochromatic morphology observed for TMX, TMXB^{S} 9–1, and TMXB^{S} 9–4. (Arrows represent centromere positions.)

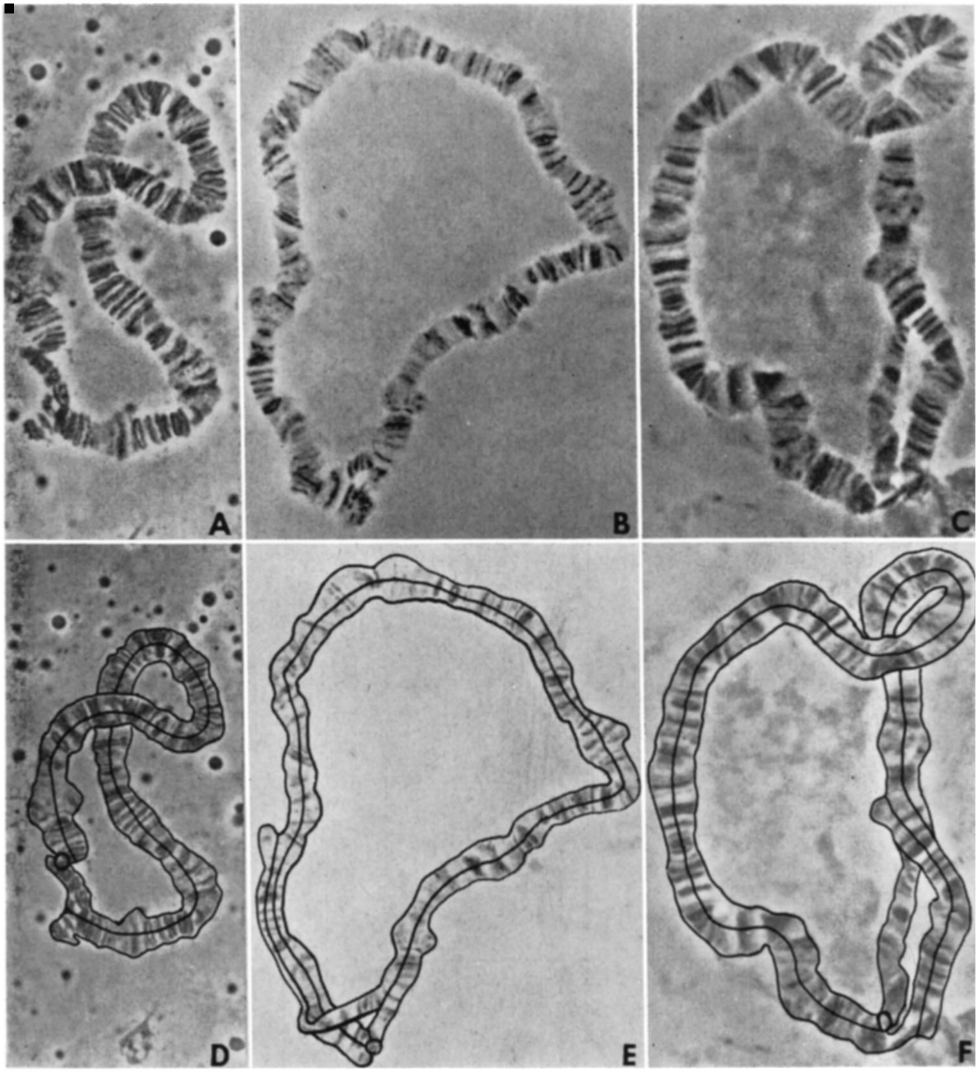


FIGURE 4.—Polytene configurations of TMX, y (**A**), TMXB^{S} 9–1 (**B**), and TMXB^{S} 9–4 (**C**) and line drawings of their interpretations with centromere positions designated by circles (**D**, **E**, and **F**, respectively).

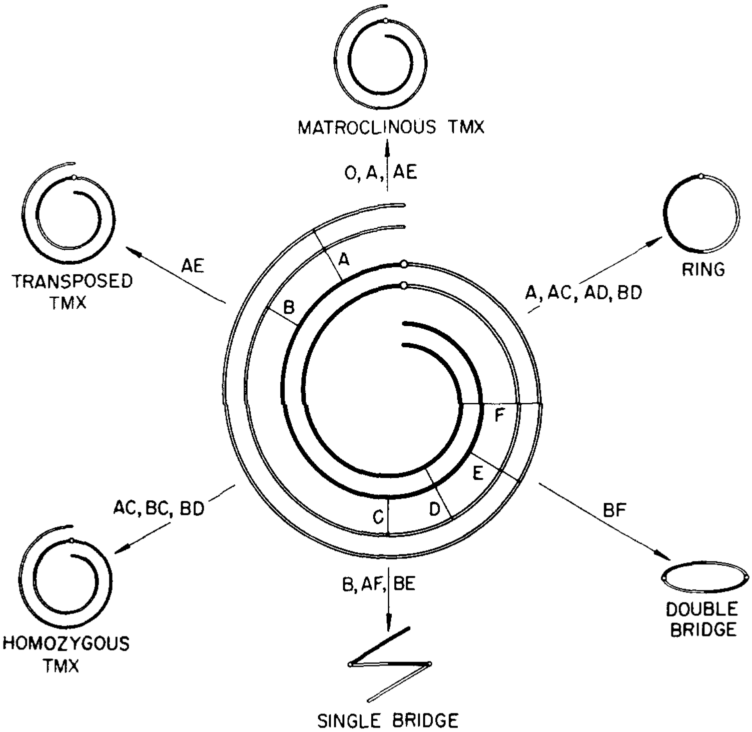


FIGURE 5.—The centric meiotic products of tandem metacentric compound X chromosomes with no, single, and double exchange. The tetrad types from which each product may be derived are indicated.

tached to sister centromeres (Exchange B, Figure 5) and will be referred to as *nonreciprocal* or *diagonal.* As there are two types of single exchange between the arms of a tandem metacentric compound, so too are there two types of two- and four-strand double exchanges, i.e., those in which both exchanges are reciprocal (Exchanges AE and AD, Figure 5) and those in which both are diagonal (Exchanges BC and BF, Figure 5). Three-strand double exchanges always involve one reciprocal and one diagonal exchange (Exchanges AC, AF, BD, and BE, Figure 5).

Three different classes of tandem metacentric chromosomes may be derived from a tandem metacentric. The first, the *homozygous TMX*, is homozygous for regions that were heterozygous in the parental TMX. The other two are treated as a single class in the analysis of the data and are referred to collectively as *nonhomozygous TMX's*; they differ from each other in that in one, the *transposed TMX*, the phase (i.e., the coupling relations) of the markers is altered as the consequence of diagonal two-strand double exchange (Exchange AE, Figure 5), whereas in the other, the *matroclinous TMX*, the phase of the markers is the same as in the parental TMX.

The four products of meiosis in TMX/FR-2 (FR-2 = $y^{+}Y^{L\cdot}$)-bearing females following the various types of exchange shown in Figure 5 and their expected

TABLE 1

Consequences of exchange and regular disjunction in TMX/FR-2 females. Crossovers involved are shown in Figure 5

Tetrad types		Products of meiosis and the probability that each will be included in the functional egg nucleus			
		First meiotic division			
Rank and frequency	Crossover involved	Second meiotic division		Second meiotic division	
E_0		Matroclinous TMX = ¼	Matroclinous TMX = ¼	FR-2 = ¼	FR-2 = ¼
½ E_1	A	Ring = ½ *c*	Matroclinous TMX = ½ (1-*c*)	FR-2 = ¼	FR-2 = ¼
½ E_1	B	Single bridge = ½		FR-2 = ¼	FR-2 = ¼
⅛ E_2	AC	Ring = ½ *c*	Homozygous TMX = ½ (1-*c*)	FR-2 = ¼	FR-2 = ¼
⅛ E_2	AD	Ring = ¼	Ring = ¼	FR-2 = ¼	FR-2 = ¼
⅛ E_2	AE	Transposed TMX = ¼	Matroclinous TMX = ¼	FR-2 = ¼	FR-2 = ¼
⅛ E_2	AF	Single bridge = ½		FR-2 = ¼	FR-2 = ¼
⅛ E_2	BC	Homozygous TMX = ¼	Homozygous TMX = ¼	FR-2 = ¼	FR-2 = ¼
⅛ E_2	BD	Ring = ½ *c*	Homozygous TMX = ½ (1-*c*)	FR-2 = ¼	FR-2 = ¼
⅛ E_2	BE	Single bridge = ½		FR-2 = ¼	FR-2 = ¼
⅛ E_2	BF	Double bridge = ½		FR-2 = ¼	FR-2 = ¼

TABLE 2

Regular progeny produced by the cross TMX/FR-2 *female* × XY/0 *male. Products of oogenesis taken from Table 1*

Products of oogenesis		Types and frequencies of sperm	
Type	Frequency	XY $=p$	0 $=1-p$
Matroclinous TMX	$\frac{1}{2}[E_0+\frac{1}{2}(1\text{-}c)E_1+\frac{1}{16}E_2]$	Superfemale	Matroclinous TMX-bearing female
Transposed TMX	$\frac{1}{2}(\frac{1}{16}E_2)$	Superfemale	Transposed TMX-bearing female
Homozygous TMX	$\frac{1}{2}[\frac{1}{8}(3\text{-}2c)E_2]$	Superfemale	Homozygous TMX-bearing female
Ring	$\frac{1}{2}[\frac{1}{2}cE_1+\frac{1}{8}(1+2c)E_2]$	Ring-bearing female	Ring-bearing male
Double bridge	$\frac{1}{2}(\frac{1}{8}E_2)$	Exceptional patroclinous male (or lethal?)	Lethal
Single bridge	$\frac{1}{2}(\frac{1}{2}E_1+\frac{1}{4}E_2)$	Lethal	Lethal
FR-2	$\frac{1}{2}(E_0+E_1+E_2)$	Regular patroclinous male	Lethal

frequencies of recovery are given in Table 1, where E_i is the frequency of tetrads of rank i ($\sum_i E_i = 1$) and c is the coefficient of nonrandomness, i.e., the probability of recovering the ring in the egg nucleus when a ring separates from a TMX at second anaphase (NOVITSKI 1951). The unsplit TMX centromere proceeds toward one pole at the first meiotic division and all egg nuclei developing from that pole will be considered *presumptive X-bearing ova* whether or not they contain an X chromosome. Egg nuclei developing from the other half of the first meiotic division will be considered *presumptive Y-bearing ova* whether or not they carry FR-2.

The terms in Table 1 were collected to yield expressions for the expected frequencies of ova carrying each of the possible derivatives of a TMX; (see Columns 1 and 2, Table 2). The types of zygotes produced when TMX/FR-2 females are crossed with XY/0 males are shown in Columns 3 and 4 of Table 2, where p and $1-p$ represent the frequencies of functional XY-bearing and nullo-XY sperm, respectively; p may be estimated directly from the proportion of females among the progeny of crosses between XY/0 males and normal females. If data are corrected for any inequalities in proportions of functional XY-bearing and nullo-XY sperm by multiplying the numbers of flies observed in classes resulting from fertilization with nullo-XY sperm by $p/1-p$, then the expression of each zygotic class is a function of E_i and c multiplied by $\frac{1}{2}p$. Considering ratios of classes or groups of classes leads to equations in c and E_i alone.

EXPERIMENTAL RESULTS

The TMX/0 daughters recovered from the irradiated females described in the section on TMX origin were crossed to $Y^SX{\cdot}Y^L$, *In(1)EN, y B*/FR-2 males; the resulting TMX/FR-2 daughters were crossed to $Y^SX{\cdot}Y^L$, *In(1)EN, y B*/0 males (XY, *y B*/0, or XY/0) and their progeny scored (Table 3). In the next generation, TMX/0 females were crossed to XY, *y B*/0 males to give the data shown in Table 4.

Females from the two $TMXB^S$ lines (9–1 and 9–4) were crossed to both XY/FR-2 and XY/0 to produce $TMXB^S$/FR-2 and $TMXB^S$/0 daughters. These daughters were crossed to XY, *y B*/0 males and their progenies are recorded in Tables 5 and 6.

Additional classes of progeny: It is evident in Tables 3 to 6 that a small fraction of the products are indicated as having arisen from triple and quadruple exchange. These events were not considered in the discussion of the expected behavior of TMX. Because tetrads of rank greater than two certainly constitute less than 2 percent of all tetrads, the precision to be gained from their consideration in the analysis does not seem to justify the complication that would result. It has therefore been assumed that $E_0 + E_1 + E_2 = 1$.

Other infrequent classes, not considered in the discussion of the expectations, that appear in Tables 3 and 5 are the exceptional TMX- and X^c-bearing progeny resulting from nondisjunction of TMX from FR-2. The reciprocal products of such nondisjunction are nullo-X nullo-Y ova, which may produce exceptional

TABLE 3

Results of the cross TMX, $\underline{\mathrm{In(1)sc^{4L}, EN^{R}, y\ sc^{4}\ sn\ g/y\ cv\ v\ sd}}$*/FR-2 females* × $Y^{S}X{\cdot}Y^{L}$, In(1)EN, y B/*0 males*

Class of progeny	Phenotype of progeny	Observed number
Regular patroclinous males	*B*	6230
Exceptional patroclinous males	*y B*	143
Regular nonhomozygous TMX-bearing females	*y*	1307
Exceptional nonhomozygous TMX-bearing females	+	7
Regular homozygous TMX-bearing females	*y cv*	5
	y v	36
	y sd	2
	y cv v	48
	y v sd	14
	y cv v sd	7
	y sn	28
	y g	33
	y sn g	60
	*y sn sd**	1
Regular ring-bearing females	*y B/y* +	2127
Exceptional ring-bearing females	*B*/+	8
Regular single-crossover-ring-bearing males	*y cv v sd*	365
	y v sd	338
	y sn v sd	591
	y sn sd	414
	y sn g sd	228
	y sn g	458
Exceptional single-crossover-ring-bearing males	*cv v sd*	1
	sn g	3
Regular triple-crossover-ring-bearing males	*y v*	5
	y sn v	1
	y cv v	2
Exceptional triple-crossover-ring-bearing males	*cv v g*	1

* Quadruple crossover.

patroclinous males. Thus exceptional patroclinous males come, in part at least, from primary nondisjunctional presumptive Y-bearing ova. Finally, in Table 5, there are females that carry a tandem ring (TRX) derivative of the TMXB^{S} chromosomes and are characterized by the simultaneous loss of the terminal markers from both arms of the tandem metacentric, i.e., of y^{+} and B^{S}. The origin of TRX from TMXB^{S} and the behavior of TRX have also been investigated in detail by SANDLER and LINDSLEY (unpublished). In the analysis of the data, tandem rings are considered to be nonhomozygous TMX's. It may be noted in this connection that there is a dramatic effect of FR-2 on tandem ring generation. Tables 5 and 6 show that the incidence of tandem rings per regular patroclinous male in TMXB^{S} 9–1 is increased from 0/3648 to 3/3382 by addition of FR-2 and in TMXB^{S} 9–4 from 0/4176 to 11/2907.

The results presented also indicate that TMXB^{S} 9–4 generates TRX's at a higher rate than TMXB^{S} 9–1, suggesting that the difference in the structure of

TABLE 4

Results of the cross TMX, In(1)sc^{4L}, EN^R, y sc^4 sn g/y cv v sd/*0 females*
× $Y^SX{\cdot}Y^L$, In(1)EN, y B/*0 males*

Class of progeny	Phenotype of progeny	Observed number
Patroclinous males	*y B*	6519
Nonhomozygous TMX-bearing females	*y*	1254
Homozygous TMX-bearing females	*y cv*	6
	y v	40
	y sd	11
	y cv v	30
	y v sd	16
	y cv v sd	10
	y sn	19
	y g	30
	y sn g	53
Ring-bearing females	*y B/y* +	1980
Single-crossover-ring-bearing males	*y cv v sd*	313
	y v sd	336
	y sn v sd	398
	y sn sd	359
	y sn g sd	163
	y sn g	315
Triple-crossover-ring-bearing males	*y cv v*	1
	y v	4
	y v g	1
	y sd	1

these two compounds that can be demonstrated cytologically is correlated with differences in behavior. The relative proportions of the various classes of progeny from TMXB^S 9–1 and TMXB^S 9–4, in Tables 5 and 6, provide further genetic evidence of this nonidentity. This comparison of 9–1 and 9–4 can be extended to the tandem rings that they generate, where there are also differences in behavior, which will be discussed in a future paper (SANDLER and LINDSLEY unpublished).

Estimation of sperm frequencies: Analysis of the data requires an estimate of p and $1-p$ (see Table 2), i.e., of the relative proportions of X- and non-X-bearing sperm in the fertilizing population. Past experience has indicated that males carrying the Y^{S}X·Y^L chromosome with no homolog (i.e., XY/0) produce more functional nullo-XY than XY-bearing sperm, whereas XY/FR-2 males produce equal numbers of XY- and FR-2-bearing sperm (SANDLER and BRAVER 1954). Is this true in these experiments? In TMX crosses, the relative proportion of XY to nullo-XY sperm is given by the relative recovery of ring-bearing females (the yellow, wide Bar female class) and ring-bearing males (the *y* male classes) because a ring is recovered as a male or female, depending only on whether the ring-bearing egg is fertilized by an XY or a nullo-XY sperm (see Table 2). The amount of loss of the XY chromosome will be given by the difference in relative recovery of these two classes when the parental male is XY/0 as contrasted to when it is XY/FR-2. Data from crosses to TMX/0 female × XY/0 male produce

TABLE 5

Results of the cross TMXB^{S}, In(1)sc^{SL}, EN^{R}, sn g/*Dp(1;1)B*^{S} *TAG*, B^{S} y cv v sd/*FR-2 females*
× *Y*^{S}*X*·*Y*^{L}, In(1)EN, y B/*0 males*

Class of progeny	Phenotype of progeny	Observed number	
		TMXB^{S} 9–1	TMXB^{S} 9–4
Regular patroclinous males	*B*	3382	2907
Exceptional patroclinous males	*y B*	117	123
Nonhomozygous TMXB^{S}-bearing females	*B*^{S}	962	663
Homozygous TMXB^{S}-bearing females	*cv B*^{S}	3	3
	v B^{S}	8	4
	sd B^{S}	3	1
	cv v B^{S}	10	4
	v sd B^{S}	4	3
	cv v sd B^{S}	2	3
	sn B^{S}	17	3
	g B^{S}	4	3
	sn g B^{S}	4	5
TRX-bearing females	*y*	3	11
Regular ring-bearing females	*y B/y* +	969	990
Exceptional ring-bearing females	*B*/+	6	4
Regular single-crossover-ring-bearing males	*y cv v sd*	207	215
	y v sd	239	211
	y sn v sd	298	266
	y sn sd	168	161
	y sn g sd	63	38
	y sn g	51	42
Exceptional single-crossover-ring-bearing males	*v sd*	1	0
	sn v sd	2	0
	sn g sd	0	1
	sn g	0	1
Regular triple-crossover-ring-bearing males	*y v*	3	3
	y cv sd	0	1
	y cv sn g sd	1	1
	y cv v	5	0
	y v g	1	0
Exceptional triple-crossover-ring-bearing males	*cv g sd*	1	0
Others	*y v* females	0	1

single ring-bearing sons and daughters in the ratio of 1891:1980 (Table 4). From crosses of TMX/0 female × XY/FR-2 male the ratio was 192:182. The results give no indication of loss of the XY chromosome. We do not understand in what way the XY stock has changed so that loss is no longer manifest (although the XY chromosome was rebalanced before these experiments were undertaken). Whatever the reason, however, it is evident that the two classes of sperm produced by the XY/0 males used in these experiments may be taken as equally frequent.

It might be added that similar crosses were performed by MR. JOHN MERRIAM several months after the experiments reported here using the same XY chromosome and females carrying a tandem acrocentric X chromosome with Y^{L} attached as a second arm, i.e. TAX·Y^{L}/0 females. Such females produce X·Y^{L}-bearing eggs in much the same way that TMX-bearing females pro-

TABLE 6

Results of the cross TMXB^S, In(1)sc^{8L}, EN^R, sn g*/Dp(1;1)B^S TAG*, B^S y cv v sd*/0 females × Y^{S}X·Y^L*, In(1)EN, y B*/0 males*

Class of progeny	Phenotype of progeny	Observed number TMXB^S 9–1	 TMXB^S 9–4
Patroclinous males	*y B*	3648	4175
Nonhomozygous TMXB^S-bearing females	*B^S*	1196	1130
Homozygous TMXB^S-bearing females	*cv B^S*	1	3
	v B^S	12	6
	sd B^S	7	0
	cv v B^S	3	4
	v sd B^S	1	0
	cv v sd B^S	1	0
	sn B^S	9	12
	g B^S	3	1
	sn g B^S	3	1
	*sn sd B^S**	1	0
	*cv sd B^S**	0	1
TRX-bearing females	*y*	0	0
Ring-bearing females	*y B/y* +	748	1083
Single-crossover-ring-bearing males	*y cv v sd*	138	157
	y v sd	196	248
	y sn v sd	235	257
	y sn sd	133	140
	y sn g sd	59	47
	y sn g	58	32
Triple-crossover-ring bearing males	*y v*	1	0
Others	*y v* females	1	0
	B/+ females	4	0
	sn g males	2	1

* Quadruple crossovers.

duce X^c-bearing eggs. TAX·Y^L/0 female × XY/0 produced X·Y^L-bearing sons and daughters in the ratio of 572:638 and TAX·Y^L/0 female × XY/FR-2 produced them in the ratio of 77:89. Thus in quite a different system both classes of sperm are recovered equally frequently.

Distribution of exchange in TMX: The proportions of single ring-generating exchanges that occur in the six regions of TMX/FR-2 and TMXB^s/FR-2 females are shown in Figure 6. In TMX, the values do not depart seriously from the normal map distribution, which reading counter clockwise from the centromere, is 21, 11, 18, 17, 11, and 22 relative map units. The slight relative deficiency apparent in the lengths of the regions around the centromere of the TMX, *y* may be partially attributed to the proportionally greater contribution from two-exchange tetrads to normal map values as compared to the ring-generating exchanges in tandem metacentrics. In TMXB^s however, there is a clockwise shift in the distribution toward the centromere, presumably owing to the reduction of recombination in the proximal portion of the X caused by the *B^S* duplication. Since TRX generation is a rare event, the reduction in crossing over caused by

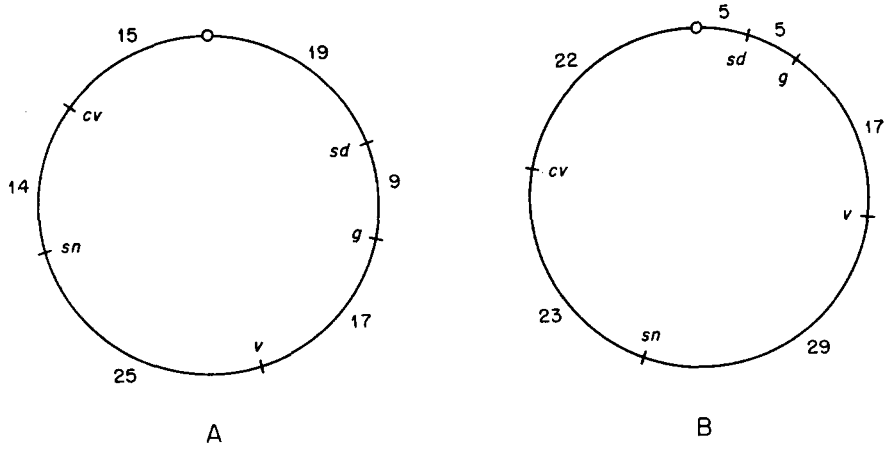


FIGURE 6.—Distribution of ring-generating exchanges for TMX, y (**A**) and TMXB^S (**B**). The proportions of ring-generating exchanges in each region among all ring-generating exchanges are indicated.

the B^S duplication implies that the duplication interferes with crossing over without itself being involved in exchange. This agrees with the experience of E. H. GRELL (1964). The distribution of exchange is quite insensitive to the presence or absence of FR-2.

Estimation of frequency of homozygosis: Homozygous TMX-bearing daughters provide a direct estimate of E_2; consequently it is important to know how well the markers used in the present experiments estimate total homozygosis. The females tested were always of the constitution shown in the lower part of Figure 1; the phase of the markers is such that any TMX that becomes simultaneously homozygous for more than one recessive has, as a complementary product either of the same exchange (BC, Figure 5) or of a complementary exchange (AC and BD, Figure 5), a TMX homozygous for some other recessive marker. Compounds homozygous for only one marker, however, may have a complementary product homozygous for only the normal allele of that marker; consequently, the complementary product will not be scored as a homozygote. To estimate the frequency of this complementary product, a sample of females homozygous for a single marker were progeny tested to determine the proportion that were heterozygous for all other markers and thus whose complement must have been homozygous for no recessive marker. From the data in Table 7, it can be seen that total homozygosis in these TMX experiments is best estimated by adding to the multiply homozygous classes the singly homozygous classes multiplied by 136/128. Of course, 8/128 of the singly homozygous class must be subtracted from the matroclinous female class. Because this correction leads to inconsequential changes in the estimate of homozygosis frequency, it has not been used.

Determination of TMX genotype for estimation of transposition frequency: Another measure of two-exchange tetrads is supplied by the incidence of transposed tandem metacentrics; as mentioned previously, a transposed compound is

TABLE 7

Tests of TMX-bearing females homozygous for single mutant alleles to determine the proportion in which the markers in repulsion remain heterozygous, i.e., the proportion whose complement is homozygous for only the normal allele of the marker in question and thus not scored as a homozygote

Female homozygous for	Number tested	Number heterozygous for all other markers
cv	4	0
sn	32	1
v	47	2
g	42	4
sd	3	1
Total	128	8

one that remains heterozygous for all the markers but in which the coupling relations have been changed by crossing over. This particular product is phenotypically indistinguishable from the matroclinous tandem metacentrics, but it can be detected by progeny testing. A single ring generated by a TMX compound can be considered as having arisen from a single crossover between the two arms of the compound attached to the same centromere. This is so irrespective of whether the crossover under consideration was part of a single- or a double-exchange event. If all the markers that are carried heterozygously in a TMX are known, then for a particular ring derivative recovered, the concomitantly produced acentric can be specified. If the point of the ring-generating exchange could be specified, the distribution of markers between the two arms of the TMX would be established. Any observed single ring is consistent, in these experiments involving five heterozygous markers, with six distributions of the five markers between the two arms of the TMX compound—one specified by assuming that the observed ring was the result of a crossover in each of the six crossover regions in the TMX. Two single rings will differ from each other in such a way that one of them must be assumed to have a crossover in a specific region and the other from a crossover in another specific region. But since it cannot be determined which ring arose from the crossover in which of the two regions in question, two possible parental compounds are consistent with the two rings. A third ring will be compatible with but one of these alternatives. Therefore, three distinct single rings produced by one TMX compound heterozygous for all the markers completely specifies the coupling relations of all the markers.

Considered in another way, a sample of three different single rings generated from a tandem metacentric will be alike for a distance on either side of the centromere. Proceeding from the centromere, say along the normal arm, the markers carried by the three rings will be the same until the point of the most proximal exchange that produced one of the three rings is reached. At this point the alleles carried by that ring will become the alternatives of those carried by the other two; i.e., from this point of departure in marker content of one ring from two others arising from the same TMX, the point of the exchange that generated that ring can be determined. As stated previously, a single ring derivative with a known point of ring-generating exchange unambiguously specifies the TMX from which it arose if all the heterozygous markers present in the TMX are known. This analysis applies to tandem compounds with any number of heterozygous markers greater than one. Triple crossover rings that result from triple exchanges represent exceptions to these generalizations, but they occur so much less frequently than single crossover rings that in practice they do not cause ambiguity (see Tables 3–6).

Only data from compounds carrying the mutants *sn* and *g* on the inverted arm and *cv*, *v*, and *sd* on the normal arm have been included in Tables 3 to 6. Enough single ring types were produced by every tested female to specify the TMX, so that no bias is introduced into the data by elimination of transposed TMX's. And, since pedigrees were kept, the frequency of transposition could be determined. The results listed in Table 8 show that a small but significant proportion of the nonhomozygous tandem metacentrics are in fact transposed.

Estimation of single ring viability: A final point that must be considered before we can proceed with the analysis pertains to the viability of the ring derivatives of the TMX's. Euchromatically, they should be identical to X^c since the TMX's are derived from *In(1)EN*, which in turn arose from X^c exclusively by heterochromatic events (see NOVITSKI 1949). They will differ heterochromatically, however, according to the compound-generating exchange that produced the TMX from which they were derived (see Figure 3). It can be argued from the roughly equal numbers of ring-bearing males and females that there are no major viability problems with the ring X's. This argument is strengthened by the normal viability observed in the single ring derivatives of the tandem ring (which are identical to those of TMXB^S 9–4) in crosses designed specifically to measure the relative viability of this element (SANDLER and LINDSLEY unpublished).

Analysis of results: The theoretical basis of the analytical methods was fully developed in the section on the expected behavior of tandem metacentrics. The data to be analyzed are presented in Table 9; they represent the known crosses of TMX females heterozygous for markers and carrying a marked homolog, accompanied where possible by data from the same TMX but without a homolog. The fifth row (TMX, *Hw f*) is a composite of NOVITSKI's data (1951, 1955) that

TABLE 8

Results of progeny tests to determine the incidence of transposed tandem metacentrics among nonhomozygous compounds

Genotype of mother	Number tested	Number transposed	
		Observed	Expected*
TMX, $y/0$	82	9	6.3
TMX, y/FR-2	7	7	5.6
TMXB^S 9–1/0	131	7	1.5
TMXB^S 9–4/0	124	3	1.1

* Expectations based on the incidence of homozygosis (see text).

TABLE 9

Summary of TMX crosses in which the compound is heterozygous for markers and carries a marked homolog with data from the same compounds with no homolog

	Classes of progeny					
	Compound-bearing females		Ring-bearing		Patroclinous males	
Genotype of mother	Non-homozygous	Homozygous	Females	Males	Regular	Exceptional
TMX, *y*/FR-2	1314	234	2135	2407	6230	143
TMXB^S 9–1/FR-2	965	55	975	1040	3382	117
TMXB^S 9–4/FR-2	674	29	994	940	2907	123
*RMX, *In(1)y*^{4}/+ /FR-2	871	96	1460	0	4241	100
†TMX, *Hw f*/FR-2	567	114	1248	1205	3288	162
TMX, *y*/0	1254	215	1980	1891	6519	. . .
TMXB^S 9–1/0	1196	41	748	820	3648	. . .
TMXB^S 9–4/0	1130	28	1083	881	4175	. . .
*RMX, *In(1)y*^{4}/+ /0	1080	100	1240	0	5585	. . .

* Data from NOVITSKI and SANDLER 1956.

† Data combined from NOVITSKI (1952, 1955) as explained in text; also corrected for unequal production of nullo XY- and XY-bearing sperm.

we constructed as follows: The numbers used are from Table 1 of his 1955 results, but since there were no heterozygous markers in those crosses, we had to use the data in Table 1 of his 1951 paper to compute the proportion of TMX-bearing females that were homozygous. It can be shown that the combined frequency of *cv* + *v* daughters from TMX, *cv* +/+ *v* mothers is equal to *cv* + *v* + 2 *cv v* daughters from TMX, *cv v*/+ + mothers. We may thus determine the proportion of the homozygotes observed in TMX, *cv v sd*/*sn g* females that would have been detected had the females been TMX, *cv* +/+ *v*, as used by NOVITSKI (1951), and thereby arrive at a factor by which his observed homozygosis should be multiplied to estimate total homozygosis. Such an estimate was used to apportion the TMX-bearing daughters in NOVITSKI's 1955 data among homozygotes and non-homozygotes. A similar procedure was used in estimating total homozygosis in the RMX, *In(1)y*^{4}/*y v f* crosses. In addition, the rings generated by RMX, *In(1)y*^{4}/+ are duplicated for the region proximal to the right breakpoint of *In(1)y*^{4} (i.e., salivary regions 18A through 20); this duplicated ring is inviable in the male and shows reduced viability in heterozygous females. Consequently, the recovery of the ring from RMX, *In(1)y*^{4}/+ was corrected upward to be equivalent to that of X^{c2}, the ring generated by TMX, *Hw f* (see NOVITSKI and LINDSLEY 1950). The data used in making the correction are given in Table 4 of NOVITSKI and SANDLER (1956).

NOVITSKI and SANDLER (1956) showed that recovery of the single X derivative from a tandem compound is higher when the compound has a homolog (FR-2 or a Y chromosome) than when it has not. They postulated that the absence of a homolog results in the inviability of zygotes carrying a single X derivative of the tandem compound rather than a change in the parameters of meiosis because of the relative insensitivity of the proportion of matroclinous females to the presence

TABLE 10

Effect of the presence of a homolog (FR-2) on recovery of ring chromosome derivatives of tandem metacentrics compared with the recovery of tandem metacentrics

Genotype of females	Total rings	Total tandem metacentrics
TMX, y/0	0.59	0.23
TMX, y/FR-2	0.71	0.24
TMXB^S 9–1/0	0.43	0.34
TMXB^S 9–1/FR-2	0.58	0.29
TMXB^S 9–4/0	0.47	0.28
TMXB^S 9–4/FR-2	0.64	0.23
RMX, $\underline{In(1)y^4/+}$/0	0.22	0.21
RMX, $\underline{In(1)y^4/+}$/FR-2	0.34	0.22

Recovered classes are expressed as the proportion of all patroclinous males.

or absence of a homolog. That this is the case in the data presented in Table 9 may be seen by comparing the proportions of ring-bearing and TMX-bearing progeny from TMX/0 and TMX/FR-2 (see Table 10). The mechanism of this effect of a homolog on ring recovery eludes understanding. However, because the incidence of single rings recovered from TMX/0 females is suspect and because it is not possible to score exceptional patroclinous males unless the compound-bearing females carry a marked homolog, initial analysis will be made from data from crosses in which the females carried FR-2.

Least-squares estimates of the parameters in the equations in Table 2 were obtained for the TMX/FR-2 crosses in Table 9, on the assumption that double second-anaphase bridges result in exceptional patroclinous males. The expected numbers of individuals in the different classes were computed from the estimated parameters and compared with observations by chi-square. In every instance the probability of obtaining a chi-square as high as or higher than the one computed was less than 0.05. Furthermore, almost the entire value of chi-square came from homozygous TMX-bearing females and the exceptional patroclinous males. There were more homozygotes and fewer exceptional patroclinous males than expected among the progeny of TMX, y females, whereas the converse was true in the remainder of the cases.

Because the homozygous females represent a direct measure of E_2, whereas the relation between exceptional patroclinous males and E_2 is hypothetical, we attempted fits by assuming that double bridges are lethal and disregarding the exceptional patroclinous males. In this case the fits were good and the estimates of the parameters were reasonable (summarized in Table 11). The agreement between TMX, y and TMX, $Hw\ f$ is reasonable, as is that between TMXB^S 9–1 and 9–4. RMX, $\underline{In(1)y^4/+}$ and the two TMXB^S chromosomes show the reduction in total exchange predicted from their structure. Finally, TMXB^S 9–1 and 9–4 yield lower estimates of c than the others. The estimates from TMX, y agree rather well with similar estimates from tandem acrocentric and tandem ring compounds, which in turn resemble those from normal unattached X's except

TABLE 11

Results of tetrad analysis of progeny from TMX/FR-2 crosses presented in Table 9

Compound	E_0	E_1	E_2	c	Map length
TMX, *y*	0.159	0.574	0.267	0.94	0.554
TMXB^S 9–1	0.177	0.738	0.085	0.74	0.454
TMXB^S 9–4	0.135	0.809	0.056	0.78	0.461
RMX, *In(1)y*^{4}*/+*	0.154	0.695	0.151	0.91	0.498
TMX, *Hw f*	0.104	0.673	0.223	0.88	0.559

Exceptional patroclinous males are assumed to be surviving presumptive lethal zygotes and are omitted from the data. (Map length is computed as $\frac{1}{2}E_1 + E_2$.)

that total map distance in somewhat reduced (SANDLER and LINDSLEY 1963, unpublished).

From the number of homozygotes observed per nonhomozygous compound-bearing female, we can estimate the proportion of nonhomozygotes that should carry transposed TMX's and compare this expectation with observation. The equations in Table 2 show that homozygous TMX females should be 2(3–2c) times as frequent as transposed females; thus the ratio of homozygous TMX females to nonhomozygous TMX females should be larger by the same factor than the ratio of transposed TMX females to nonhomozygous TMX females. Knowing the former ratio and *c*, we may therefore compute the number of transposed TMX females expected in a particular sample of nonhomozygous TMX females. The homozygosis data from Table 9 and estimates of *c* from Table 11 were used in computing the expected numbers of transposed TMX females shown in Table 8. The observed number is higher than expected in every instance; but, because the numbers involved are small, we attribute this deviation to sampling error and are inclined to believe that the homozygotes and transposes form a consistent set of observations yielding comparable estimates of E_2.

The foregoing analysis suggests that persistence of double second-anaphase bridges is not the explanation of the exceptional patroclinous males, but it provides little insight into the source of this class, except to show that the data are compatible with the hypothesis that some fraction of the presumptive lethal zygotes survive as exceptional patroclinous males. One source of exceptional patroclinous males that has been mentioned before is from nondisjunction of the TMX from FR-2 at the first meiotic division. The incidence of exceptional patroclinous males arising from nondisjunction may be estimated from the frequency of the reciprocal products, i.e., the products that carry both a TMX or a TMX derivative and FR-2. The incidence of such trisomic exceptions is very low, as can be seen for TMX-bearing daughters of TMX, *y* females and X^c progeny of both TMX, *y* and TMXB^S females (see Tables 3 and 5). In these cases, nondisjunction accounts for perhaps as much as 20 percent of the exceptional patroclinous males. The involvement of exchange in the origin of the remaining exceptional patroclinous males is suggested by NOVITSKI's observation (1955) that heterozygosis for *In(1)dl-49* (i.e., TMX, *In(1)dl-49/+*) drastically reduces the incidence of such males and homozygosis for the uninverted arm results in a return of high production of exceptional patroclinous males. It may be noted that there is a rough inverse relation between the number of exceptional patroclinous males in Table 9 and the values of c in Table 11. This has suggested to us that perhaps loss of the ring chromosome from presumptive X^c-bearing zygotes gives rise to a sizable fraction of the exceptional patroclinous males, which would lead to reduced recovery of X^c and thus to an underestimate of c. To inquire into the compatibility of such a hypothesis with the data, we added the exceptional patroclinous male class to the X^c-bearing females and again obtained least-squares estimates of the parameters. This procedure results in higher estimates of E_0 and E_2 and lower estimates of E_1 than those in Table 11; the estimates of c are also increased and cluster around unity. In his initial work on nonrandom disjunction in TMX chromosomes, NOVITSKI (1951) recognized that his data were compatible with some loss of newly generated rings and higher values of c than those calculated on the assumption of no ring loss.

In the foregoing discussion it was pointed out that data from TMX/0 crosses agree with the earlier data that led NOVITSKI and SANDLER (1956) to postulate preferental mortality of the single X chromosomes generated by exchange in tandem compound X chromosomes (TCX) in TCX/0 females compared with TCX/FR-2. Perhaps the data could be explained equally well by postulating chromosome loss rather than zygote mortality. Suppose that a fraction of the single X derivatives from TCX-bearing females were lost and that this fraction were higher in TCX/0 than in TCX/FR-2 females. The zygotes from which an X was lost would appear as exceptional patroclinous males in TCX/FR-2 crosses but would be indistinguishable from the regular patroclinous male classes in TCX/0 crosses. To test this hypothesis, we fitted the data from both the TMX/FR-2 and TMX/0 crosses simultaneously to the equations in Table 2 to obtain a single estimate of E_i and c for both sets of data. X^c loss for TMX/FR-2 was estimated directly from exceptional patroclinous males; for TMX/0 the patroclinous males were considered to be the sum of presumptive non-X-bearing eggs and that fraction of the presumptive ring-X-bearing ova from which the ring had been lost, and ring loss was estimated from the data. The agreements between observation and expectation based on this model were quite good in TMX, y and RMX, $\underline{In(1)y^4/+}$, but not in the two TMXB^S chromosomes. In TMXB^S 9–1 and 9–4, the high chi-square values are derived almost exclusively from the nonhomozygous TMX-bearing female classes; this class is lower than expected from TMXB^S/FR-2 crosses and higher than expected from TMXB^S/0 crosses (this result is reflected in the last column of Table 10). Estimates of the parameters based on this model are presented in Table 12. It should be pointed out that X^c loss in TMX/FR-2 is overestimated to the extent that nondisjunction of TMX from FR-2 contributes exceptional patroclinous males. Actually, these estimates based on both the TMX/FR-2 and TMX/0 results agree quite closely with those from the TMX/FR-2 results alone when the ring-loss model is used. Because the expectations based on this model and the observations agree very well in TMX, y and RMX, $\underline{In(1)y^4/+}$ and diverge in a systematic way in the case of TMXB^S 9–1 and 9–4, we believe the

TABLE 12

Estimates of parameters from progenies TMX/FR-2 and TMX/0 females presented in Table 9

Compound	E_0	E_1	E_2	c	X^c loss from TMX/FR-2	X^c loss from TMX/0
TMX, *y*	0.182	0.485	0.333	1.06	0.063	0.181
TMXB^S 9–1	0.311	0.571	0.118	1.01	0.107	0.291
TMXB^S 9–4	0.291	0.624	0.085	1.09	0.110	0.302
RMX, *In(1)y^4/+*	0.164	0.690	0.146	0.92	0.064	0.324

Parameters were derived from simultaneous fitting of data from TMX/FR-2 and TMX/0 to the hypothesis that loss of X^c from presumptive X^c/XY zygotes produces exceptional patroclinous males among progeny of TMX/FR-2 females and adds to the patroclinous male class among progeny of TMX/0 females. For a particular TMX, the parameters E_i and c are assumed to be the same for TMX/FR-2 and TMX/0 females, but the loss of newly generated rings is assumed to vary.

model is probably valid and that, in TMXB^S, an additional factor is coming into play for which we have not adequately accounted in the model. Actually if we were to relax some of the constraints in the model, i.e., that E_i and c be identical in TMX/FR-2 and TMX/0 crosses, the agreement in TMXB^S would undoubtedly improve. This model has the unifying virtue that it attempts to account for the exceptional patroclinous males and the differences in the ratios of observed classes from TMX/FR-2 versus TMX/0 females by the same mechanism.

We wish to express our thanks to MRS. AVERIL ROSENFELD and MR. JOSEPH OREM for their invaluable assistance in collecting the data presented in this report, and to MR. HERBERT ARMENTROUT for his assistance in preparing the cytological figures.

SUMMARY

Well marked tandem metacentric compound X chromosomes of two structural types (see Figure 1) were synthesized and their behavior in crosses was investigated. In addition to the data from these newly synthesized tandem metacentrics, previously published data on other tandem metacentrics were considered. The following conclusions emerge from an analysis of tandem metacentric data: (1) The data do not fit the hypothesis that nullo-X eggs (detected as exceptional patroclinous males) result from the exclusion of double second-anaphase bridges from the egg nucleus; such bridges, therefore, probably result in inviable zygotes. (2) The data are compatible with the hypothesis that nullo-X eggs arise through the loss of a fraction of the newly generated single-ring X chromosomes and that ring loss in lower in the progeny of tandem metacentric X-bearing females that carry a marked Y-chromosome fragment than of those that carry none. (3) The exchange distribution in tandem metacentrics, as in other tandem compounds, is comparable with that of free X chromosomes, and the coefficient of nonrandomness approximates unity.

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