ON RECOMBINATION-DEFECTIVE MEIOTIC MUTANTS IN *DROSOPHILA MELANOGASTER*[1]

ADELAIDE T. C. CARPENTER[2] AND L. SANDLER

Department of Genetics, University of Washington, Seattle, Washington 98195

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ABSTRACT

The genetic effects of four recombination-defective meiotic mutants in *D. melanogaster* on recombination, segregation and the relationship between the two have been examined. The results suggest the following. (1) The anomalous meiotic segregation observed in females carrying recombination-defective meiotic mutants is a normal consequence of the reduction in exchange; each recombination-defective mutant can, therefore, be defined by a single lesion in the control of recombination. (2) Of the operations used to date to characterize this lesion, the most informative is whether the decrease in recombination is uniform along the chromosome arm or nonuniform; in particular, if the formation of recombinants is visualized as a two-step process consisting of the establishment of possible exchange points (exchange preconditions) followed by exchange itself, then mutants that uniformly decrease crossing over involve defects in the second step while mutants that result in a nonuniform decrease involve defects in the establishment of exchange preconditions. (3) Of the fourteen loci identified by recombination-defective meiotic mutants, only one (with two alleles) is involved in exchange itself; the others all reduce recombination most drastically in distal regions, suggesting that the establishment of exchange preconditions involves polar processes. (4) A very general description of the polar establishment of exchange preconditions is presented; this description has the property that if a precondition meiotic mutant affects interference, the coefficient of coincidence will be increased in proportion to the decrease in recombination which is what is observed for all recombination-defective meiotic mutants studied to date.

IN *D. melanogaster* there have so far been recorded seventeen meiotic mutants, representing fourteen loci, that result in marked decreases in recombination for all chromosome pairs in females (they have no recombinational or disjunctional effects in males). The phenotype of these recombination-defective meiotic mutants, in addition to the decrease in crossing over, is anomalous meiotic chromosome segregation. However, the evidence indicates that each mutant can be characterized by a single lesion in the control of recombination with the segregational abnormalities being the consequence of the normal processes of disjunction acting in meiocytes with abnormal recombination. For tabulations of meiotic mutants, discussion of the points raised here, and references, see reviews by BAKER and HALL (1974) and SANDLER and LINDSLEY (1974).

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[2] Present address: Department of Zoology, University of Wisconsin, Madison, Wisconsin 53706.

With respect to recombination, it is possible to separate recombination-defective mutants according to four criteria. (1) The decrease in crossing over can be uniform along a chromosome arm or nonuniform; when nonuniform, the decrease is always most marked distally. (2) The decrease in recombination may be accompanied by a change in the coefficient of coincidence or not; when coincidence is altered, it is always increased. (3) The mutants may or may not exhibit dominant effects on recombination. (4) The interchromosomal effect of heterozygous heterologous inversions on recombination may be manifested or abolished in mutant individuals.

It has been suggested that those mutants that result in an altered coefficient of coincidence are involved in the establishment of preconditions for exchange while the others may affect the process of exchange itself (LINDSLEY *et al.* 1968; SANDLER *et al.* 1968). By this criterion, it is found that most mutants affect exchange preconditions and also exhibit a nonuniform reduction in recombination, while mutants at one locus affect exchange directly and exhibit a uniform reduction. Among the former, the interchromosomal effect may be manifested or not, while in the latter instance it is probably not (see below). These observations suggest that recombination-defective meiotic mutants can be separated into at least three groups: interchromosomal-effect-sensitive precondition mutants, interchromosomal-effect-insensitive precondition mutants, and exchange mutants. While these categories are operational, the distinction between preconditions and exchange raises two problems. Firstly, it is not clear why the coefficient of coincidence should be increased—implying relatively more frequent multiple exchanges—in every precondition mutant. Secondly, this analysis in its most simple form suggests that chromosome *4* would be insensitive to the effects of recombination-defective meiotic mutants because chromosome *4* does not undergo exchange in wild-type (or presumably in mutant) individuals and segregates by the exchange-independent process of distributive disjunction (for a review of the distributive system and references, see GRELL 1969). In fact, however, chromosome *4* segregates anomalously under the influence of every recombination-defective meiotic mutant.

For these reasons, it seems worthwhile to consider alternative criteria for establishing a sequence of action of the normal alleles of recombination-defective meiotic mutants. To this end, we have examined the meiotic behavior of two recombination-defective meiotic mutants exhibiting nonuniform decreases in crossing over (*abo* = abnormal oocyte and *mei-218*) and the two alleles of the gene that result in a uniform decrease (*mei-9* and *mei-9^{b}*).

MATERIALS AND METHODS

All crosses were performed on standard Drosophila cornmeal-molasses-agar medium at 25° (unless otherwise noted) utilizing one female and 2–3 male parents per shell vial. Parents were transferred to fresh medium after five days and discarded after an additional five days; all progeny emerging before day 18 were scored (introduction of parents = day 0). Crosses to measure recombination frequencies and most other crosses were initiated with females of uniform age (12–14 hours after eclosion). Progeny of the following types are excluded from the tabulations presented: haplo-*4*, triploid, intersex, metafemale. The relatively rare haplo-*4*/diplo-*4*

mosaics and gynandromorphs are tabulated as the presumptive original diploids. Tetra-*4* progeny are considered to be lethal in calculations of frequencies of fourth chromosome nondisjunction. (Fourth chromosome nondisjunction = (*#44* + *#0*/total), compensated as below for lethal *X* exceptional zygotes.) If the viability of tetra-*4* progeny (MOORE and GRELL 1972) were taken into account, the frequency of fourth chromosome nondisjunction would be increased slightly. All frequencies of nondisjunction are expressed as gametic frequencies; the lethality of triplo-*X* and nullo-*X* zygotes is compensated for by doubling the observed numbers of *X*-exceptional progeny before further computation. For descriptions of chromosomes and mutants used in this study, see LINDSLEY and GRELL (1968).

The mutant *abo* is a second chromosome recessive that maps three units proximal to *J* which is at 41 on the standard map (MANGE and SANDLER 1973). It has two apparently independent phenotypes (see Table 1): a maternal effect that results in egg mortality with a probability that is a function of the amount of sex-chromosome heterochromatin carried either by a mutant mother or by her nonmutant progeny (SANDLER 1970, 1972) and a meiotic effect, operative in females only, resulting in increased nondisjunction and decreased recombination for all chromosome pairs studied (SANDLER *et al.* 1968; MANGE and SANDLER 1973). The two effects have not yet been genetically separable. In this report, we will ignore the maternal effect.

The meiotic mutants *mei-9*, *mei-9^b*, and *mei-218* are sex-linked recessives that result in increased nondisjunction and decreased recombination for all chromosome pairs (BAKER and CARPENTER 1972). The mutant *mei-9* is at approximately 5 on the standard map (*7 pn mei-9 cv+*, 6 *pn mei-9+ cv+*, 9 *pn+ mei-9 cv*, and 4 *pn+ mei-9+ cv* recombinants among 302 unselected chromosomes examined from *y mei-9/y pn mei-9+ cv m f·Dp(1,1)sc^{V1}, y+* females); *mei-9^b* also maps to approximately 5 (10 *pn mei-9^b cv+*, 12 *pn mei-9+ cv+*, 11 *pn+ mei-9^b cv*, and 2 *pn+ mei-9+ cv* recombinants among 369 unselected chromosomes tested from *y mei-9^b nod/y pn mei-9+ cv* (*m nod+*) *f·y+* females). The mutants are allelic because *mei-9/mei-9^b* females exhibit high frequencies of nondisjunction of chromosomes *1* and *4* (24% and 11%, respectively; data not presented). The mutant *mei-218* maps to 57 on the basis that no recombinants between it and *f* (56.7) were found among 61 recombinants between *m* and *Dp(1,1)sc^{V1}, y+* from *y mei-218/y pn cv m* (*f mei-218+*)·*y+* females (196 unselected chromosomes tested).

RESULTS AND DISCUSSION

In this study, we have examined segregation, recombination, and their interrelation under the influence of the four meiotic mutants under investigation. Data on the segregation of chromosomes *1* and *4* in homozygous *abo* females were presented in Table 1. Analogous data for the case of *mei-9^b*, including sex-chromosome segregation in *XXY* females, are presented in Table 2. Recombination data for *X* chromosomes marked at the tip, middle, and centromere under the influence of *abo*, with and without a heterozygous heterologous inversion, are given in Table 3; *abo* recombination data for more densely-marked *X* chromosomes are given in Table 4. In Table 5 are presented *X*-chromosome recombination and *X* and fourth-chromosome segregation data for the mutants *mei-9* and *mei-218*, including the effects of heterozygous heterologous inversions. The results of experiments monitoring *X*-chromosome segregation and second-chromosome recombination in *mei-9*, *mei-9^b*, and *mei-218* females, both in the heterozygous and homozygous condition, are shown in Table 6. In Table 7, the segregation of chromosomes *1* and *4* is followed along with recombination in an interval on chromosome *3* in *mei-9* and *mei-218* females. The data on the relationship between recombination in one chromosome and the disjunction of a different chromosome are summarized for *mei-9*, *mei-9^b*, and *mei-218* in Table 8. The precise genotypes of the parents in every cross are given in the table headings.

TABLE 1

Results of crosses of females of the constitution y pn v·Dp(1,1)sc^{v1}, y$^+$/y; spa^{pol}/spa^{pol} *by* Y^{S}X·Y^L, v f B/0; C(4)RM, ci ey^R/0 *males*

Type of progeny for *X* chromosomes	Fourth chromosome constitution of progeny					
	abo/+ mothers			*abo*/*abo* mothers		
	4	*44*	*0*	*4*	*44*	*0*
Regular ♀♀	2402	0	0	2842	8	15
Regular ♂♂	2250	0	0	301	4	2
Exceptional ♀♀	0	0	0	8	1	3
Exceptional ♂♂	0	0	0	14	3	2
X exceptions/total*		0			0.0192	
4 exceptions/total*		0			0.0145	
♂-recovery†			0.11			

The male progeny are not separated into crossover classes.

* *X* exceptions are here, and in the tables that follow, doubled before further computations to compensate for the fact that only one-half of *X*-exceptional gametes are recoverable as viable progeny.

† ♂-recovery is the recovery relative to regular females, of regular males from homozygous *abo* mothers relative to the heterozygous *abo* controls. The reduced recovery of *X0* males is diagnostic of the maternal effect of *abo*.

Segregation: The disjunctional behavior of chromosomes under the influence of the four meiotic mutants under consideration here are qualitatively similar. First, the nondisjunction occurs at the first meiotic division since centromere-linked markers are heterozygous in exceptional progeny (BAKER and CARPENTER 1972 for the case of *mei-9*, *mei-9^b*, and *mei-218*; footnote to Table 3 for the case of *abo*).

Secondly, chromosomes that nondisjoin are mostly or exclusively nonrecombinant. For *abo* this too is seen from the footnote to Table 3. In the case of *mei-9*, a sample of diplo-*X* exceptional females from the *SM1*$^+$, *TM2*$^+$ crosses recorded in Table 5 were examined and progeny-tested to determine their *X*-chromosome constitutions. Of 1243 such females, 1083 were fertile and carried noncrossover nonsister chromosomes; 147 were semisterile or sterile, but phenotypically wild-type; 10 carried one crossover and one noncrossover *X* chromosome; 2 carried reciprocal crossovers; and one was an equational exception. Thus, there were 14 recombinants recovered among 2486 chromosomes that had nondisjoined, which is tenfold lower than expected from the recombination frequency among *X*-regular sons. Moreover, since there was but one equational exception, nondisjunction occurs at the first division.

The same conclusion can be drawn concerning *X*-chromosome nondisjunction in *mei-218* females. Each of the 436 + 390 diplo-*X* exceptional females observed in the crosses in Table 5 was phenotypically wild-type, indicating that nondisjunction occurs exclusively at the first meiotic division and strongly suggesting

TABLE 2

Results of crosses of females of the constitution X/X/(y+Y); spa^{pol}/spa^{pol} *carrying the indicated sex chromosomes by* Y^{s}X·Y^{L}, y v f B*/0; C(4)RM, ci ey^{R}/0 *males*

		Sex chromosomes of parental female					
		y/y	*y/y/y^{+}Y*		*y cv g^{b}/y cv g^{b}+*	*y cv g^{b}/y cv g^{b}/y^{+}Y*	
	Y gamete type of females:	-	*Y*	*0*	-	*Y*	*0*
X, 4 gamete types females	males						
X 4	*XY 44*	3080	336	1675	1181	3	557
X 4	*0 44*	4267	1909	2201	942	444	425
X 44	*XY 0*	1	0	153	35	0	95
X 44	*0 0*	0	4	128	20	13	46
X 0	*XY 44*	4	41	3	33	0	26
X 0	*0 44*	0	116	5	19	26	16
XX 4	*0 44*	5	0	98	82	18	378
XX 44	*0 0*	0	0	2	3	9	26
XX 0	*0 44*	6	0	1	12	7	14
0 4	*XY 44*	6	59	1	125	230	34
0 44	*XY 0*	5	4	0	22	25	8
0 0	*XY 44*	0	0	0	22	17	17
Total		7374	6736		2496	2434	
$\frac{XXO + OY}{X}$ exceptions			164/165			690/783	
$\frac{44O + OY^{**}}{4}$ exceptions			244/253			72/101	
Nondisjunction							
X		0.0059	0.0478		0.1926	0.4868	
4		0.0037	0.0672		0.0815	0.1455	

* A spontaneous *y* derivative of the *Y^{s}X·Y^{L}, v f B* chromosome.
† *mei-9*, *mei-9^{b}*, and *mei-218* will, in this and subsequent tables, be listed as *9*, *9^{b}* and *218*.
** Calculated among *X*-regular males.

that nondisjunction involves primarily or exclusively no-exchange tetrads. Thus, if nondisjunction and exchange were independent, exchange tetrads should be as frequent among *X*-exceptional females as among *X*-regular males; half of the diplo-*X* exceptions resulting from nondisjunction of exchange tetrads should be phenotypically detectable; consequently 15/436 (3.4%) and 30/390 (7.7%) of the diplo-*X* exceptional daughters of *mei-218* mothers recorded in Table 5 should have been homozygous for one or more of the *X*-linked recessive visibles, but none were.

Although *X*-nondisjunction involves primarily or exclusively no-exchange tetrads, only a fraction of such tetrads are recovered as *X*-exceptional progeny.

TABLE 3

Results of crosses of females of the constitution y pn v·Dp(1,1)sc^{v1}, y+/y *carrying the indicated second and third chromosomes by* B/Y; +/+; +/+ *males*

Progeny type*	Autosomal constitution of parental females: $\frac{abo}{+}$;$\frac{+}{+}$	$\frac{abo}{abo}$;$\frac{+}{+}$	$\frac{abo}{+}$;$\frac{TM2}{+}$	$\frac{abo}{abo}$;$\frac{TM2}{+}$
Regular ♀♀	9878	4399	3537	1740
Exceptional ♀♀	0	39†	0	5
Exceptional ♂♂	2	17	1	7
Regular ♂♂ Total	9754	3315	3434	1361
Noncrossover	4449	1986	1317	619
Single Crossover				
1	2455	498	841	330
2	2166	716	839	300
Double Crossover	684	115	437	112
Total Progeny	19634	7770	6972	3113
Map:				
1	32.2	18.5	37.2	32.5
2	29.2	25.1	37.2	30.3
Total Map	61.4	43.6	74.4	62.8
C	0.75	0.75	0.92	0.84
Map relative to control:				
1	1	0.58	1.16	1.01
2	1	0.86	1.27	1.04
Total	1	0.71	1.21	1.02

* Region 1 is *pn-v;* region 2 is *v-y*+.

† 26 of these females were progeny-tested and all proved to carry two nonsister noncrossover *X* chromosomes; all 39 were phenotypically *y*+.

This can be seen most easily by noting that, for each mutant, the number of no-exchange *X* tetrads among regular progeny is higher than is the number of *X*-exceptional gametes among all gametes. If the two homologs of all no-exchange tetrads disjoined randomly, the two numbers would be equal.

Although these mutants are characterized by an increase in primary nondisjunction, it seems that the distributive system is operative in that nonhomologous chromosomes segregate from one another in agreement with the properties of the distributive pairing system; the lines of supporting evidence for *mei-9*, *mei-9^b*, and *mei-218* are found in BAKER and CARPENTER (1972). An additional corroborating observation is the pattern of sex-chromosome segregation in *XXY* females homozygous for *mei-9^b* (Table 2). Here distributive disjunction can be seen in two ways. First, as in the controls, *X* (and *4*) nondisjunction is higher in *mei-9^b*,

TABLE 4

Results of crosses of females of the constitution y pn cv m f·Dp(1,1)sc^{v1}, y+/y *carrying the indicated second chromosomes by* B/Y; +/+ *males*

Progeny type*	Second chromosome constitution of parental females *abo/+*	*abo/abo*		Second chromosome constitution of parental females *abo/+*	*abo/abo*
Regular ♀♀	7186	2576	Map:		
Exceptional ♀♀	0	27	1	11.6	5.3
Exceptional ♂♂	2	19	2	28.7	17.3
Regular males, Total	6908	1653	3	13.6	11.1
Noncrossover	3106	993	4	8.8	10.1
Single Crossover			Total	62.7	43.8
1	562	68	C(1,2)	0.21	0.33
2	1663	241	C(2,3)	0.52	0.54
3	668	151	C(3,4)	0.21	0.27
4	380	135	Map relative to control		
Double Crossover			1	1	0.46
1,4	79	4	2	1	0.60
1,3	113	11	3	1	0.82
1,2	47	5	4	1	1.15
2,4	135	23	Total	1	0.70
2,3	137	17			
3,4	15	5			
Triple Crossover	3	0			

* Region 1 is *pn-cv*; region 2 is *cv-m*; region 3 is *m-f*; and region 4 is *f-y+*.

XXY females than in *mei-9^b*, *XX* females. Second, again as in the control, the vast majority of *X*-exceptional gametes from *mei-9^b XXY* females are of the types expected from *XX*-from-*Y* nonhomologous segregations. That not all *X*-exceptions in *mei-9^b* can be attributed to *XX*-from-*Y* segregations is likely a consequence of the high frequency of no-exchange autosomes which can also disjoin distributively from the *X*'s. This same disjunctional pattern is also seen, but to a lesser extent, for *44*-from-*Y* segregations.

Finally, it will be noted that nondisjunction of chromosomes *1* and *4* are positively correlated (Tables 1, 2, and 5), but, unlike the cases involving two major chromosomes (BAKER and CARPENTER 1972), the correlation does not appear to be the result of nonhomologous segregations because there is no excess of diplo-nullo exceptions over the diplo-diplo and nullo-nullo classes. Such an excess is the diagnostic criterion of nonhomologous disjunction—the tendency for two nonhomologs to disjoin.

In summary, then, recombination-defective meiotic mutants show the following segregational properties: nondisjunction occurs at the first meiotic division,

TABLE 5

Results of crosses of females of the constitution X/X; spa^{pol}/spa^{pol} *carrying the indicated* X, *second and third chromosomes by* $Y^{S}X{\cdot}Y^{L}$, v f B/0; C(4)RM, ci $ey^{R}/0$ *males. For* a, X-*chromosome markers are* y pn + + +·-/y + cv m f·Dp(1,1)sc^{V1}, y^{+}; *for* b, *markers are* y pn + + +·Dp(1,1)sc^{V1}, y^{+}/y^{2} + cv v wy·-

X, second and third chromosome constitution of parental females and fourth chromosomes of progeny

	a							b					
Progeny type*	$\frac{+\ +\ +}{X^{1}\ 2^{+}\ 3^{+}}$ ♀	$\frac{♀\ +\ +}{3^{2}\ 2^{+}\ 3^{+}}$ ♀	♂	$\frac{+\ SM1\ TM2}{X^{1}\ 2^{+}\ 3^{+}}$ ♀	♂	$\frac{♀\ SM1\ TM2}{3^{2}\ 2^{+}\ 3^{+}}$ ♀	♂	$\frac{+\ +\ +}{X^{1}\ 2^{+}\ 3^{+}}$ ♀	$\frac{218\ +\ +}{218^{1}\ 2^{+}\ 3^{+}}$ ♀	♂	$\frac{+\ SM1\ TM2}{X^{1}\ 2^{+}\ 3^{+}}$ ♀	$\frac{218\ SM1\ TM2}{218^{1}\ 2^{+}\ 3^{+}}$ ♀	♂
Regular ♀♀	2526	9907	1301	914	5	1225	288	1217**	2424	342	945**	1161	283
Exceptional ♀♀	0	1367	336	0	0	249	120	0	332	104	0	260	130
Exceptional ♂♂	0	1512	774	0	0	244	196	0	462	249	0	308	295
Regular ♂♂, Total	2589	9686	904	919	6	1008	193	1284	2559	261	1193	1258	273
Noncrossover	1226	8891	886	237	1	799	186	578	2461	259	290	1146	273
Single crossover													
1	-	-	-	-	-	-	-	2	0	0	9	3	0
2	222	167	2	91	0	50	2	88	9	1	106	16	0
3	585	368	10	155	1	96	2	226	24	1	159	24	0
4	255	134	2	100	1	37	1	85	14	0	65	16	0
5	128	120	4	58	2	23	2	221	49	0	179	50	0
Double crossover													
Σ1,2-1,5	-	-	-	-	-	-	-	0	0	0	12	0	0
2,5	23	2	0	34	0	0	0	27	1	0	72	1	0
2,4	40	0	0	56	0	0	0	2	0	0	25	0	0
2,3	23	0	0	28	0	1	0	1	0	0	31	0	0
3,5	38	2	0	46	0	0	0	41	0	0	132	0	0
3,4	39	2	0	56	0	2	0	3	0	0	29	0	0
4,5	8	0	0	24	0	0	0	9	0	0	34	1	0
Triple crossover	2	0	0	34	1	0	0	1	0	0	50	1	0
Quadruple crossover	0	0	0	0	0	0	0	0	1	0	0	0	0
Total Progeny	5115	25787		1844		3523		2501	6733		2138	3968	
# Parental ♀	42	536		22		165		20	118		20	117	
Map: †													
1	-	-		-		-		0.31	0.050		3.86	0.238	
2	11.94	1.173		25.08		2.637		9.27	0.302		22.88	0.674	
3	26.54	2.620		34.49		5.025		21.18	0.655		32.27	0.990	
4	13.29	0.947		28.00		1.990		7.71	0.378		15.51	0.713	
5	7.65	0.878		20.65		1.244		23.29	1.260		39.56	2.100	
Total	59.42	5.618		108.22		10.896		61.76	2.645		114.08	4.715	
Map relative to control:													
1	-	-		-		-		1	0.161		12.45	0.768	
2	1	0.098		2.10		0.221		1	0.033		2.47	0.073	
3	1	0.099		1.30		0.189		1	0.031		1.52	0.047	
4	1	0.071		2.11		0.150		1	0.049		2.01	0.092	
5	1	0.114		2.69		0.162		1	0.054		1.70	0.090	
Total	1	0.095		1.82		0.183		1	0.043		1.85	0.076	

* For *a*, region 1 is unmarked; region 2 is *pn-cv*; region 3 is *cv-m*; region 4 is *m-f*; and region 5 is *f-y*+. For *b*, region 1 is *y-pn* (only half of the crossovers in this region are detectable); region 2 is *pn-cv*; region 3 is *cv-v*; region 4 is *v-wy*; and region 5 is *wy-y*+.

† Calculated among males + *X*-exceptions.

** Includes 1 fourth-chromosome exception.

TABLE 6

The results of crosses of females of the constitution X/X; al dp b pr cn/+ + + + +; spa^{pol}/spa^{pol} *carrying the indicated* X *chromosomes by* +/Y; al dp b pr cn/al dp b pr cn; +/+ *males*

	X-chromosome constitution of parental females and of ova										
Progeny type†	y/y* / X	y cv g^b/y cv g^b / X		y g/y g / X		y 218/y 218 / X		y/y / X	y cv g^b/y / X	y g/y / X	y 218/y / X
			y cv g^b/+ / XX+0		y g/+ / XX+0		y 218/+ / XX+0				
Noncrossover	6308	22046	2404	10960	1448	12107	2520	4090	2902	2608	3245
Single crossover											
1	1365	499	37	146	9	100	19	917	559	483	695
2	2977	1137	53	258	17	216	22	1998	1329	1123	1620
3	416	205	8	53	2	66	14	327	222	190	316
4	151	64	3	46	4	124	16	72	56	41	93
Double crossover											
1,4	24	1	0	0	0	0	0	17	11	4	22
1,3	61	4	0	0	0	1	0	34	23	20	43
1,2	84	8	1	4	0	0	0	57	28	17	48
2,4	50	2	0	0	0	0	0	23	27	15	38
2,3	48	4	0	1	0	0	0	39	19	20	49
3,4	9	1	0	0	0	0	0	4	1	3	7
Triple crossover	2	0	0	0	0	0	0	3	6	1	4
Total Progeny	11495	26477		12948		15205		7581	5183	4525	6180
Map											
1	13.36	2.08		1.23		0.79		13.56	12.06	11.60	13.11
2	27.50	4.55		2.16		1.57		27.96	27.18	25.99	28.43
3	4.65	0.84		0.43		0.53		5.34	5.17	5.17	6.78
4	2.04	0.27		0.39		0.92		1.56	1.93	1.39	2.65
Total	47.55	7.74		4.21		3.81		48.42	46.34	44.15	50.97
Map relative to control											
1	1	0.156		0.092		0.059		1	0.889	0.855	0.967
2	1	0.165		0.079		0.057		1	0.972	0.930	1.017
3	1	0.181		0.092		0.114		1	0.968	0.968	1.270
4	1	0.132		0.191		0.451		1	1.237	0.891	1.700
Total	1	0.163		0.089		0.080		1	0.957	0.912	1.053

* Data from BAKER and CARPENTER (1972).

† Region 1 is *al-dp*; region 2 is *dp-b*; region 3 is *b-pr*; and region 4 is *pr-cn*.

involves primarily no-exchange tetrads, involves only a fraction of these, and can involve distributive disjunction. These observations suggest that the segregational anomalies characterizing recombination-defective meiotic mutants are a secondary consequence of the reduced recombination and not a second direct effect of the mutants (BAKER and CARPENTER 1972). Another, and rather strong, argument in favor of this conclusion is the comparison of the extent of the reduction in recombination (measured, for example, as the total map length of a chro-

TABLE 7

Results of crosses of females of the constitution X/X; Ly Pr/+ +; spa^{pol}/spa^{pol} *carrying the indicated* X *chromosomes by* $Y^{S}X\cdot Y^{L}$, v f B/0; C(4)RM, ci $ey^{R}/0$ *males*

Maternal *X* and *4* constitution of progeny	*X*-chromosome constitution of parental females and third chromosome constitution of progeny*							
	y/y		*y 9/y 9*		*y 9/y 9* (19°)†		*y 218/y 218*	
	P	R	P	R	P	R	P	R
X *4*	2078	1139	5341	408	521	38	490	26
X *44*	1	0	408	11	26	0	49	1
X *0*	0	1	452	8	23	0	70	0
XX *4*	0	0	379	18	32	3	43	3
XX *44*	0	0	36	0	0	0	7	0
XX *0*	0	0	65	1	4	0	11	0
0 *4*	0	0	470	17	48	4	49	3
0 *44*	1	0	102	4	1	0	9	0
0 *0*	0	0	143	0	12	0	26	0
Total Progeny	3220		7863		712		787	
Nondisjunction								
X	0.001		0.271		0.255		0.322	
4	0.001		0.174		0.102		0.241	
Map	35.4		5.94		6.32		4.19	

* P = Parental (*Ly Pr* and + +); R = Recombinant (*Ly* + and + *Pr*).
† Parental females raised and tested at 19°C.

mosome arm in mutant individuals divided by the same parameter in controls) with the frequencies of nondisjunction of chromosomes *1* and *4*. This comparison for the four mutants under consideration here is:

	Mutant			
	abo	*mei-9*	*mei-9*^{b}	*mei-218*
Map (mutant ÷ control)	0.70	0.09	0.16	0.08
X-exceptional gametes	0.02	0.27	0.19	0.29
4-exceptional gametes	0.01	0.15	0.08	0.17

The relevant points are three: (1) the greater the reduction in recombination, the more nondisjunction there is (even for the two alleles of the same locus); (2) *X*-chromosome nondisjunction is always greater than nondisjunction of chromosome *4*; and, most strikingly, (3) *mei-9* and *mei-218* both reduce recombination to the same extent and, although this quantitative similarity is almost surely coincidental because the reduction in *mei-9* is uniform along the chromosome arm but is nonuniform in *mei-218* (see below), the segregational properties resulting from the two mutants are almost identical.

TABLE 8

Comparisons of nondisjunction between gametes crossover or noncrossover for a heterologous chromosome

	Mutant					
	9		*9^b*		*218*	
Crossover status of heterolog*	CO	NCO	CO	NCO	CO	NCO
X-nondisjunction among						
2L†	0.112	0.209	0.096	0.179	0.219	0.294
*3***	0.158	0.278	___	___	0.308	0.323
4 nondisjunction among						
X; ++ ††	0.022	0.091	___	___	0.020	0.095
X; SM1; TM2 ††	0.032	0.189	___	___	0	0.192
3 **	0.057	0.181	___	___	0.026	0.250

* CO = crossover; NCO = noncrossover.
† Data from Table 6.
** Data from Table 7.
†† Data from Table 5, calculated among *X*-regular males only.

Recombination: Although each of the four recombination-defective meiotic mutants reduces crossing over, *abo* and *mei-218* do so such that the decrease is most striking in distal regions while in *mei-9* and *mei-9^b* the decrease is the same for all regions. Thus, in the case of the relatively weak mutant effect of *abo* (total map 70% of the control value), the most distal region has less than one-half the control rate of recombination, the most proximal segment slightly exceeds the control rate, and centrally-located regions have intermediate values (Tables 3,4). The nonuniformity of *mei-218* is even more striking: for chromosome *2*, the total map is reduced to 8% of control with the most distal segment having 6% of the control rate of recombination and the most proximal segment showing 45% (Table 6). The *X*-chromosome results suggest a similar pattern (Table 5), although the most proximal region is too large to resolve the striking centric response observed with chromosome *2*. A uniform reduction in exchange, on the other hand, is observed both for the weaker allele *mei-9^b* (16% the control rate of recombination) and the more extreme *mei-9*, in which recombination occurs at about 9% of the control frequency (Tables 5, 6).

These results suggest that the wild-type alleles of *abo* and *mei-218* on the one hand, and the *mei-9* alleles on the other, are concerned with basically different processes, both of which are necessary for normal recombination. Two further experiments were performed to explore potential differences between the two types om mutants: the first examined dominant effects on crossing over, the second examined the response to the interchromosomal effect of inversions on crossing over.

In order to determine whether *mei-9*, *mei-9^b*, and *mei-218* exhibited any dominant effects on crossing over (the weak response of *abo* was not examined in this connection), crossing over along *2L* was monitored in heterozygous females. In order to insure relative homogeneity between mutants and control so as to eliminate, as far as possible, extraneous modifiers of recombination, the mutant and control females tested were half-sibs. The experiment was initiated with females of uniform age (0–24 hours post-eclosion) and serially transferred at two-day intervals for a total of 10 days' laying; each vial was individually scored. The changes in crossing over with increasing maternal age were similar in all four crosses; hence the broods have been summed (Table 6). The mutants do appear to have a dominant effect on the overall frequency of crossing over; *mei-218* significantly increases the total map, *mei-9* significantly decreases the total map, and *mei-9^b* (the weaker allele) also decreases the total map, but not significantly. Thus, the *mei-9* alleles and *mei-218* exhibit different dominant effects on crossing over.

To assay for the interchromosomal effect of inversion heterozygosity in the mutants, the effect of inversion heterozygosity for chromosome *2* (*SM1*) and *3* (*TM2*) on crossing over on the *X* was examined in *mei-9* and *mei-218* females and controls (Table 5); the effect on heterozygosity for *TM2* was examined in *abo* females and controls (Table 3). The former will be discussed first.

In the controls (Table 5), the interchromosomal effect is quite striking; the map length of the *X* chromosome in females carrying both inverted autosomes is nearly twice that observed with normal autosomes. In the controls for the *mei-9* experiment, the increase in crossing over was, as expected (LUCCHESI and SUZUKI 1968), most pronounced in the proximal and distal regions; in the experiment involving *mei-218*, the proximal increase in the controls was less pronounced, possibly owing to undetected double crossovers in the very long proximal region. For both control experiments, the increase in crossing over results from the addition of an average of one exchange per tetrad and the coefficient of coincidence is increased. Finally, although females bearing inversions are somewhat less fertile than females without inversions, the increase in crossing over is accompanied by an increase in the absolute number of crossovers recovered per female parent from 37 to 46 and from 40 to 68 in the two experiments. Consequently, there are four criteria that may be used to ascertain whether the interchromosomal effect on recombination is expressed in *mei-9* and *mei-218*: (1) an approximately twofold increase in map length and exchanges; (2) a nonuniform distribution of crossovers similar to the respective controls; (3) an increase in the number of crossovers per female parent; and (4) an increase in the coefficient of coincidence.

The responses of the two mutants to inversion heterozygosity are quite similar. There are approximately twofold increases in map length and frequency of exchanges, but the crossovers are not distributed as in the controls; in fact, in the presence of either *mei-9* or *mei-218* the distributions of crossovers in the presence of inversions are not significantly different from the distributions without inversions, but are significantly different from the control distributions with inver-

sions (tested by $2 \times n$ contingency tests of the numbers of crossovers recovered in the various regions). Moreover, there is no increase in the number of crossovers per female parent—819 crossovers/536 females = 1.5 *vs.* 219/165 = 1.3 for *mei-9*; 104/118 = 0.9 *vs.* 116/117 = 1.0 for *mei-218*. Finally, too few double crossovers were recovered to determine whether coincidence was altered in either mutant. Consequently, two of the three applicable criteria indicate that inversion heterozygosity has no appreciable effect on crossing over in *mei-9* and *mei-218* females.

Furthermore, the following consideration suggests that the apparent increases in map length and exchange frequency may be artifacts. In the controls, inversion heterozygosity decreases fertility (as *X*-regular males per female parent) slightly—51 and 64 *vs.* 42 and 60, respectively. This decrease in fertility presumably reflects the increased frequency of nonrecoverable ova nondisjunctional for the second and/or third chromosomes. The decrease in fertility in the mutants is much more drastic. For *mei-9*, the decrease is from 19.7 to 7.9, a 2.5-fold reduction; for *mei-218*, the decrease is from 24.7 to 13.1, a 1.9-fold reduction. Here, also, the reductions are presumably the result of increased frequencies of ova nondisjunctional for the second and/or third chromosomes. As will be discussed below, in these mutants nondisjunction for one chromosome pair is correlated with noncrossover status of a heterolog; therefore, the nonrecoverable ova nondisjunctional for major autosomes may nonrandomly contain a noncrossover *X*. Consequently, it is possible that the apparent increase in map length in *mei-9* and *mei-218* females carrying inversions is due to decreased recovery of noncrossover strands.

Although these considerations suggest that inversion heterozygosity has little effect on crossing over in either *mei-9* or *mei-218* females, another possible interpretation of the data should be mentioned. The values for the various regions from the ratio (map *mei-218* with inversions)/(map *mei-218* without inversions) are virtually identical with those obtained from (map control with inversions)/(map control without inversions), suggesting that the interchromosomal effect is added to the *mei-218* effect (or *vice versa*). These values for *mei-9* give similar results for three of the four regions monitored. Unfortunately, the numbers of crossover progeny recovered from both mutants are too small for these comparisons to be statistically meaningful. Nevertheless, however the data are interpreted, it seems clear that *mei-9* and *mei-218* respond in the same way to inversion heterozygosity, and thus the response to the interchromosomal effect does not permit differentiation between these mutants.

On the other hand, inversion heterozygosity does effect crossing over in *abo* on the basis of the four criteria discussed above. First, in the control (Table 3) in the presence of the multiply-inverted chromosome *TM2*, map length increases 1.2-fold; in homozygous *abo* females, map length increases 1.4-fold. Second, the coefficient of coincidence is increased both in the control and in *abo* (Table 3). Third, the number of crossover progeny per parental female is increased slightly in the control (from 78.8 to 85.1) and dramatically in *abo* (from 13.4 to 30.5). Fourth, there is a nonuniform distribution of crossovers in *abo* with inversions

relative to *abo* without inversions; however, the altered distribution in *abo*—a greater increase distally—is not similar to that observed in the control. This suggests that the *abo* effect and the interchromosomal effect do not interact in a simple additive fashion.

The final aspect of recombination that has been examined in the four mutants under consideration is the coefficient of coincidence (C). It has been suggested that recombination-defective mutants that restrict the possibility of exchanges (preconditions for exchange) might, although not necessarily will, change C as well as the overall amount of recombination; on the other hand, mutants that reduce the probability of exchange itself would reduce the amount of recombination, but leave coincidence unaltered (SANDLER *et al.* 1968; LINDSLEY *et al.* 1968). The fact, in the case of *abo*, is easy to establish because many recombinants, including double-crossovers, are recovered. Here coincidence is not changed, as can be seen from the comparison in Table 3 and from the three comparisons in Table 4; thus, *abo* may, by this analysis, be a mutant that directly reduces the probability of exchange. Unfortunately, in the case of *mei-9*, *mei-9^b*, and *mei-218*, crossing over is so drastically reduced that reliable estimates of coefficients of coincidence are difficult to obtain. An alternative, but related, procedure for distinguishing between these two types of mutants will be presented below.

Recombination and segregation: We have noted above that nondisjunction involves primarily or exclusively noncrossover chromosomes, that nondisjunction of nonhomologous chromosome pairs is positively correlated in these mutants, and that at least for *mei-9*, *mei-9^b* and *mei-218*, at least some of the nondisjunction appears to be the result of nonhomologous segregations.

In fact, it may be that all of the irregular segregation is due to nonhomologous separations. That nonhomologous associations do occur can be inferred directly from the observation that, among *X-2* and *X-3* double exceptions, nonhomologous segregations predominate—the numbers of (diplo-nullo + nullo-diplo) progeny are much greater than the numbers of diplo-diplo + nullo-nullo) progeny (BAKER and CARPENTER 1972). However, most of the nondisjunction in these mutants is not due to detectable nonhomologous segregations. The exceptional progeny not directly attributable to nonhomologous segregations include progeny exceptional for a single chromosome pair and all *X-4* double exceptions, since here there is no excess of nonhomologous segregations (BAKER and CARPENTER 1972; see also Tables 1 and 2). Exceptions for a single chromosome pair are, however, nonrandomly recovered among progeny in which a nonhomolog is noncrossover (Table 8); it is therefore possible that such nondisjunction is also the result of nonhomologous associations in meiocytes with at least two no-exchange tetrads—the nondisjunctional pair plus one other.

Because the fourth chromosomes do not show nonhomologous segregation (at least not from the *X*), there is thus far no direct evidence in these mutants that the fourth chromosomes can form nonhomologous associations with (other) no-exchange chromosomes. However, nearly half of the fourth-chromosome exceptions are recovered as *X-4* double exceptions (Tables 1, 2, 5 and 7), and, more-

over, fourth chromosome exceptions are preferentially recovered among gametes containing a noncrossover nonhomolog (Table 8). These observations suggest that fourth chromosome nondisjunction is also a result of nonhomologous associations with no-exchange nonhomologs, but that such associations do not lead to nonhomologous segregations. HALL (1972) reached this same conclusion based on data involving the recombination-defective meiotic mutant *c(3)G*.

There are two further observations that suggest that fourth chromosome nondisjunction is the result of nonhomologous associations. The first is that, in *mei-9*^{b} and control *XXY* females (Table 2), the fourth chromosomes do show some nonhomologous from the *Y* chromosome. The second is that, in *mei-9* females, fourth chromosome nondisjunction is lower at 19° than at 25°, although crossing over on the third chromosome is the same at the two temperatures (Table 7). HALL (1972) found a similar effect of temperature on fourth chromosome nondisjunction in *c(3)G*, a female meiotic mutant that eliminates meiotic crossing over at both temperatures; HALL, moreover, determined that the temperature-sensitive stage for fourth-chromosome nondisjunction in *c(3)G* was at the time the eggs were laid (Metaphase I), much later than the probable time of exchange (Prophase I).

INTERPRETATION

Recombination-defective meiotic mutants are those mutants that decrease the frequency of crossing over, alter the distribution of crossovers, or both. Of the fourteen known recombination-defective loci in *D. melanogaster*, (1) all reduce crossing over, (2) all that have been examined reduce crossing over to approximately the same (characteristic for the mutant) extent on all chromosomes, and (3) all increase nondisjunction of all chromosome pairs at the first meiotic division. This nondisjunction involves primarily or exclusively no-exchange tetrads.

There are three ways in which the recombinational and disjunctional attributes of these mutants might be related. (1) Independent: each "mutant" might involve two defective loci, one defective in exchange, the other in disjunction. This is vanishingly unlikely for seventeen independently isolated mutants at fourteen loci. (2) Identical: if the same processes are required at one time for normal disjunction and at another time for normal recombination, then each of the fourteen loci might be defective in such processes. (3) Dependent: the increased nondisjunction might be an indirect effect of the recombinational defect owing to the increased frequencies of no-exchange tetrads. There are four lines of evidence which argue in favor of the latter. First, increased frequencies of nondisjunction are observed in non-meiotic-mutant females when the frequency of exchange is decreased by means of inversion heterozygosity on two or more chromosomes (see, for example, ZIMMERING 1958). Second, as discussed above for the mutants *mei-9* and *mei-218*, much if not all of the nondisjunction in recombination-defective mutants may be the result of nonhomologous associations. Third, as discussed by BAKER and CARPENTER (1972) and BAKER and HALL (1974), the rules governing these nonhomologous associations (at least of the *X*, second, and third

chromosomes) in the mutants examined are quite similar to those of the distributive system in the absence of meiotic mutants. Finally, as illustrated in this report, the pattern of nondisjunction for chromosomes *1* and *4* is the same in *mei-9* and *mei-218* females whose recombinational phenotypes are alike only in the frequency of no-exchange tetrads produced. More generally, a regular relationship between the frequency of no-exchange tetrads and nondisjunction for all recombination-defective meiotic mutants has been exhibited by BAKER and HALL (1974). Thus, it is most probable that the nondisjunction observed in recombination-defective mutants is a secondary effect and likely results from the normal process of distributive disjunction.

As has been repeatedly pointed out (BAKER and CARPENTER 1972; HALL 1972; PARRY 1973), the high frequency of nondisjunction of chromosomes *4* in these mutants is difficult to explain under such an hypothesis, since distributive disjunction depends upon similarity in size (GRELL 1964) and the fourth chromosomes are distinctively smaller than the other chromosomes. There are two alternatives. Either the same processes are required at different times for disjunction and for recombination (in which case, since the fourth chromosomes do not recombine, all known recombination-defectives must be defective in such processes) or else the presence of no-exchange nonhomologs can interfere with the distributive segregation of the fourth chromosomes despite the great difference in size. There are three observations that support the latter possibility. First, in nonmutant females, inversion heterozygosity for the *X* and second chromosomes increases fourth chromosome nondisjunction more than tenfold relative to uninverted or singly-inverted controls (HALL 1972—his Tables 1 and 9); interestingly, inversion heterozygosity for the second and third chromosomes has little effect on fourth-chromosome nondisjunction (Table 5). Second, fourth-chromosome nondisjunction can be increased in *XXY* females despite the size difference between the *Y* and fourth chromosomes (HALL 1972; CARPENTER 1973; and Table 2; but see ROBBINS 1971); such nondisjunction appears to be attributable to *Y-44* distributive disjunction. Third, in these mutants gametes containing a noncrossover nonhomolog are much more likely to be exceptional for the fourth chromosome than are gametes containing a crossover nonhomolog (Table 8). Thus, although not predictable from the size-dependent property of distributive disjunction (GRELL 1964) and not directly demonstrable from the patterns of segregation, it is possible that the high levels of fourth-chromosome nondisjunction observed in these mutants is also a secondary effect of reduced recombination and involves the normal process of distributive disjunction.

With respect to mutant effects on recombination, it has previously been suggested (LINDSLEY *et al.* 1968; SANDLER *et al.* 1968; BAKER and CARPENTER 1972) that the distinction between mutants affecting exchange preconditions and those affecting exchange itself could be made on the basis of the coefficient of coincidence——the former possibly altering C, the latter not. This procedure is not particularly useful in the present instance. In the first place, C is very difficult to measure accurately in many recombination-defective mutants because of the rarity of recovered double crossovers (*mei-9* and *mei-218* are cases in point).

Secondly, and more fundamentally, the procedure can be misleading since, if C is not altered, the defect may effect either an exchange precondition or exchange. This is illustrated by the case of *abo*. Consequently, a different, but related, method of differentiating between the two theoretically-possible types of recombination defects has been employed. This method follows from the analysis of CHARLES (1938) (see also STEPHENS 1961), who, by an extension of WEINSTEIN's (1936) general method of tetrad analysis, compared the *X*-chromosome map derived from consideration of only no-exchange and single-exchange tetrads to the map derived from all tetrads. He found that crossovers from single-exchange tetrads tend to be localized in the medial region of the chromosome arm, whereas the crossovers from multiple-exchange tetrads tend to be localized proximally and distally. That is, in the case of single-exchange tetrads, the modal position of the chiasma is toward the middle of the arm, whereas if there are two chiasmata per arm, the modal position of one is proximal and the other distal. In wild type, then, the distribution of crossovers along a chromosome arm reflects the relative frequency of single *vs.* multiple exchange tetrads because of their different modal positions of chiasmata. It should therefore be possible to deduce information about the type of defect in a meiotic mutant from the observed pattern of crossing over along a chromosome arm. In theory, at least three types of defects might be distinguishable. Letting "node" stand for the establishment of an exchange possibility, (1) a mutant that reduces the probability of node formation without affecting the modal position of nodes that do form should yield a pattern of crossing over approaching that obtained by considering only single-exchange tetrads in wild type; (2) a mutant that reduces the probability of exchange per node without affecting the frequency or modal position of nodes should yield a pattern of crossing over similar to that obtained by considering all tetrads in wild type; (3) a mutant in which the distribution of nodes is abnormal should yield other patterns (a random distribution of nodes, for example, would yield a pattern more representative of physical distances between markers than does wild type).

It should be noted that these considerations assume that the probability of exchange per node is constant and therefore that the difference in modal positions of chiasmata in single and double exchange tetrads is due to a shift in the modal positions of nodes—in other words, that interference in wild type is a property of the exchange preconditions, not of exchange.

The patterns of crossing over observed in the mutants can be conveniently compared with wild type graphically. The plots in Figures 1 and 2 are presented as experimental map relative to control map *vs.* control map. Normalization to the control map compensates for unequal lengths of regions monitored; plotting against the control map permits visualization of the pattern along the chromosome arm. The nonmutant plots, which represent the contribution of crossovers from single-exchange tetrads to the total crossovers observed for each interval, show the expected distribution; crossovers in the middle of the arm are most likely to have been derived from single-exchange tetrads, whereas proximal and distal crossovers are less likely to have been so derived. None of the mutants appear

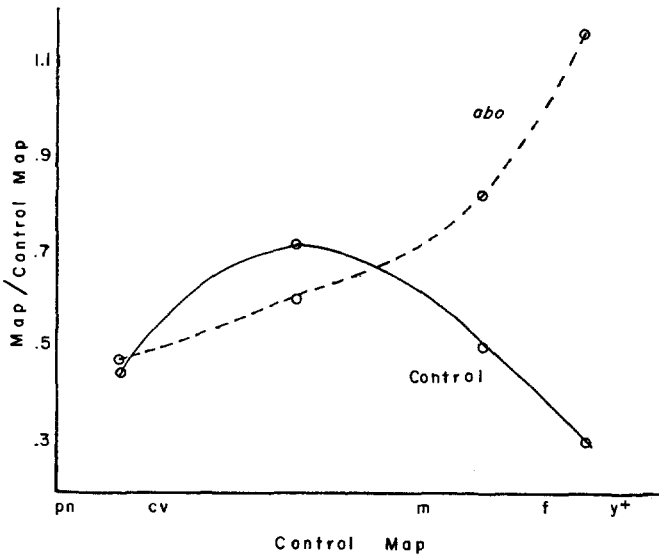

FIGURE 1.—Recombination along the *X* chromosome in *abo*. Map intervals are drawn to scale on the abscissa; ordinate values are (experimental maps for an interval) ÷ (control map for that interval). "Control" curve depicts the contribution of crossovers from single exchange tetrads only.

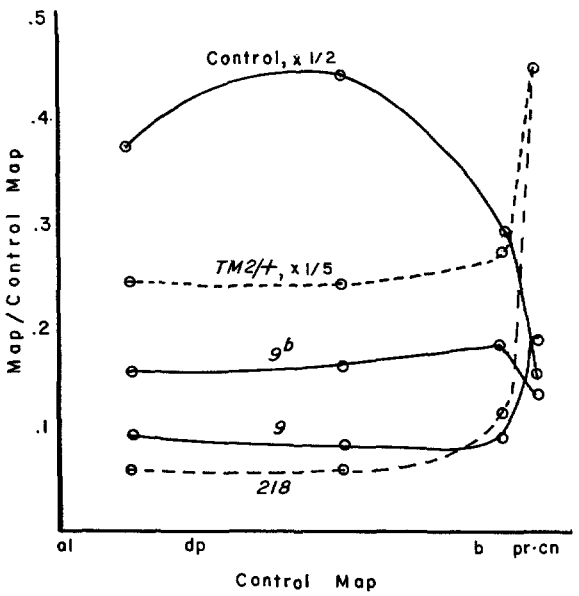

FIGURE 2.—Recombination along the second chromosome in *mei-9*, *mei-9*^{b}, and *mei-218*. Ordinate and abscissa same as Figure 1. "Control" curve depicts the contribution of crossovers from single-exchange tetrads only; the value for each point has been halved to consolidate the figure. Data for the "*TM2*/+" curve from CARPENTER (1973; her table 1, cross 6; the values have been divided by five).

to have this distribution, suggesting that neither the *mei-9* alleles nor *mei-218* nor *abo* lower the number of crossovers by simply decreasing the frequency of nodes.

The *mei-9* alleles both produce relatively uniform reductions in crossing over in all regions, and thus appear to be defects in the probability of exchange per node; the frequency and modal positions of nodes are not affected (type 2, above).

The mutants *mei-218* and *abo*, on the other hand, both produce nonuniform reductions in crossing over along the chromosome; the reductions are polar, being less extreme in centric regions, and thus each appears to be a mutant whose defect results in a lowered frequency and altered distribution of nodes along the chromosome (type 3, above).

Recombination under the influence of *abo* is unique among meiotic mutants in that crossing over is decreased nonuniformly but coincidence is unaltered. It is possible to rationalize these two properties based on the observation that the mutant effect of *abo* is relatively weak and on the assumption that the nonuniform decrease in exchange implies a defect in the polar establishment of exchange preconditions. Thus, suppose that the chromosome arm is divided into two segments (as in the first two columns in Table 3) such that the preconditions for exchange are established in neither segment in a fraction y of meiocytes, are established only in the proximal segment in x of the meiocytes, and are established in both segments in $1 - x - y$ of meiocytes. Suppose, further, that an exchange occurs with probability p in the proximal segment only, d in the distal segment only, and m in both regions simultaneously provided that the preconditions in a segment have been established. Then, the observed rates of crossing over will be

$$\text{distal} = (1 - x - y)(d + m)$$
$$\text{proximal} = (1 - y)(p + m),$$

and the coefficient of coincidence will be

$$C = \frac{(1 - x - y)m}{[(1 - y)(d + m) - x(d + m)][(1 - y)(p + m)]}.$$

In this formulation, C has two interesting properties. If $y = 0$ (that is, if the mutant is relatively weak), C is independent of x and will therefore be constant even though there is a polar decrease in recombination. Thus, for example, the *abo* data in Table 3 are satisfied by an $x = 0.425$, $y = 0$, $p = 0.205$, $d = 0.257$ and $m = 0.066$. Secondly, if $y \neq 0$ (that is, in the case of stronger recombination-defective mutants), the coefficient of coincidence exhibited by the mutant will be greater than in the control and, under this precise formulation, will be greater by a factor of $(1 - y)$, implying that the stronger the mutant effect, the greater the increase in C. This is, in fact, generally observed, as can be seen for the following precondition mutants (data from BAKER and CARPENTER 1972, their Tables 6 and 8).

Mutant	Total map (*al–cn*)	Region *al–dp–b* C	*al–dp–b* *1-y*	*dp–b–pr* C	*dp–b–pr* *1-y*
control	47.6	0.20	1*	0.33	1*
mei-41†	22.8	0.86	.23	1.74	.19
mei-195†	31.5	0.71	.28	0.71	.46
mei-251	38.8	0.40	.50	0.48	.69
mei-352	47.1	0.31	.65	0.42	.79

* By definition.
† Allelic.

These considerations, then, suggest in the specific instance that *abo* is best interpreted as a defect in the establishment of exchange preconditions and in general suggest that the uniformity or nonuniformity in the decrease in exchange caused by recombination-defective meiotic mutants is more reliable than the coefficient of coincidence as an indicator of whether any particular mutant is involved in precondition defects or defects in exchange itself.

It should be noted that in the formulation of the polar establishment of preconditions used here, we have imagined that in mutant individuals nodes can only be subtracted from the wild-type condition, and are subtracted most distally and less proximally. It is the case that neither of these conditions need obtain in reality. Thus, we cannot distinguish between this model and one in which the disestablishment of preconditions occurs prematurely—first in distal regions, later in proximal regions. More importantly, this precise formulation implies that in no region will nodes exist in mutant individuals that are not present in wild type. In fact, very proximal regions do sometimes exhibit more exchange in mutant individuals than in wild type (BAKER and CARPENTER 1972); it might well be, therefore, that nodes can be differently distributed in mutant and wild-type meiocytes. Indeed, as indicated above and suggested by BAKER and HALL (1974), the effect of recombination-defective mutants might be to relax constraints on the spatial distribution of nodes. This could lead to the observed polarity because of the existence of polar constraints in wild type (such as, for example, those involved in the centromere effect (BEADLE 1932)). Moreover, if interference is the consequence of such restraints, then their relaxation in mutant individuals would lead to the increase in coincidence as observed; JONES (1974) proposes that this is the case in rye, based on his observations of altered chiasma distributions in rye meiotic mutants. In any event, it is clear that the best distinction between recombination-defective meiotic mutants affecting exchange preconditions and those affecting exchange itself is made on the basis of the uniformity or nonuniformity in the decrease in exchange, and that the polar nature of (at least some) precondition events accounts for the increase in the coefficient of coincidence in mutant meiocytes.

In summary, then, of the fourteen loci identified by recombination-defective meiotic mutants, only *mei-9* exhibits a decrease in exchange not accompanied by a change in the spatial distribution of the recovered recombinants; the others, most of which have been adequately studied, give evidence of nonuniformity in the decrease—with the property, in all cases, that distal regions are most affected

(LINDSLEY *et al.* 1968; BAKER and CARPENTER 1972; PARRY 1973). The most reasonable interpretation of these observations is that *mei-9* is a defect in the control of the exchange events themselves, while the other loci are involved in the establishment of preconditions for exchange. Two corollaries follow from this interpretation. The establishment of these exchange preconditions must be basically a polar event and the nondisjunction of chromosome *4* in *mei-9* (and by inference in recombination-defective meiotic mutants in general) is the consequence of the disruption of normal chromosome *4* segregation by nonhomologs, presumably mediated by the distributive system.

The four recombination-defective mutants so far examined for dominant effects on recombination have all exhibited such effects. The mutant *mei-9* and its allele *mei-9^{b}* both decrease crossing over when heterozygous; the observed decrease is uniform along the chromosome arm and C is not affected, suggesting that the dominant effect reflects a defect in exchange, as does the much greater recessive effect. The mutants *c(3)G* (HINTON 1966; also see LINDSLEY *et al.* 1968) and *mei-218* both increase crossing over when heterozygous; the observed increase is polar and C is increased, suggesting that these dominant effects reflect defects in exchange preconditions, as has been proposed for the recessive effects (for *mei-218*, see above; for *c(3)G*, see HALL 1972). Thus, at least for the mutants examined, the type of lesion inferred from the dominant effect on recombination is congruent with that inferred from the recessive effect; this relationship may prove useful in the analysis of very strong recombination-defectives (such as *c(3)G*). However, this approach may not be useful in the analysis of weaker mutants, since possible dominant effects may not be detectable—note that the dominant effect of *mei-9^{b}*, the weaker allele, is less than that observed in *mei-9*.

Although examined here, the interpretation of interchromosomal effects of heterozygous inversions on recombination in recombination-defective mutants is not straightforward, for several reasons. First, the mode of action of interchromosomal effects is itself poorly understood, although it apparently affects a precondition or preconditions for exchange (for a review of interchromosomal effects, see LUCCHESI and SUZUKI 1968). Second, although mutants can be subdivided into those that respond to the interchromosomal effect and those that do not, even those that respond do not exhibit the same response as wild type. As discussed above, *abo* exhibits a greater increase in recombination than the controls; another recombination-defective mutant, *mei-S282*, exhibits a lesser increase than the controls (PARRY 1973).

Consideration of interchromosomal effects in the mutants suggests a confounding possibility. It is conceivable that the recombinational difficulties caused by a recombination-defective meiotic mutant might trigger the interchromosomal effect response in the mutant itself, thus complicating the interpretation of the defect. For example, the phenotype of a mutant that decreased the probability of exchange per node but which secondarily triggered the interchromosomal effect (which, in effect, "adds on" nodes nonrandomly) might mimic a mutant defective in an exchange precondition—i.e., exhibit nonrandom reduction in crossing over along the chromosome and altered coincidence. Consequently, the nonuniform reduction in crossing over observed in *mei-218* may be either

a direct result of the defect in the mutant (in which case *mei-218* is defective in an exchange precondition) or an indirect effect resulting from the interchromosomal effect (in which case *mei-218* may be defective in either an exchange precondition or in exchange itself). The uniform reduction in crossing over observed in *mei-9*^{b} suggests that this mutant is defective in exchange and that this defect does not trigger the interchromosomal effect response. It should be noted, however, that the slight departures from uniform reduction observed in the allele *mei-9*, which shows a two-fold greater reduction in crossing over than *mei-9*^{b}, are very similar to those expected from a mild interchromosomal effect (compare the patterns observed from *mei-9* in Figure 2 with those observed in controls heterozygous for the multiply-inverted third chromosome *TM2*).

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Corresponding editor: G. LEFEVRE