MEIOTIC CHROMOSOME BEHAVIOR INFLUENCED BY MUTATION-ALTERED DISJUNCTION IN *DROSOPHILA MELANOGASTER* FEMALES

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ABSTRACT

The effects of a female-specific meiotic mutation, altered disjunction (*ald*: 3-61), are described. Although *ald* females show normal levels of meiotic exchange, sex- and 4*th*-chromosome nondisjunction occurs at an elevated level. A large proportion of the nondisjunction events is the result of nonhomologous disjunction of the sex and 4*th* chromosomes. These nonhomologous disjunction events, and probably all nondisjunction events occurring in *ald* females, are the result of two anomalies in chromosome behavior: (1) X chromosomes derived from exchange tetrads undergo nonhomologous disjunction and (2) the 4*th* chromosomes nonhomologously disjoin from larger chromosomes. There is at best a marginal effect of *ald* on the meiotic behavior of chromosomes 2 or 3. The results suggest that the ald^+ gene product acts to prevent the participation of exchange X chromosomes and all 4*th* chromosomes in nonhomologous disjunction events. The possible role of ald^+ in current models of the disjunction process is considered.

TO account for the occurrence of nonhomologous disjunction, GRELL (1962a; reviewed by GRELL 1976) proposed that two pathways of meiotic disjunction exist in Drosophila females. Homologs that have recombined will regularly disjoin via the *exchange disjunction* pathway. A second mode of disjunction, known as *distributive disjunction*, is also utilized. Only chromosomes that have not secured a disjunction partner by exchange are available for distributive disjunction. Thus, this mode is only used by the 4*th* chromosomes, which do not recombine, other chromosomes that have failed to recombine, and special rearrangements such as compound chromosomes. Unlike exchange disjunction, distributive disjunction partners are not established by homology; this system, therefore, supports the disjunction of both homologs and nonhomologs. Similarity in the sizes of chromosomes, at least for chromosomes approximately the size of the 4*th* chromosome, is important in establishing disjunctional relationships (GRELL 1964; MOORE and GRELL 1972). It is also known that distributive relationships are not limited to pairs of chromosomes—a metacentric chromosome will disjoin distributively from two acrocentric chromosomes (COOPER 1948; GRELL 1962b), and in many other genotypes trivalent formation is also evident (GRELL 1976).

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The properties of meiotic mutants are consistent with the existence of two modes of disjunction. Recombination-defective mutants exhibit increased levels of nondisjunction of all chromosomes as a consequence of a reduction in meiotic exchange; it is likely that the distributive system in these mutants is "overloaded" with nonexchange chromosomes and cannot support regular disjunction (BAKER and HALL 1976). The meiotic mutant *nod* is defective in distributive disjunction (CARPENTER 1973). The *4th* chromosomes, which always disjoin via the distributive system, are frequently lost in homozygous *nod* females; the behavior of the other (mostly exchange) tetrads is much more normal. In *nod* females, the X chromosomes nondisjoin only about 2.5% of the time; this is the frequency expected if the 5% nonexchange X-chromosome tetrads usually disjoining via the distributive system are segregating at random.

Although work with wild-type females and meiotic mutant females demonstrate the existence of two modes of disjunction, the relationship between exchange disjunction and distributive disjunction is not clear (GRELL 1976; NOVITSKI and PURO 1978). In this report, the characterization of a new meiotic mutant, altered disjunction (symbol: *ald*), is presented. This analysis allows new insights into the working of the two disjunction pathways of Drosophila females.

MATERIALS AND METHODS

All mutations and chromosomes referred to in this report are described in LINDSLEY and GRELL (1968) except for the following. *Dp(3;3)S462* is a duplication of region 89D1-2 to 90D1 on the left arm of chromosome 3 at 64E; it is derived from *Tp(3)S462* by recombination (E. B. LEWIS, unpublished). *Dp(1,4)1021* (PARKER 1969) is a duplication of the y^+ euchromatic tip of the X chromosome on the heterochromatic left arm of chromosome 4. The *4th*-chromosome mutation spa^{pol} will be referred to as *pol* throughout this report.

Nondisjunction frequencies, except where noted, are calculated as the sum of exceptional progeny classes divided by the sum of all progeny classes. In crosses in which the female test parent contained free X chromosomes, exceptional-X progeny are doubled before computations are made to correct for the inviability of triplo-X and nullo-X progeny.

Exchange rank distributions are calculated by the method of WEINSTEIN (1936) for regular-X progeny and by the method of MERRIAM and FROST (1964) for exceptional-X progeny.

Nonhomologous disjunction frequencies are calculated in the following manner. If two pairs (*A;B*) of chromosomes are being assayed, the frequency of nonhomologous disjunction is computed as: $[(AA;0 + 0;BB) - (AA;BB + 0;0)] \div$ total progeny. If disjunction of one pair of chromosomes (*AA*) from a third chromosome (*B*) is being assayed, the formula used is $[(AA;0 + 0;B) - (AA;B + 0;0)] \div$ total progeny. These equations may measure only a fraction of nonhomologous disjunction events. This is satisfactory for the analysis presented here, because these frequencies will be used to (1) document the occurrence of these events and (2) compare the frequency of these events in females of similar genotypes.

The rationale for using these equations for nonhomologous disjunction frequency is as follows. Given two *A* and two *B* chromosomes, A_1 disjoins from B_1 ($A_1 \leftrightarrow B_1$) at a certain frequency. To specify the occurrence of this event it is necessary that A_2 be recovered with A_1 (to be sure they were not disjunctional partners) and likewise B_2 with B_1. How often these two criteria are met may be only a fraction of the $A_1 \leftrightarrow B_1$ frequency. For instance, if A_2 and B_2 segregate randomly when $A_1 \leftrightarrow B_1$, $(AA;0 + 0;BB) = \frac{1}{4}(A_1 \leftrightarrow B_1)$. If $A_2 \leftrightarrow B_2$ when $A_1 \leftrightarrow B_1$, $(AA;0 + 0;BB) = \frac{1}{2}(A_1 \leftrightarrow B_1)$. Higher order associations are possible; here also only some $A_1 \leftrightarrow B_1$ nonhomologous disjunction event will generate *AA;0 + 0;BB* gametes. Note that no type of nonhomologous disjunction event involving only *A* and *B* chromosomes will generate *AA;BB* and *0;0* gametes. These gametes will occur as frequently as *AA;0* and *0;BB* gametes if *A,B* nonhomologous disjunction is not occurring and so are subtracted from *AA;0 + 0;BB* before computing the nonhomologous disjunction frequency. The second equation, used to assay the disjunction of a pair of chromosomes (*AA*) from a third chromosome (*B*), is similar.

RESULTS

ald is an EMS-induced 3*rd*-chromosome mutation recovered in the laboratory of D. L. LINDSLEY on the basis of showing increased levels of X- and 4*th*-chromosome nondisjunction. It maps to a single site at 61 on the standard map (one *ald-sr* crossover among ten *cu-sr* crossovers in + *ald* +/*cu* + *sr* females). In agreement with this genetic mapping, the *ald*$^+$ locus was shown to be located on *Dp(3,3)S462*; this places the *ald* locus in the salivary region 89D-90D.

As shown in Table 1, X-chromosome nondisjunction occurs at 9.5%, and 4*th*-chromosome nondisjunction occurs at 6.0% in XX;*ald/ald* females. X- and 4*th*-

TABLE 1

X- and 4th-chromosome nondisjunction in ald *females*[a]

Male gametes	Female gametes	Sex and 3rd chromosomes of females								
		XX;+/+	XX; *ald*/+	XX;*ald/ald*	XXY;+/+		XXY;*ald*/+		XXY;*ald/ald*	
	X 4 Y				0	Y	0	Y	0	Y
$\overline{XY}$ $\overline{44}$	X 4	3553	2289	2109	2339	394	1554	231	563	114
0 $\overline{44}$	X 4	4408	2753	2394	2747	2027	1664	1435	633	421
$\overline{XY}$ 0	X 44	0	0	50	10	0	6	0	207	7
0 0	X 44	0	0	38	4	0	7	0	157	10
$\overline{XY}$ $\overline{44}$	X 0	0	0	34	0	5	0	1	25	65
0 $\overline{44}$	X 0	0	1	49	0	1	0	5	12	108
0 $\overline{44}$	XX 4	3	1	77	122	2	77	0	106	2
$\overline{XY}$ $\overline{44}$	0 4	4	1	100	4	113	5	68	4	90
0 $\overline{44}$	XX 0	0	0	26	0	0	2	0	16	1
$\overline{XY}$ 0	0 44	0	0	42	0	0	0	0	1	28
0 0	XX 44	0	0	1	1	0	0	0	16	0
$\overline{XY}$ $\overline{44}$	0 0	0	0	0	0	0	0	0	1	10
Total:		7968	5045	4920	7769		5055		2597	
% Nondisjunction[b]										
	X	0.2	0.1	9.5	4.8		4.7		17.0	
	4	0	0	6.0	0.1		0.4		22.3	
% Nonhomologous disjunction										
	X,4	0	0	2.6	0		0.1		1.2	
	X,Y				4.6		4.4		15.9	
	Y,4				0.1		0.3		14.0	

[a] The crosses are *y/y w*^{a} *ct m f/(y*$^+$*Y); pol/pol* females carrying the indicated third chromosomes by $Y^S X \cdot Y^L$, *In(1)EN, y B/0; C(4)RM, ci* $ey^R/0$ males.

[b] Since XXYY female progeny are relatively inviable, X-chromosome nondisjunction is computed as exceptional-X progeny/(regular males + exceptional-X progeny) and 4*th*-chromosome nondisjunction is computed among male and exceptional-X progeny in all XXY crosses.

chromosome nondisjunction events occur exclusively at the reductional (first) meiotic division. This was demonstrated by constructing *ald* females that were heterozygous for a centromere marker on either the X (*y/Dp(1;1)sc*^{VI}, *y·y*$^{+}$) or the *4th* chromosome (*Dp(1;4)1021, y*$^{+}$*·pol/ci ey*^{R}) and progeny testing their exceptional progeny. In both cases, all diplo-exceptional progeny (X: 23 tested, *4*: 37 tested) were heterozygous for the centromere marker. To examine the effect of *ald* in male meiosis, *y/y*$^{+}$*Y;pol/pol* males carrying +/+ or *ald/ald* 3rd chromosomes were crossed to *y pn/y pn;C(4)RM, ci ey*^{R} females. In these crosses, *ald* males did not exhibit increased sex (X,Y)- or *4th*-chromosome nondisjunction: *ald*$^{+}$ males exhibited 0.2 and 0.1% (total = 6600), and *ald* males exhibited 0.1 and 0.2% (total = 7741) sex- and *4th*-chromosome nondisjunction, respectively. Therefore, *ald* is one of a large number of female-specific mutants that increase nondisjunction only at the first meiotic division (see BAKER and HALL 1976 for review).

It is evident from the results of the XX crosses in Table 1 that X- and *4th*-chromosome nondisjunction events are correlated in two ways in *ald* females. First, the frequencies of nondisjunction are not independent: X,4 double exceptions are five times more frequent than expected on the basis of independence. Second, X,4 nonhomologous disjunction is occurring: XX;*O* and *O*;44 gametes comprise 99% of the total X,4 double exceptions. Furthermore, although there is no evidence for X,4 nonhomologous disjunction in the control cross, 2.6% of the total gametes are derived from X,4 nonhomologous disjunction in *ald* females. The occurrence of X,4 nonhomologous disjunction makes *ald* unusual among meiotic mutants; only one other such mutant is known (ROBBINS 1971). All recombination-defective mutations also increase X- and *4th*-chromosome nondisjunction nonindependently, but they exhibit little or no evidence of X,4 nonhomologous disjunction. For example, *c(3)G*^{17} produces 4.3% XX;*O* and *O*;44 gametes and 4.6% XX;44 and *O*;*O* gametes (HALL 1972).

Recombination in ald

Recombination was monitored on the X and *2nd* chromosomes in *ald* females. These results, summarized in Table 2, demonstrate that *ald* does not decrease the frequency of recombination. Recombination occurs at normal levels on the *2nd* chromosome and at slightly elevated levels on the X chromosome.

By progeny testing exceptional females, it is possible to determine the exchange status of tetrads that give rise to X-chromosome exceptions in *ald* females. Twenty-three of the 28 diplo-X exceptions were successfully tested from the *y/y pn cv m f·y*$^{+}$*; ald/ald* females; ten of these contained at least one recombinant chromosome. Exchange events occurred in each region monitored: 2 between *pn* and *cv*, 6 between *cv* and *m*, 1 between *m* and *f*, and 4 between *f* and the centromere. Therefore, the occurrence of an exchange event does not prevent an X-chromosome bivalent from nondisjoining in *ald* females.

Although exchange tetrads nondisjoin, the E_0 tetrad class is most likely to nondisjoin in *ald* females. When the procedure of MERRIAM and FROST (1964) is used, it is possible to estimate the exchange rank distribution of tetrads that give rise to X exceptions. These values are: E_0 = 48%, E_1 = 33%, E_2 = 19% and E_3 = 0%. Almost half of the exceptional-X gametes are derived from the E_0 tetrad

TABLE 2

X- and 2nd-chromosome recombination in ald females[a]

	y/y pn cv m f·y⁺				*al dp b pr cn/+*		
			ald/ald			*ald/ald*	
	+/+	+/*ald*	4	44 + 0	+/*ald*	X	XX + 0
NCO	1301	1390	411	19	2332	1181	60
SCO 1	177	176	60	2	483	247	6
2	589	687	231	6	1031	529	18
3	334	380	106	4	213	92	8
4	156	189	78	5	42	25	4
DCO 1,2	7	11	7	0	30	14	0
1,3	20	34	14	1	28	13	3
1,4	13	27	10	0	6	2	0
2,3	37	54	17	0	19	16	2
2,4	61	59	28	0	20	11	0
3,4	1	4	9	1	2	2	0
TCO 1,2,3	1	1	1	0	1	0	0
1,2,4	1	2	3	0	1	0	0
1,3,4	0	0	2	0	0	0	0
2,3,4	1	1	1	0	0	0	0
Total progeny	2699	3015	1016		4208	2233	
Map distances							
Region 1	8.1	8.3	9.8 (9.6)[b]		13.0	12.8	
2	25.8	27.0	28.9 (28.4)		26.2	26.4	
3	14.6	15.7	15.4 (14.8)		6.3	6.1	
4	8.6	9.4	13.5 (13.4)		1.7	2.0	
Total	57.1	60.4	67.6 (66.2)		47.2	47.3	
Exchange rank							
E_0	0.07	0.05	0.02 (0.04)		0.16	0.17	
E_1	0.73	0.71	0.67 (0.65)		0.74	0.72	
E_2	0.19	0.23	0.26 (0.26)		0.09	0.11	
E_3	0.01	0.01	0.06 (0.05)		0	0	

[a] The crosses are *y/Dp(1;1)sc*^{v1}, *y pn*(1)*cv*(2)m(3)f(4)·*y*$^+$; *pol/pol* females carrying the indicated 3rd chromosomes by *Y*^{S}X·*Y*^{L}, *In(1)EN, v f B/0; C(4)RM, ci ey*^{R}*/0* males for X-chromosome recombination and *y/y; al*(1)*dp*(2)*b*(3)*pr*(4)·*cn/+* females carrying the indicated 3rd chromosomes by *+/Y;al dp b pr cn/al dp b pr cn* males for 2nd-chromosome recombination. X-chromosome recombination is measured only in the regular male progeny.

[b] Values in parentheses are the map distances and the exchange rank distribution computed from the regular male progeny and 23 exceptional female progeny (five exceptional females were not successfully progeny tested) of this cross. The exchange rank distribution is calculated as the weighted sum of the male data and twice the exceptional female data.

class, whereas only 2% of the regular-X gametes are derived from this class. Since regular-X gametes and exceptional-X gametes are 94 and 6% of the total in this cross, approximately equal numbers of E_0 tetrads are recovered as regular-X gametes (94% × 0.02 = 2% regular-X E_0 tetrads) and exceptional-X

gametes (6% × 0.48 = 3% exceptional-X E_0 tetrads). Similar calculations suggest that only 4% of the exchange-X tetrads nondisjoin in *ald* females.

Overall map distances and exchange rank distributions can be estimated for the X chromosome by combining the regular male and exceptional female data. These values, given in parentheses in Table 2, show that X-chromosome recombination occurs at an elevated frequency in *ald* females. The exchange rank distribution analysis shows that the increase in recombination is primarily a result of an increase in the frequency of the multiple exchange tetrads. As expected from the increased occurrence of multiple exchange tetrads (CHARLES 1938), *ald* females show the increased levels of recombination primarily in the distal and proximal intervals.

A more extensive XX experiment was performed as a control for XXY;*ald*/*ald* females; these results are presented in Table 3. The data are shown in two parts: (1) the recombination values and exchange rank distribution of tetrads computed from regular male progeny and (2) the exchange rank distribution of

TABLE 3

X-chromosome recombination and tetrad distribution in ald *females*[a]

	Sex and 3rd chromosomes of females					
	XX;+/+	XX;*ald*/+	XX;*ald*/*ald*[b]	XXY;+/+	XXY;*ald*/+	XXY;*ald*/*ald*[b]
No. of regular male progeny	4408	2754	2481	4779	3111	1335
Map distances						
Region 1 (w^a-*ct*)	19.6	16.4	24.1	22.2	21.1	23.2
2 (*ct*-*m*)	14.8	15.2	16.3	16.0	16.8	17.9
3 (*m*-*f*)	16.7	15.8	16.0	17.7	16.3	16.1
Total	51.1	47.4	56.4	55.9	54.2	57.2
Exchange rank						
E_0	13.9	18.3	10.0	7.2	5.6	11.3
E_1	70.1	69.2	67.0	74.0	80.4	65.6
E_2	15.8	11.9	22.4	18.4	13.7	23.1
E_3	0.2	0.6	0.6	0.3	0.3	0
No. of exceptional female progeny tested[c]	0	0	72	112	73	111
Exchange rank						
E_0			23.2	90.1	96.4	23.4
E_1			47.0	7.4	3.6	54.0
E_2			29.4	2.5	0	21.0
E_3			0	0	0	1.6

[a] The crosses are given in Table 1. X-chromosome recombination is determined from the regular male progeny, and tetrad distributions are determined separately for the regular male progeny and the exceptional-X progeny.

[b] The recombination data for the regular male and exceptional female progeny of these crosses are given in Table 5.

[c] All exceptional females that were successfully progeny tested are included in this analysis.

tetrads computed from exceptional female progeny. In agreement with the previous X-chromosome recombination experiment, nondisjoining X chromosomes are derived from all tetrad ranks in XX;*ald/ald* females. There is an enrichment of chromosomes derived from E_0 tetrads among exceptional progeny and a corresponding depression of X chromosomes derived from this rank among the regular progeny.

With respect to the exchange tetrad classes, the relative frequencies of X chromosomes from E_1 and E_2 tetrads are similar in the exceptional female and regular male progeny. Moreover, the proportion of exchanges in regions 1, 2 and 3 is 43, 29 and 28% in the regular male progeny and 42, 29 and 30% in the exceptional female progeny. These results imply that all exchange tetrads, irrespective of the number or location of the exchange events, have an equal probability of giving rise to nondisjunctional X chromosomes in *ald* females.

Disjunction of the major autosomes

Three sets of crosses to males carrying attached autosomes were performed to determine whether *ald* increases nondisjunction of the major autosomes. In these crosses, only ova exceptional for the tested autosome(s) can be recovered, so nondisjunction frequencies are estimated from the number of progeny per mother. In crosses to males bearing compound-3*rd* chromosomes [*C(3L)RM, se* h^2 rs^2; *C(3R)RM, sbd gl e*], only a two-fold increase in 3*rd*-chromosome nondisjunction occurred in *ald* females: 240 *ald* females yielded three offspring and 170 wild-type females yielded one offspring. There is no increase in 2*nd*-chromosome nondisjunction (Table 4 left, rows 1–3); however, the control frequency is higher than that expected based either on the *ald/+* females or previous reports (0.01%: CARPENTER 1973). To ascertain whether the major autosomes nondisjoin only simultaneously, *ald* and ald^+ females were crossed to y^2/Y; *C(2L)RM, sp; C(2R)RM, px; C(3L)RM,* h^2 rs^2; *C(3R)RM,* + males. In these crosses, *ald* also showed only a three-fold increase in autosomal nondisjunction: 380 *ald* females yielded four progeny, and 600 wild-type females yielded two progeny. The *ald* females had very good fertility in these crosses: sisters that were crossed to *B*/Y males yielded 112 (*ald*) and 145 (ald^+) progeny per mother. Therefore, a difference in fertility is not a major complicating factor in these experiments. Table 4 (left, rows 4–6) also contains the results of crosses in which the female parent was heterozygous for a multiply inverted second chromosome *In(2LR)SM1*. Since the presence of *SM1* in these females increases the frequency of E_0 2*nd* chromosomes, an effect of *ald* on this tetrad class will be more pronounced in this cross relative to the cross in which the 2*nd* chromosomes are of normal sequence. However, in the *SM1/+* crosses, *ald* females show only a modest increase (fourfold) in the level of 2*nd*-chromosome nondisjunction.

These results show that, although there is a small increase in autosomal nondisjunction in *ald* females, this effect is small when compared with the increased nondisjunction of the X and 4*th* chromosomes. The results in Table 4 show that *ald* causes only a fourfold increase in 2*nd*-chromosome nondisjunction; this is much less than the 40- to 60-fold increases seen for the X and 4*th* chromosomes (Table 1).

TABLE 4

The effect of ald *on* 2nd-*chromosome nondisjunction*[a]

2nd and 3rd chromosomes of female	X/X					$\overline{XX}$/Y					
	Female gametes					Female gametes					
	X;22 + X;0	XX;0 + X;22	XX;22 + 0;0	No. of mothers	Gametes per mother[b]	$\overline{XX}$;22 + Y;0	$\overline{XX}$;0 + Y;22	$\overline{XX}$Y;0 + 0;22	$\overline{XX}$Y;22 + 0;0	No. of mothers	Gametes per mother
+/+;+/+	3	1	0	105	0.05	3	1	15	0	180	0.11
+/+;*ald*/+	0	0	0	90	0	0	1	1	0	75	0.03
+/+;*ald*/*ald*	7	0	0	164	0.04	0	1	0	0	48	0.02
SM1/+;+/+	9	4	1	110	0.17	35	135	534	6	180	3.94
SM1/+;+/*ald*	8	16	1	80	0.53	10	35	137	2	39	4.72
SM1/+;*ald*/*ald*	72	16	0	155	0.67	18	50	90	4	66	2.45

[a] The crosses are *y*/*y*;*pol*/*pol* and *C(1)RM*, *y pn v*/*y*$^+$Y females carrying the indicated *2nd* and *3rd* chromosomes by *C(2L)RM,dp*; *C(2R)RM, px* males.

[b] Female gametes exceptional for the X chromosomes are doubled before this calculation is made to correct for inviability of nullo-X and triplo-X progeny.

These crosses also examine the independence of autosomal and X-chromosomal nondisjunction. The data are too few for *SM1*$^+$ females to make a judgment in this regard; however, in *SM1*/+ females there is no difference in the frequency of X,2 nonhomologous disjunction in the *ald* and *ald*$^+$ crosses: 31 and 32% of the *2nd*-chromosome exceptions are due to X,2 nonhomologous disjunction in these two crosses, respectively. Thus, in contrast to its effect on the *4th* chromosome, *ald* does not increase the frequency that the *2nd* chromosomes nondisjoin as a result of participating with the X chromosome in an nonhomologous disjunction event. This does not rule out the possibility that the major autosomes interact with the X chromosomes in a manner that increases nondisjunction of the X chromosome but not the major autosomes. However, if it is supposed that an increased frequency of nonhomologous interaction will result in increased levels of nondisjunction, these results imply that the X-chromosome exceptions recovered in *ald* are not the result of nonhomologous interactions with the major autosomes.

The basic phenotype of ald

The analysis has revealed the following properties of the *ald* mutation.

(1) *ald* increases X- and *4th*-chromosome nondisjunction, and 27% of X-chromosome nondisjunction events and 43% of *4th*-chromosome nondisjunction events are due to X,4 nonhomologous disjunction. It is possible that a larger percentage, perhaps even all, of the nondisjunction events are due to X,4 nonhomologous disjunction because it may be that only some of these events are detectable (see MATERIALS AND METHODS).

(2) Recombination occurs at normal levels in *ald* females.

(3) The X-chromosome exceptions of *ald* females are derived from all tetrad ranks, but the E_0 tetrad class is most likely to nondisjoin. Among exchange tetrad classes, the number or location of exchange events does not affect the probability that an exchange tetrad will nondisjoin.

(4) The *2nd* and *3rd* chromosomes show only slightly increased levels of nondisjunction, and there is no increase in the rate of X,2 nonhomologous disjunction in *ald* females. Thus, the major effect of the the *ald* mutation is on the X and *4th* chromosomes.

(5) *ald* has no detectable effect on male meiosis.

These results show that *ald* is a disjunction-defective mutant. It affects the disjunctional decisions made by the X and *4th* chromosomes, allowing frequent X,4 nonhomologous disjunction. The defect in *ald* females can be ascribed to two properties of the distributive system: size recognition and exchange exclusion. Size recognition is the process that exists in wild type to prevent the *4th* chromosomes from participating in nonhomologous disjunction events with larger nonexchange chromosomes (GRELL 1964). Exchange exclusion prevents exchange X chromosomes from participating in nonhomologous disjunction events. Therefore, it appears likely that processes that normally limit nonhomologous disjunction events are defective in *ald* females. This hypothesis is examined in the following experiments.

The effect of ald *in* XXY *females*

By examining a genotype in which nonhomologous disjunction occurs in *ald*$^+$

females, it is possible to compare the nature of nonhomologous disjunction events that occur in *ald* and *ald*$^+$ females. XXY females are one such genotype: the presence of a Y chromosome in an otherwise wild-type female causes X chromosomes derived from E_0 tetrads to disjoin from the Y chromosome (BRIDGES 1916).

Tables 1 and 3 contain the disjunction and recombination results, respectively, of XXY females carrying +/+, +/*ald*, and *ald/ald 3rd* chromosomes. Since the females carry *y/y* w^a *ct m f* X chromosomes in these crosses, the *f*-centromere interval is not monitored and, therefore, the frequency of the E_0 tetrad class is overestimated, and other tetrad classes are underestimated. The results of the XXY;+/+ cross are consistent with previous work on XXY females (BRIDGES 1916; COOPER 1945): X-chromosome nondisjunction occurs at a rate of 5%, virtually all exceptional progeny are derived from the E_0 tetrad class, and X-chromosome nondisjunction events are the result of X,Y nonhomologous disjunction. However, in XXY;*ald/ald* females, X-chromosome nondisjunction occurs at a higher rate (17%), not all exceptional progeny are derived from E_0 tetrads, yet almost all (94%) of X-chromosome exceptions are due to X,Y nonhomologous disjunction.

In XXY;+/+ females 4.3% of the total gametes are E_0 tetrads that were recovered in exceptional progeny. In XXY;*ald/ald* females, the corresponding value is 4.0%. Thus, the frequency of E_0 tetrads recovered in the exceptional progeny of XXY;*ald/ald* females equals that from XXY;+/+ cross, and these exceptional progeny are the result of X,Y nonhomologous disjunction. X chromosomes derived from E_0 tetrads are, therefore, showing proper distributive disjunction from the Y chromosome in XXY;*ald/ald* females. It was shown earlier that only approximately half of the E_0 tetrads nondisjoin in XX;*ald/ald* females, and that these exceptions comprised 2.2% of the total gametes. Therefore, approximately half of the X chromosomes from E_0 tetrads segregate properly in XX;*ald/ald* females but segregate XX from Y in XXY;*ald/ald* females.

The results of the XXY;*ald/ald* cross confirm that exchange-X chromosomes participate in nonhomologous disjunction: the X-chromosome exceptions are almost entirely due to X,Y nonhomologous disjunction and are frequently derived from exchange tetrads. Since the behavior of these exchange chromosomes is identical with that of nonexchange X chromosomes in *ald*$^+$ females, the defect in *ald* females includes the failure to exclude exchange X chromosomes for nonhomologous disjunction; nonhomologous disjunction processes *per se* appear to be normal.

In XXY;*ald/ald* females, as in XX;*ald/ald* females, the location of exchange events does not affect the probability that an exchange tetrad will nondisjoin in *ald* females, since the proportion of exchanges in regions 1, 2 and 3 is the same in the regular male progeny and the exceptional female progeny (41, 31, and 28% *vs.* 38, 29 and 33%, respectively). Moreover, like the E_0 class, half of the chromosomes from exchange-X tetrads that segregate XX from Y in XXY;*ald/ald* females must segregate X from X in XX;*ald/ald* females since XXY;*ald/ald* females have nearly twice the X-chromosome nondisjunction frequency of

XX;*ald/ald* females, yet the tetrad distributions of the exceptional progeny are similar in these two crosses.

These experiments also assess whether X,4 nonhomologous disjunction is dependent on the exchange status of the X chromosome. Table 5 lists the *4th*-chromosome composition of the regular male and the exceptional female gametes recovered from XX;*ald/ald* and XXY;*ald/ald* females. The exceptional female data are arranged using the nomenclature of MERRIAM and FROST (1964) in which the N_0 class is comprised of exceptional females containing two nonrecombinant chromosomes, and classes N_1–N_{10} are comprised of females carrying the possible combinations of at least one recombinant chromosome. Thus, classes N_1–N_{10} are derived from exchange X-chromosome tetrads. Although the data are few, the *4th*-chromosome exceptions appear to occur without regard to the exceptional female class in XX;*ald/ald* females. Since the X,4 double exceptions are the result of X,4 nonhomologous disjunction in these females (Table 1), recombinant X chromosomes are capable of disjoining from the *4th* chromosomes in *ald* females.

These crosses also examine the effect of *ald* on Y,4 nonhomologous disjunction. Y,4 nonhomologous disjunction has been observed occasionally at a low

TABLE 5

4th-chromosome composition of gametes from ald *females*[a]

	XX;ald/ald		*XXY;ald/ald*		
	4	*44 + 0*	*4 + Y4*	*44 + Y*	*0 + Y44*
Regular males					
NCO	1183	36	520	136	10
SCO	1073	42	466	117	9
DCO	136	9	68	12	3
TCO	2	0	0	0	0
Total	2394	87	1054	265	22
Exceptional females[b]					
N_0	23	5	34	7	5
N_1	13 (2)[c]	3	34 (2)	3	5
N_2	12	3	8	0	0
$N_3 + N_4$	7 (4)	3 (1)	8 (3)	2	1 (1)
N_5	0	0	2	0	0
N_6	2	0	1	0	0
N_{10}	1	0	1	0	0
Total	64	15	93	12	12

[a] These data are from the *ald/ald*;XX and *ald/ald*;XXY crosses presented in Table 1.

[b] See MERRIAM and FROST (1964) for a description of these exceptional female classes.

[c] The numbers given in parentheses represent exceptional females that are accounted for by an exchange occurring between *f* and the centromere before reductional nondisjunction occurred. Alternatively, these females could be the result of equational nondisjunction, but this is less likely because no *ald*-induced equational nondisjunction was observed in other experiments (see text).

level in previous work on XXY females [HALL (1972) reports a level of 1.5%; CARPENTER (1973) reports 5.1%]. The occurrence of Y,4 nonhomologous disjunction was examined in this work in two separate crosses involving XXY females. In the crosses reported in Table 1, the XXY females carried X chromosomes in normal sequence, whereas in a separate experiment described in Table 6, the females were heterozygous for the X-chromosome inversion *In(1)dl-49*. The major difference in these two crosses is the frequency of nonexchange X-chromosome tetrads. When the X chromosomes are of normal sequence, only 5% of X-chromosome tetrads are E_0, but *In(1)dl-49* heterozygotes show a much higher frequency of E_0 tetrads. From the data of STURTEVANT and BEADLE (1936) and of NOVITSKI and BRAVER (1954), the E_0 class can be estimated as approximately 60%. At least 54% appear to be E_0 in the crosses reported here because the frequency of secondary nondisjunction in the control cross is 54%.

The results of the two control crosses (Tables 1 and 6) show that Y,4 nonhomologous disjunction occurs only at the low level of 0.1% in both the XXY and X/*In(1)dl-49*/Y females. In contrast, Y,4 nonhomologous disjunction occurs frequently in XXY;*ald/ald* females that either carry normal sequence X chromosomes or are heterozygous for *In(1)dl-49*. However, the frequency of Y,4 nonhomologous disjunction only accounts for 63 and 38% of the *4th*-chromosome nondisjunction events in XXY and X/*In(1)dl-49*/Y females, respectively. Because Y,4 nonhomologous disjunction is more frequent in XXY females, in which 5% of the X-chromosome tetrads are nonexchange, than in X/*In(1)dl-49*/Y females, in which 60% of the X-chromosome tetrads are nonexchange, it seems likely that the participation of the X chromosomes in nonhomologous disjunction diminishes the occurrence of Y,4 nonhomologous disjunction. Indeed, Y,4 nonhomologous disjunction is more frequent among regular X progeny (17.7 and 14.6% for females carrying normal sequence X chromosomes and *In(1)dl-49* heterozygotes, respectively) than among exceptional X progeny (0 and 1.9%, respectively). In spite of this, the frequency of *4th*-chromosome nondisjunction (22.3 and 22.9% for females carrying normal sequence X chromosomes and *In(1)dl-49* heterozygotes, respectively) is constant in these two crosses and remains constant when measured only in X-exceptional progeny (26.6 and 23.5%, respectively). This suggests that the *4th* chromosomes are not more likely to become disjunctional partners in meiocytes in which the X chromosomes disjoin from the Y chromosome.

Two further points can be made from the crosses reported in Tables 1 and 6. First, X/*In(1)d1-49*;*ald/ald* females have twice as much X-chromosome nondisjunction as *ald* females carrying X chromosomes in normal sequence, confirming that nonexchange X-chromosome tetrads are more sensitive to the *ald* defect than exchange tetrads. Second, although X/*In(1)d1-49*;*ald/ald* females show higher levels of X,4 nonhomologous disjunction than *ald* females with X chromosomes in normal sequence, X- and 4th-chromosome single exceptions are increased as well. Since inversion heterozygosity increases only the number of X chromosomes in the distributive system, it is likely that single *4th*-chromosome exceptions in *ald* females are the result of nonhomologous interactions involving the the X and *4th* chromosomes.

TABLE 6

X- *and* 4th-*chromosome nondisjunction in* In(1)d1-49 *heterozygotes*[a]

Male gametes	Female gametes	Sex and 3rd chromosomes of females								
		XX;+/+	XX; *ald*/+	XX;*ald*/*ald*	XXY;+/+		XXY;*ald*/+		XXY;*ald*/*ald*	
	X 4 Y				0	Y	0	Y	0	Y
$\overline{XY}$ $\overline{44}$	X 4	1667	1708	495	472	112	526	241	252	150
0 $\overline{44}$	X 4	1571	1838	466	412	364	553	555	297	214
$\overline{XY}$ 0	X 44	0	2	17	2	0	25	0	111	12
0 0	X 44	1	7	18	0	0	22	0	67	9
$\overline{XY}$ $\overline{44}$	X 0	0	6	22	0	0	0	6	13	46
0 $\overline{44}$	X 0	2	7	14	0	2	0	16	17	55
0 $\overline{44}$	XX 4	6	6	46	457	0	645	0	258	4
$\overline{XY}$ $\overline{44}$	0 4	3	11	50	3	454	1	446	9	175
0 $\overline{44}$	XX 0	0	2	14	0	0	3	0	29	4
$\overline{XY}$ 0	0 44	2	4	15	0	0	1	3	4	33
0 0	XX 44	0	0	4	0	0	7	0	41	1
$\overline{XY}$ $\overline{44}$	0 0	0	0	1	0	0	0	5	0	25
	Total	3252	3591	1162	2278		3055		1826	
% Nondisjunction[b]										
	X	0.7	1.3	20.1	54.0		49.2		46.9	
	4	0.2	0.9	10.8	0.1		2.5		22.9	
% Nonhomologous disjunction										
	X,4	0.1	0.3	3.7	0		−0.2		0.2	
	X,Y				53.7		49.0		43.4	
	Y,4				0.1		2.0		8.6	

[a] The crosses are *y/In(1)d1-49, y sc v g f/(y*$^+$*Y);pol/pol* females carrying the indicated 3rd chromosomes by $Y^S X \cdot Y^L$, *In(1)EN, y B/0;C(4)RM, ci ey*^{R}*/0* males.

[b] See footnote to Table 1.

Disjunction in attached-X females

PURO (1978) has shown that the *4th* chromosomes will nonhomologously disjoin from an attached-X chromosome at a low frequency. This is an alternative means to compare the nature of *4th*-chromosome nonhomologous disjunction in *ald* and *ald*$^+$ females. For this reason, control and *ald* females bearing an attached-X chromosome and also carrying either *Dp(1;f)3*, a Y chromosome, or no sex-chromosome homolog were monitored for sex- and *4th*-chromosome nondisjunction. [*Dp(1;f)3* is a free duplication consisting of the centromere, the entire heterochromatin and the euchromatic y$^+$ tip of the X chromosome.] These results are given in Table 7.

TABLE 7

Sex- and 4th-chromosome nondisjunction in attached-X females[a]

	$\overline{XX}$/0		$\overline{XX}$/Dp3		$\overline{XX}$/Y	
Female gametes	+/+	*ald/ald*	+/+	*ald/ald*	+/+	*ald/ald*
$\overline{XX}$ *4*	1031	525	2020	116	2609	419
E 4	872	459	1587	45	2167	352
$\overline{XX}$ *44*	0	9	3	10	9	92
E 0	0	6	1	10	5	61
$\overline{XX}$ *0*	7	106	3	15	4	51
E 44	5	180	1	25	14	82
$\overline{XX}$*E 4*			44	37	8	31
0 4			47	34	16	34
$\overline{XX}$*E 0*			5	19	1	30
0 44			6	25	5	37
$\overline{XX}$*E 44*			0	0	0	0
0 0			0	0	0	0
Total	1915	1285	3717	336	4838	1192

Sex and *3rd* chromosomes of females	% Nondisjunction		% Nonhomologous disjunction	
	Sex	*4*	XX,*4*	XXE,*4*
$\overline{XX}$*/0;+/+*		0.6	0.6	
$\overline{XX}$*/Dp3;+/+*	2.7	0.5	0.3	0.3
$\overline{XX}$*/Y;+/+*	0.6	0.8	0.2	0.1
$\overline{XX}$*/0;ald/ald*		23.4	21.1	
$\overline{XX}$*/Dp3;ald/ald*	34.2	31.0	19.0	13.1
$\overline{XX}$*/Y;ald/ald*	11.3	29.9	3.7	5.4

[a] The crosses are *C(1)RM, y pn v/(0,Dp(1;f)3* or y^+Y*);pol/pol* females carrying the indicated *3rd* chromosomes by $Y^S X \cdot Y^L$, *In(1)EN, y B/0; C(4)RM, ci* $ey^R/0$ males. The letter "E" refers to the X-chromosome homolog [*0* (no homolog), *Dp3* or Y] in the cross.

The control crosses of *C(1)RM/0, C(1)RM/Dp3* and *C(1)RM/Y* show that the *4th* chromosomes nondisjoin at a similar frequency, slightly more than 0.5%. In the *C(1)RM/0* cross, all of the *4th*-chromosome exceptions are the consequence of nonhomologous disjunction from the attached-X chromosome. These results are similar to those of PURO (1978). For the following reasons, it is likely that all of the *4th*-chromosome exceptions resulting from the *C(1)RM/Dp3* and *C(1)RM/Y* crosses are also the result of nonhomologous disjunction from a sex chromosome. Sex,*4* double exceptions occur more frequently than expected on the basis of independence. These double-exceptional gametes are exclusively the result of sex,*4* nonhomologous disjunction events. These events are probably of several types, involving the attached-X chromosome, the sex-chromosome hom-

olog, or both, and at least one *4th* chromosome. Indeed, a comparison of these crosses shows that an additional sex chromosome, either *Dp3* or the Y chromosome, diminishes the occurrence of *C(1)RM,4* nonhomologous disjunction without lowering the frequency of *4th*-chromosome nondisjunction. This suggests that *Dp3* and the Y chromosome, as well as the attached-X chromosome, serve as nonhomologous disjunction partners for the *4th* chromosomes in females of these genotypes. Taken together, these results suggest that in attached-X females the *4th* chromosomes will nonhomologously disjoin from sex chromosomes present in the distributive system resulting in slightly less than 0.5% *4th*-chromosome nondisjunction.

In *C(1)RM/0, C(1)RM/Dp3* and *C(1)RM/Y* females homozygous for *ald*, the *4th* chromosomes nondisjoin between 23 and 31% of the time (Table 7). As in wild type, it is likely that all *4th*-chromosome exceptions are the result of nonhomologous disjunction from a sex chromosome. The strongest evidence for this comes from the *C(1)RM/0* cross in which nearly all of the 4th-chromosome exceptions are the result of *C(1)RM,4* nonhomologous disjunction. In addition, as in wild type, sex- and *4th*-chromosome double exceptions from the *C(1)RM/Dp3* and *C(1)RM/Y* crosses are the result of sex,*4* nonhomologous disjunction.

The similarity between the behavior of wild-type and *ald* females in these crosses can be summarized as follows. First, as noted before, in *C(1)RM/0* females, the *4th*-chromosome exceptions are nearly all accounted for by *C(1)RM,4* nonhomologous disjunction events. Second, in *C(1)RM/Dp3* females, about 60% of the *4th*-chromosome exceptions are accounted for by segregation of the *4th* chromosomes from the attached-X chromosome. The remainder of the *4th*-chromosome nondisjunction events in these females are presumably the result of *Dp,4* nonhomologous disjunction. Third, in *C(1)RM/Y* females, the attached-X and Y chromosomes are equally efficient in causing *4th*-chromosome nondisjunction. Notice that there is little or no evidence for *C(1)RM,4* nonhomologous disjunction events in these females; this is the expected result if the attached-X chromosome and the Y chromosome disjoin from the *4th* chromosomes at similar rates. Finally, in both wild-type and *ald* females, *C(1)RM,Y* nondisjunction (0.6 and 11.3%, respectively) is lower than the *C(1)RM,Dp3* nondisjunction (2.7 and 34.2%, respectively).

These results suggest that the difference between the control and *ald* crosses does not involve a qualitative difference in the kinds of nonhomologous disjunction events involving the *4th* chromosomes but rather a difference in the frequency with which such events occur. In wild type, less than 1% of the time the *4th* chromosomes disjoin from a sex chromosome, whereas in *ald* the *4th* chromosomes will disjoin from a sex chromosome in 30% of the meiocytes. The results support the hypothesis that *4th* chromosomes are more frequently available for nonhomologous disjunction as a result of the *ald* defect, but other aspects of the nonhomologous disjunction process are normal.

C(1)RM females were also crossed to compound-*2nd* chromosomes to assay nonhomologous disjunction of the major autosomes from the sex chromosomes. These results are given in the right columns of Table 4. Although 2*nd*-chromosome nondisjunction is higher in *C(1)RM;SM1/+* females than XX;*SM1/+*

females, there is no major effect of *ald* in these crosses. In agreement with the XX results given earlier, these results suggest that, if it is supposed that increased levels nonhomologous interactions result in increased levels of nondisjunction, increased sex-chromosome nondisjunction in *ald* females is not due to nonhomologous interactions with the major autosomes.

The effect of ald *on the size recognition process*

GRELL (1964) demonstrated that if a free-X duplication similar in size to the *4th* chromosome is present in an otherwise normal genome, the *4th* chromosomes will nonhomologously disjoin from it at a high frequency. From these observations, she concluded that the regular segregation of the *4th* chromosomes is not a consequence of their homology but rather is the result of their small size relative to the other chromosomes usually present in the genome. Therefore, a system (known as the size-recognition process) must exist by which the *4th* chromosomes choose a disjunctional partner on the basis of size similarity.

The *ald* mutation may be defective in this process because it causes a high frequency of nonhomologous disjunction events involving the *4th* chromosomes and the larger sex chromosomes. To test this possibility, experiments similar to those of GRELL (1964) were performed in *ald* females. These experiments monitor *4th*-chromosome nondisjunction in females carrying a free-X duplication in addition to the normal chromosome complement. These duplications all carry the centromere and euchromatic y^+ tip of the X chromosome but have different amounts of X heterochromatin and therefore differ in size.

The results of experiments with +/+, *ald*/+, and *ald/ald* females carrying one of a series of free-X duplications are summarized in Table 8 and displayed in Figure 1. The control crosses, in agreement with GRELL'S earlier results, show that *Dp(1;f)1144* has the highest level of *Dp,4* nonhomologous disjunction. Larger and smaller duplications show lower levels, with the actual level being dependent on the size similarity between the *4th* chromosome and the duplication.

In *ald* females, the highest level of *4th*-chromosome nondisjunction, as in wild type, is seen in *Dp(1;f)1144*-bearing females. Therefore, the size recognition process is at least partially operative in *ald* females. Larger and smaller duplications cause more *Dp,4* nonhomologous disjunction in *ald* females than is observed in the corresponding ald^+ females. These results imply that size recognition, although partially operative, does not ensure the proper disjunction of the *4th* chromosomes in some meiocytes of *ald* females.

DISCUSSION

The phenotype of ald

Altered disjunction (*ald*: 3-61) is a female-specific meiotic mutation causing nondisjunction of the sex and *4th* chromosomes at the first meiotic division. Because meiotic recombination in *ald* females is likely normal, and certainly not reduced, ald^+ must act directly on the disjunction process. The nature of this action will be considered after the phenotype of *ald* is briefly reviewed.

In wild-type females, only nonexchange X chromosomes participate in dis-

TABLE 8

Sex- and 4th-chromosome nondisjunction in X/X/Dp(1;f) females[a]

Duplication	0	1187	1205	1144	1346	3bb⁻	856	1173	3
Dp size[b]		0.3	0.7	1.0	2.0	2.0	3.0	3.3	3.7
(A) X/X/*Dp*;+/+									
Total	4276	2250	1033	1911	1750	1404	742	1591	
% Nondisjunction									
X	0.2	0.5	0.8	0.3	0.9	0.6	0.2	0.8	
4	0.3	0.7	0.7	31.3	6.0	4.9	1.9	1.0	
(B) X/X/*Dp;ald*/+									
Total	6349	2711	1750	3362	2556	2890	3380	2288	
% Nondisjunction									
X	0.1	0.2	0.3	0.3	0.6	0.3	0.4	1.2	
4	0.1	0.5	0.5	27.3	6.9	5.5	2.9	1.1	
(C) X/X/*Dp;ald/ald*									
Total	5789	1339	2304	2338	1598	1992	1061	2002	375
% Nondisjunction									
X	7.1	6.3	9.1	9.8	6.8	4.9	9.5	10.3	6.2
4	5.2	9.2	11.3	27.4	18.8	19.6	14.4	17.6	12.9
% Nonhomologous disjunction									
Dp,44		6.2	7.2	23.8	15.6	17.1	10.0	11.0	9.3
Dp,XX		0.1	0.2	2.2	1.8	1.5	8.0	7.2	4.1
XX,44	1.9	2.2	1.9	1.9	1.5	1.0	2.1	2.5	0

[a] The crosses are *y/y/Dp(1;f)*, y^+;*pol/pol* females carrying the indicated 3rd chromosomes by $Y^S X \cdot Y^L$, *y B/0;C(4)RM, ci* $ey^R/0$ males.

[b] Given as approximate size of the mitotic 4th chromosome as determined by KRIVSHENKO and COOPER (given in LINDSLEY and GRELL 1968) except for *Dp(1;f)3bb*⁻; this duplication is a *bb*-lethal derivative of *Dp(1;f)3* recovered by D. PARRY. I. DUNCAN (unpublished) has determined that *Dp(1;f)3bb*⁻ is twice the length of the 4th chromosome, in good agreement with its behavior in these experiments.

tributive disjunction. One property of *ald* females is the distributive disjunction of exchange X chromosomes. From the results with XXY females (Tables 1 and 3), it is estimated that *ald* permits chromosomes from about 15% of exchange X-chromosome tetrads, chosen without regard to the number or the position of exchange events, to disjoin via the distributive system. Chromosomes from nonexchange-X tetrads, in *ald* females as in wild type, disjoin via the distributive system. In XXY females mutant for *ald*, the exchange and nonexchange X chromosomes participating in the distributive system disjoin from the Y chromosome. Therefore, at least in XXY females, although presumably in other genotypes as well, the behavior of exchange X chromosomes that disjoin via the distributive system in *ald* females is identical with the behavior of nonexchange X chromosomes utilizing the system in wild type. In this view, nondisjunction of X chromosomes in XX females is not a direct consequence of their participation in the distributive system (X chromosomes from E_0 tetrads disjoin

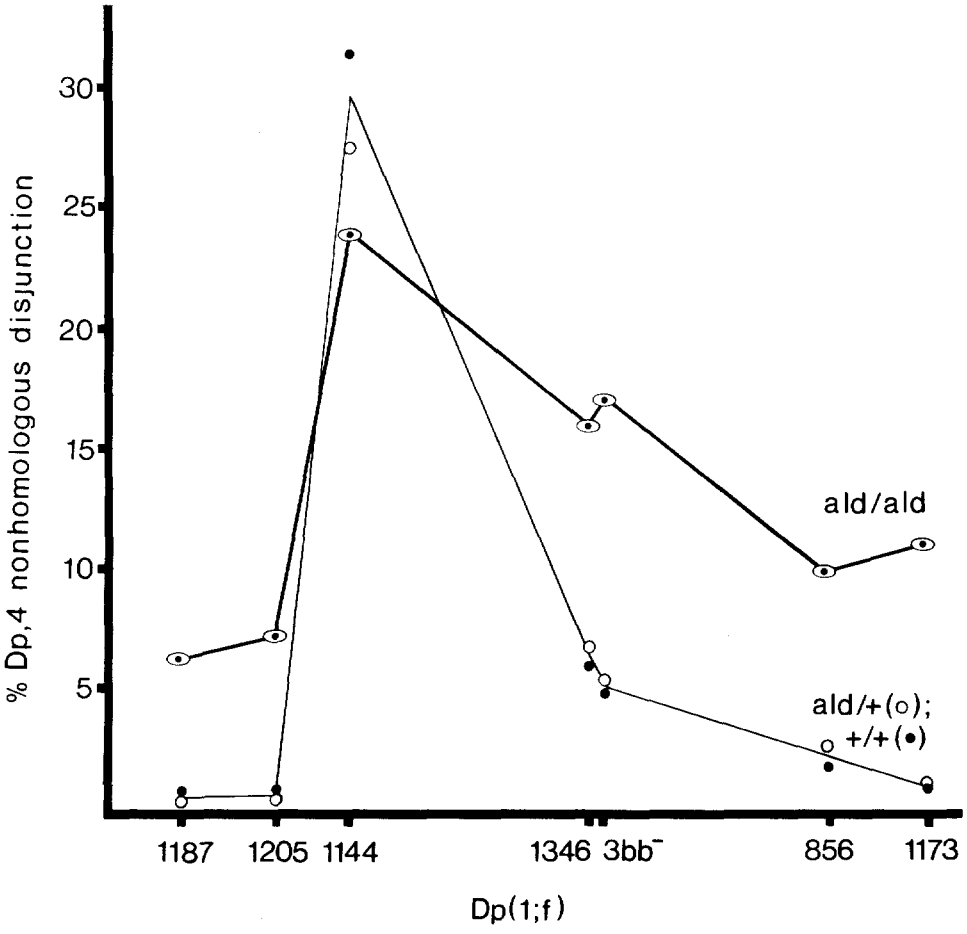

FIGURE 1.—The effect of *ald* on *Dp,4* nonhomologous disjunction. The data displayed here and a description of the free-X duplications are given in Table 8. The free-X duplications are arranged along the abscissa according to their metaphase lengths relative to the metaphase length of the *4th* chromosome.

properly via this system in wild-type females) but rather because both X chromosomes and *4th* chromosomes are available for distributive disjunction in *ald* females.

CARPENTER (1973) proposed that the distributive system could be genetically dissected into at least three components: pairing, orientation, and disjunction. She suggested that the meiotic mutation *nod* is defective only in disjunction, the final step of the process. Because *ald* allows exchange X chromosomes to participate in distributive disjunction, it defines a fourth component of the distributive system: selection of chromosomes available for distributive disjunction.

Since *ald* allows exchange X-chromosomes to disjoin via the distributive system, it is surprising that nondisjunction of the major autosomes is not increased to the same extent as the X chromosome. Two explanations that may

account for this result are as follows. First, perhaps *ald* is a leaky mutation, and the residual ald^+ activity is sufficient to prevent the participation of exchange autosomes in the distributive system. Second, it may be that the ald^+ gene product is only needed for proper disjunction of the X and *4th* chromosomes. If true, this is not because the major autosomes are metacentric and the X and *4th* chromosomes are acrocentric, for both the attached-X and Y chromosomes are metacentric and are still susceptible to the mutant effect.

Like the X chromosomes, the *4th* chromosomes exhibit an increased frequency of nonhomologous disjunction as a result of the *ald* mutation. The experiments reported here document the increased disjunction of the *4th* chromosome from the following sex chromosomes as a result of the *ald* defect: the X chromosome, the attached-X chromosome, free-X duplications, and the Y chromosome. Other than the increased participation of the 4th chromosomes, other aspects of these nonhomologous disjunction events appear to be normal. This is most clear in the *C(1)RM/0* cross (Table 7) in which all *4th* chromosome exceptions were a result of the disjunction of the *4th* chromosomes from the attached-X chromosome. Similarly, the *4th* chromosomes also disjoin from the Y chromosome at a high frequency in XXY females. In these females, the *4th* chromosomes behave just like the X chromosomes that disjoin from the Y chromosome in the same cross.

In summary, the simplest interpretation is that *4th* chromosomes are available for nonhomologous disjunction with an increased frequency as a result of the *ald* defect. As in wild type, the majority of X chromosome E_0 tetrads are available for nonhomologous disjunction in *ald* females. However, in *ald* females, some exchange-X chromosome tetrads are also available for nonhomologous disjunction. Other aspects of the nonhomologous disjunction process are apparently normal. It is these two properties of the mutation that must be accounted for when considering the action of the ald^+ gene product.

The action of ald^+

The *ald* mutation has been shown to reduce the efficiency of the size recognition process, thereby increasing the incidence of *4th*-chromosome nonhomologous disjunction. The *ald* mutation also reduces the efficiency of exchange exclusion, thereby allowing X chromosomes that have undergone exchange to participate in nonhomologous disjunction. The increase in *4th*-chromosome nonhomologous disjunction is a property *ald* shares with the synthetic meiotic mutation *mei-S51* (ROBBINS 1971). However, the effect of *ald* on exchange exclusion is not shared with *mei-S51*. These results suggest that *ald* affects a step in meiosis that is shared by the size recognition and exchange exclusion processes. Therefore, it is of interest to consider how ald^+ acts in the meiotic process. The discussion here will not treat the evidence and the theory of the Drosophila female meiosis in detail; sources of this information are the reviews of GRELL (1976) and NOVITSKI and PURO (1978).

GRELL (1962a) proposed a model of meiosis to account for both exchange and distributive disjunction. She suggested that two rounds of meiotic pairing occur. In the first round, chromosomes pair for exchange. Chromosomes undergoing exchange with a homolog form a bivalent and disjoin via the exchange disjunc-

tion pathway. All chromosomes failing to secure a disjunctional partner in the first round choose a disjunctional partner in a second round. This second round is responsible for nonhomologous disjunction events and the regular disjunction of nonexchange chromosomes.

Given this sequence of events, *ald* must affect several distinct processes. First, chromosomes that have recombined must be able to participate in the distributive system as a result of the *ald* defect. Second, the rules by which distributive disjunction occurs (*i.e.*, size recognition) must be altered to allow X,*4* nonhomologous disjunction. This is because such disjunction events rarely occur in wild type even when both the X and *4th* chromosomes disjoin via the distributive system. Finally, the proper disjunction of two nonexchange-X chromosomes and the two *4th* chromosomes via the distributive system is visualized as a consequence of two distributive bivalents in this model. However, in *ald* females, X,*4* nonhomologous disjunction was observed (Table 1), but the array of gametes produced could not be accounted for by each X chromosome disjoining from a *4th* chromosome, nor by any other paired configurations of chromosomes.

Indeed, the analysis reported here suggests that distributive disjunction in *ald* females generally proceeds from a single multichromosomal complex. In XXY;*ald/ald* females the presence of the X chromosomes as alternative disjunctional partners for the Y chromosome diminished the occurrence of Y,*4* nonhomologous disjunction. Nevertheless, *4th*-chromosome nondisjunction remained constant when measured only in exceptional-X progeny. Therefore, even when an XXY trivalent forms, the *4th* chromosomes are not more likely to form a bivalent for distributive disjunction. These results make it likely that, in *ald*, disjunction of chromosomes in the distributive system is not achieved by each chromosome finding a disjunctional partner. Rather, the distributive system in *ald* supports only the disjunction of chromosomes from one multivalent. All chromosomes using the distributive system participate in this multivalent or, possibly, move at random to either pole.

It is not clear if the *ald* mutation is causing these multichromosomal associations or increasing the frequency of associations that normally exist at a low level in wild-type females. However, the attached-X crosses reported in Table 7 do allow a comparison between *ald* and *ald*$^+$ females in this regard. In both *ald* and ald$^+$ attached-X females (Table 7), the *4th* chromosomes nondisjoin as a result of nonhomologous disjunction from the attached-X chromosome. The addition of a homolog for the attached-X chromosome failed to lower *4th*-chromosome nondisjunction in both *ald* and *ald*$^+$ females. Furthermore, the Y chromosome proved to be a better disjunctional partner for the attached-X chromosome than *Dp3*, but *4th*-chromosome nondisjunction did not change appreciably as a consequence in both types of females. These results imply that, even when the attached-X is disjoining from the Y chromosome or *Dp3*, the *4th* chromosomes are not any more likely to become disjunctional partners in either *ald* or *ald*$^+$ females. Therefore, these results suggest that *ald* is increasing the frequency of multichromosomal associations that occur at a low level in wild-type females, but that disjunction from the multivalent is similar in *ald* and *ald*$^+$ females.

If *ald* is increasing the frequency of multichromosomal associations, it does so by allowing exchange-X chromosomes and *4th* chromosomes to participate in these associations at an increased frequency. With regard to the *4th* chromosomes, NOVITSKI and PURO (1978) have suggested that the *4th* chromosomes avoid nonhomologous disjunction events because they are located in a distinct region of the nucleus. If this is true, *ald* must also be defective in the process establishing such a spatial distribution of chromosomes. Based on the behavior of *ald*, it is more economical to imagine that a size recognition mechanism (GRELL 1964) promotes the formation of the *4th*-chromosome bivalent. A second process, identical with that which renders exchange chromosomes unavailable for nonhomologous disjunction, also prevents the participation of the *4th*-chromosome bivalent in nonhomologous disjunction events. It is this second process that would be defective in *ald* females, thereby accounting for its effect on both the exchange exclusion and size recognition processes.

Therefore, adapting earlier models of the meiotic process, the characterization of *ald* suggests the following scheme of meiosis. Meiosis begins with all chromosomes associated. Recombination occurs, identifying bivalents to be removed from these associations. During this time the *4th* chromosomes identify one another as disjunctional partners by the size recognition mechanism. Exchange and size recognition are imagined to be two pathways by which bivalents are rendered unavailable for nonhomologous disjunction. In *ald*, the system that removes these bivalents is defective, causing both exchange-X chromosomes and *4th* chromosomes to participate in nonhomologous disjunction events with increased frequency. The analysis of *ald* females suggests that nonhomologous disjunction occurs via a multivalent with the minimal requirement that at least one chromosome be distributed to each pole. A second property of nonhomologous disjunction, determined from work with wild-type females (reviewed by GRELL 1976) and also governing disjunction in *ald*, is that a metacentric chromosome has the ability to orient this multivalent to bring about the disjunction of two acrocentric chromosomes from the metacentric chromosome. In this model it is supposed that nonrandom disjunction of large nonexchange chromosomes previously ascribed to the size recognition process (GRELL 1963) is also due to preferential orientation of the multivalent.

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