MUTANTS AFFECTING MEIOSIS IN NATURAL POPULATIONS OF *DROSOPHILA MELANOGASTER*[1]

L. SANDLER, D. L. LINDSLEY,[2] B. NICOLETTI AND G. TRIPPA

Department of Genetics, University of Washington, Seattle, Washington 98105; Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37831; and Istituto di Genetica, Università di Roma, Rome, Italy

Received March 25, 1968

IN Drosophila, maize, and the fungi we have precise, and indeed at times elegant, genetic descriptions of the meiotic process; furthermore, in maize, the meiotic cytology during microsporogenesis has been thoroughly studied. It is surprising, therefore, that little is known about the genetic control of meiosis (however, for an early theoretical discussion of the genetic control of meiosis see DARLINGTON 1932). For this reason, we began a systematic search for, and study of, mutations affecting one or more of the processes which together comprise meiosis. The existence of such *meiotic mutants* follows from the generally accepted induction that all cellular processes are ultimately under genic control, but it need not follow that mutants controlling a significant fraction of the steps in meiosis can be isolated by existing cytogenetic techniques. Two lines of evidence, however, suggest that at least many meiotic mutants can be resolved. First, the variable quantities of meiosis, namely the rates of crossing over and nondisjunction, are sensitive to background genotype, and these genotypic differences should be resolvable into their individual components. Second, instances are known in which specific changes in the genotype, including in some cases mutational changes, cause altered meiotic behavior.

However, the genotypic control of chromosome behavior is operationally different from that of other physiological processes in that the chromosomes both carry the controlling genes and, at the same time, respond to them. Thus, it is necessary to distinguish between aberrant control mechanisms and the aberrant response of abnormal chromosome complements to a normal control mechanism, e.g., crossing over in heterozygous inversions (STURTEVANT and BEADLE 1936). Where abnormal meiotic behavior is the result of a mutation we propose the name *meiotic* and the symbol *mei-* followed by a specific locus designation.

Reviews have appeared recently on genetic control of recombination (LINDSLEY *et al.* 1967; EMERSON 1967) and on meiotic control in general (NICOLETTI 1968). In this discussion, we shall restrict ourselves to a consideration of genetically controlled meiotic effects in Drosophila.

A striking example of genotypic influence on meiosis is sex in Drosophila

[1] Research sponsored jointly by Grant RG-9965 from the Public Health Service, the U. S. Atomic Energy Commission under contract with the Union Carbide Corporation, and the Italian National Research Council (CNR).

[2] Present address: Department of Biology, University of California San Diego, La Jolla, California 92037.

where crossing over is restricted to the female (MORGAN 1912). Concomitantly, the complex series of cytological events normally characterizing prophase I is atypical in Drosophila males (COOPER 1950). Evidently, in Drosophila, the differences in meiotic behavior between the sexes are genetically more fundamental than merely a difference in recombination rates. In females, nonhomologous chromosomes can pair and disjoin from each other; this phenomenon cannot be demonstrated in males, however (for a review of the features of nonhomologous pairing see GRELL 1967). This and similar cases, e.g., the silkworm (TANAKA 1913), may well be extreme examples of a more general phenomenon of differences in the crossover rates between the sexes [e.g., in the mouse (SLIZYNSKI 1960), in corn (RHOADES 1941), and in *Drosophila ananassae* (MORIWAKI 1937) where recombination apparently does occur in males but with a reduced frequency compared with that in females; more generally, see DUNN and BENNETT 1967].

Another effect of the genotype on meiotic behavior in Drosophila is the interchromosomal effect (see, for example, SCHULTZ and REDFIELD 1951), in which sequential heterozygosity in one chromosome pair increases the frequency of crossing over in the other chromosomes of the complement. RONEN (1964) has recently shown that, contrary to earlier indications, this phenomenon extends to mitotic crossing over.

In mitotic recombination in Drosophila (for a more general review and references, see LINDSLEY *et al.* 1967) two other kinds of genotypic controls have been elucidated. First, the class of mutation called Minutes (symbol: *M*, generally deficiencies with a dominant small-bristle phenotype that are recessive lethals), when heterozygous, increase the frequency of mitotic crossing over (STERN 1936; KAPLAN 1953), although there is no evidence that they increase meiotic crossing over (HINTON 1967). Second, WEAVER (1960) presented convincing evidence for genes on all of the chromosomes of the complement that control the frequency of mitotic recombination.

Meiotic anomalies involving the sex chromosomes in males have been discovered in a variety of Drosophila species. The first sex ratio *X* chromosome was found by GERSHENSON (1928) in *Drosophila obscura*, but examples are now known in several other species [for a recent study, see STALKER (1961)]. Males carrying a *SR X* chromosome produce mostly *X*-bearing sperm. A new sex ratio anomaly, probably different from *SR*, was recently reported in *Drosophila simulans* (FAULHABER 1967). Finally, there is the gene, *MSR*, (NOVITSKI 1947) in *Drosophila affinis* which reverses the action of *SR*; i.e., a *SR*; *MSR* male produces a preponderance of *Y*-bearing sperm.

In *Drosophila melanogaster*, five *bona fide* meiotic mutants are known; they are described briefly in the following paragraphs:

c(3)G: crossover suppressor in chromosome 3 of GOWEN: This is a recessive allele located at 57.4 on chromosome *3*, first studied by GOWEN and GOWEN (1922) and GOWEN (1928, 1933). Homozygous *c(3)G* females produce virtually no meiotic recombinants but produce a very high frequency of nondisjunction at the first meiotic division; mitotic crossing over, on the other hand, is normal

(LE CLERC 1946). Homologs do not segregate at random and the different chromosome pairs of the complement do not disjoin independently (for discussion, see LINDSLEY *et al.* 1967). Homozygous males show no meiotic irregularities. Synaptinemal complexes, normally present in early oöcytes, are absent in *c(3)G* homozygotes (MEYER 1964; SMITH and KING 1967). Heterozygotes, surprisingly, exhibit somewhat higher than normal recombination (HINTON 1966), while heterozygotes for $c(3)G^{+}$ and $Df(3R)sbd^{105} = Df(3R)88F;89B4\text{–}5$, a deficiency for *c(3)G*, exhibit lower than normal recombination.

ca^{nd}: *claret-nondisjunctional:* This is an allele of *ca* located at 100.7 on chromosome 3. The mutant was first discovered in *D. simulans* by STURTEVANT (1929), and later LEWIS and GENCARELLA (1952) found a similar allele in *D. melanogaster*. Crossing over is approximately normal in ca^{nd} females, but there is an exceedingly high incidence of nondisjunction of all pairs of homologs in the first meiotic division; however, homologs separate more often than 50%. Furthermore, chromosome loss is frequent during meiosis and probably also during the mitotic divisions. The frequency and direction of nondisjunction of the different chromosome pairs are highly correlated within cells (DAVIS 1963). The meiotic effect is cell autonomous (ROBERTS 1962), and does not depend on the *ca* phenotype, but is manifest even in the presence of the mutant, white (STURTEVANT 1956).

eq: equational producer. This gene lies near the base of the *X* chromosome and results in the production of sperm carrying 2*X* chromosomes, i.e., it causes nondisjunction of the *eq*-bearing *X* chromatids at the second meiotic division (SCHULTZ 1934). Heterozygous females are also reported to show nondisjunction, but it is unclear whether at the first or second division, and it is not known how the autosomes behave in either sex.

SD: Segregation Distorter: This locus lies near the centromere of chromosome 2; *SD*/+ males transmit the *SD*-bearing second chromosome to more than half the progeny, often 95% or more (SANDLER, HIRAIZUMI, and SANDLER 1957). *SD* has no effect in females. The regular separation of the *SD*-bearing chromosome from its homolog and the suppression of distortion by second-chromosome inversions suggest that *SD* acts at or after pairing. PEACOCK and ERICKSON (1965) have presented evidence that the mechanism of distortion is the directed segregation of the *SD*-bearing chromosome toward the meiotic pole destined to form functional sperm and the consequent segregation of SD^{+} to a nonfunctional pole. However, more recent and very convincing evidence (NICOLETTI 1968; NICOLETTI and TRIPPA 1967; NICOLETTI TRIPPA and DEMARCO 1967; HARTL, HIRAIZUMI and CROW 1968) that the number of progeny produced by an *SD* male is reduced in proportion to the amount of distortion suggests that the phenomenon of segregation distortion results from inactivation of SD^{+}-bearing sperm by *SD*.

RD: Recovery Disrupter: This locus (NOVITSKI and HANKS 1961; HANKS 1964), on the *X* chromosome, is without effect in females, but in males it results in fragmentation of the *Y* chromosome (ERICKSON 1965) and a concomitant production of an excess of female progeny.

Thus, in *D. melanogaster* we find two meiotic mutants, *c(3)G* and ca^{nd}, that

act at the first meiotic division and affect only females. It seems most probable that *c(3)G* acts first because it affects both recombination and segregation, whereas ca^{nd} causes only segregational anomalies. The control of the first division in males is clearly different; *c(3)G* and ca^{nd} are without effect, whereas *SD* and *RD* affect only males. *SD* apparently acts during or following conjugation; the situation is not clear with respect to *RD*. *eq* acts during the second meiotic division and may affect meiosis in both sexes; however, the available data are insufficient for firm conclusions. It will be shown later that a meiotic mutant affecting the second meiotic division does act in both sexes, suggesting identical control of at least some aspects of chromosome behavior during the second meiotic division in the two sexes.

To extend our understanding of the genetic control of meiosis it seems clear that an intensive study of more meiotic mutants would be very useful, and to this end an experiment to detect meiotic mutants was devised. It seemed desirable in the first instance to try to find meiotic mutants in natural populations because, in addition to collecting the mutants themselves, it should be possible to get some idea of how frequent they are. Accordingly, a series of second and third chromosomes were collected from natural populations near Rome, Italy. One second and one third chromosome are referred to as a *two-three complement* or a *test complement*. Two-three complements were made homozygous (1) in females heterozygous for well-marked *X* chromosomes and homozygous for marked fourth chromosomes all derived from laboratory stocks, and (2) in males carrying a laboratory-derived *X* and the marked fourth-chromosome pair. The marked, laboratory-derived chromosome pairs are referred to collectively as the *sex-four complement* or the *diagnostic complement*. In females, the effects of the two-three complements on crossing over between the diagnostic complement *X*'s and on segregation of both pairs of chromosomes of the diagnostic complement were followed; in males the effect of the two-three complements on segregation of diagnostic complement fourth chromosomes was followed.

The results indicate the following: Of 118 two-three complements examined in females, 11 had a detectable effect on the meiotic behavior of the diagnostic complement; all of these affect segregation, while two decrease and one increases recombination. Of 123 two-three complements and 177 half complements (either chromosome *2* or *3*) tested in males, four had an effect on segregation of the diagnostic complement fours. Of these, two cases proved to be allelic and one had an effect in females also and was, therefore, enumerated above. In addition, a new occurrence of the segregation-distorter (*SD*) gene was found. Further, a comparison of the variance in crossing over among individuals carrying the same test and diagnostic complements with that among individuals carrying the same diagnostic complement but different two-three complements indicates that a significant fraction of the total variance in crossing over in these natural populations is attributable to genetic differences among the two-three complements.

From these findings, it seems clear that there exist many meiotic mutants, affecting a variety of meiotic processes, detectable by standard cytogenetic tech-

niques. Moreover, although the intensive investigation of the behavior of these mutants has only just begun, several new principles about recombination and segregation can be inferred and a general outline, in the nature of a flow chart of the genetic control of chromosome behavior during meiosis, can be constructed. This outline exhibits both the relationships between the meiotic mutants and between the meiotic mutants and chromosome behavior during the germ-line cell divisions.

EXPERIMENTAL DESIGN

The wild-type flies from which the test complements were extracted were collected from two localities on the outskirts of Rome, Italy, during October, 1965. The Via Ostiense population was collected in the city's wholesale fruit market on the southwest edge of the city, and the Via Salaria population was collected in a winery, about 15 kilometers northeast of Rome, during the grape harvest. A small number of two-three complements were also selected from flies collected near the University of Rome on the east side of the city (Via Tiburtina).

The method utilized for making two-three complements (2_i; 3_i) homozygous in a genotype in which meiotic parameters could be measured is outlined in Figure 1. The exact procedure varies slightly depending on the source of 2_i; 3_i. Since in the present experiments two-three complements were extracted from natural populations, individual males were used in the first generation mating, and a single son was selected from the progeny of each first generation male for the second generation cross. Thus a single two-three complement was selected from each population male sampled. When mutagen-treated two-three complements are to be tested, the multiplicity of treated males used in the first cross is immaterial; furthermore any number of sons may be utilized in the second generation cross, but they must be crossed individually since each second generation male carries an independently-treated two-three complement (assuming that postmeiotically treated cells are sampled). If the presence of mosaicism is likely, e.g. following chemical-mutagen treatment, then y/Y_i; $2_i/T(2;3)S9$, *bw e*/3_i; $spa^{pol}/4_i$ sons produced by the generation-1 cross may be back-crossed individually to females with the maternal genotype y/y; *SM1*/*T(2;3)S9*, *bw e*/*TM2*; spa^{pol}/spa^{pol}, and a single y/Y_i; $2_i/T(2;3)S9$, *bw e*/3_i; spa^{pol}/spa^{pol} son chosen from each culture for crossing in generation 2. This amounts to selecting a half chromatid from a treated two-three complement for further crossing. In actual practice we made varying numbers of such backcrosses to preserve some two-three complements while others were being passed through later generations of the scheme. If, in one of these backcross generations, reversed-compound-*X*/marked-*Y* females (e.g. *C(1)RM*/$y+Y$) are substituted for the free-*X* (i.e. y/y) females, then Y_i is replaced by $y+Y$ wherever Y_i appears in subsequent generations of the crossing scheme. For all procedures described, several males heterozygous for the same two-three complement are available for use in a mass mating in generation 3.

The males from the natural populations were crossed in the first generation to y/y; *SM1*/*T(2;3)S9 bw e*/*TM2*; spa^{pol}/spa^{pol} females from stock. *SM1* is a second-chromosome balancer of constitution *In(2LR)SM1*, al^2 *Cy* cn^2 sp^2, where *In(2LR)SM1* represents *In(2LR)22A3-B1; 60B-C* on *In(2L)22D1–2;33F5–34A1* + *In(2R)42A2–3;58A-B1*, formed by superimposing the pericentric inversion upon *In(2L+2R)Cy*. *TM2* is a third-chromosome balancer of constitution *In(3LR)Ubx*^{130}, *Ubx*^{130} e^s, where *In(3LR)Ubx*^{130} = *In(3LR)61A-C;74;89D-E;93B;96A*. We induced *T(2;3)S9* in a *bw*; *e* stock. It has both breaks in the chromocentral heterochromatin and is homozygous lethal. Its use was intended to guarantee the recovery in viable zygotes, of only *T(2;3)*- and *2;3*-bearing gametes; however, we failed to consider that crosses between *T(2;3)S9* heterozygotes would produce complementary aneuploid types, and except for the first generation, this feature of the scheme was ineffective. In the second generation, *FM6*/*multex*; *SM1*/*T(2;3) S9*, *bw e*/*TM2*; spa^{pol}/spa^{pol} females from stock are employed. *FM6* is an *X*-chromosome balancer of constitution *In(1)FM6*, y^{31d} sc^8 *dm B* where *In(1)FM6* was produced by superimposing first *In(1)3C;4EF* and second *In(1)15D-E;20* on *In(1)*sc^8+*dl-49* = *In(1)1B2–3;20B-D1*

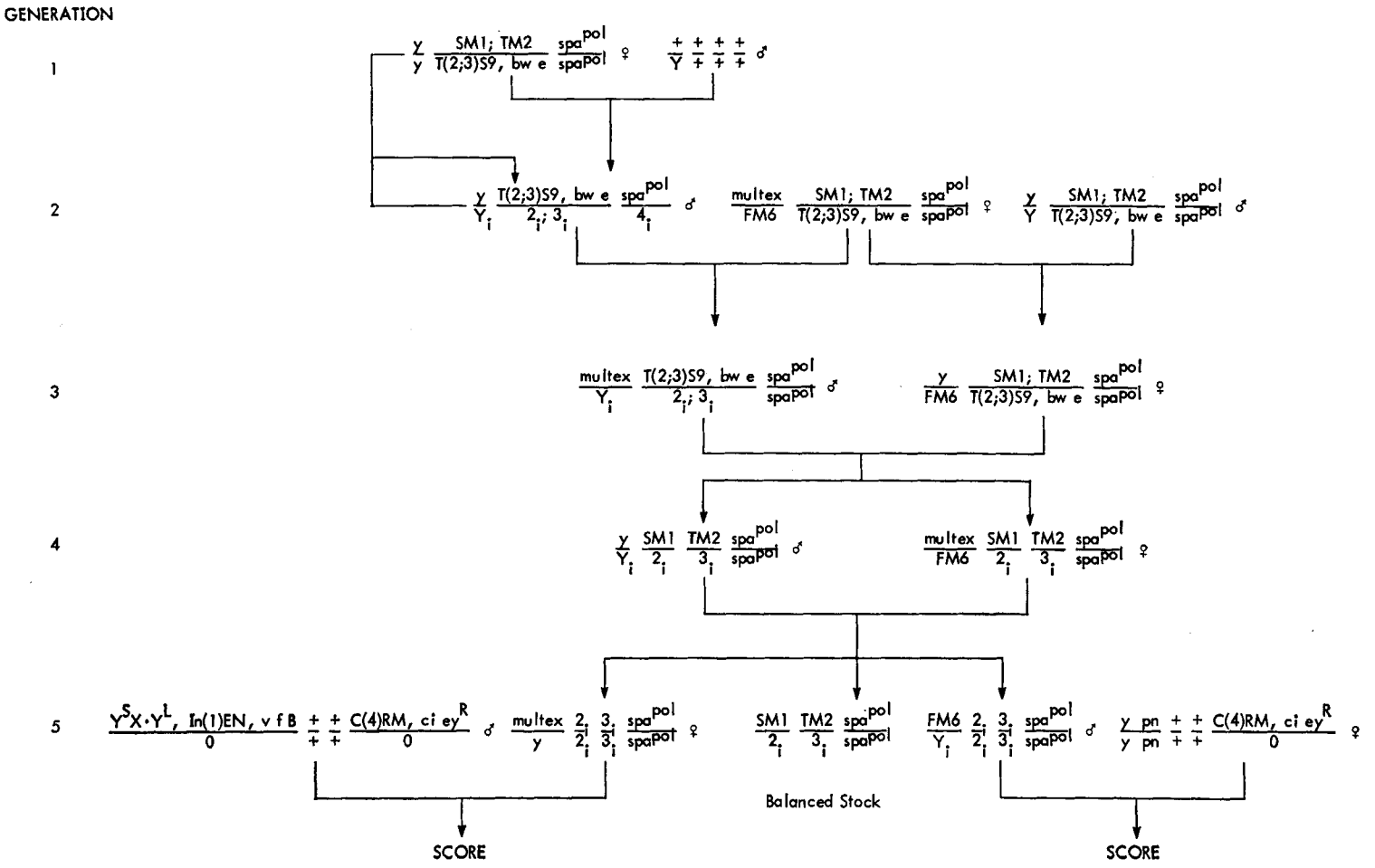
GENERATION
1
2
3
4
5
SCORE
Balanced Stock
SCORE

TABLE 1

Phenotypes of females homozygous for autosomal pairs derived from natural populations at Via Ostiense (VO) and Via Salaria (VS), Rome, Italy
Viability information is presented on the left side of the table; information on the fertility of lethal-free autosomal pairs is presented on the right side

	Viability of homozygous autosomal pairs					Female fertility of +; + autosomal pairs				
							Sterile on chromosome			
Population	+; +	l(2); +	+; l(3)	l(2); l(3)	Σ	Fertile	2	3	not tested	not tested
VO	31	21	18	11	81	18	6	4	2	1
VS	140	80	97	72	389	100	8	9	19	4
Σ	171	101	115	83	470	118	14	13	21	5

+ *In(1)4D7-E1;11F2–4*. Since *In(1)3C;4E-F* virtually reinverts *In(1)4D7-E1;11F2–4*, *FM6* is not a very effective balancer, especially in the presence of heterozygous *SM1* and *TM2*. The symbol, *multex*, designates *In(1LR)sc^{V1}, y pn cv m f.y+;* owing to the balancing inefficiency of *FM6*, *m* was lost frequently and *cv* somewhat less frequently from *multex* in the stock mentioned above. On the basis of our initial experience, we feel that replacement of the original *multex* with *In(1LR)sc^{V1}, y pn v·y+* considerably simplifies the procedure without appreciable loss of resolution owing to failure to detect multiple recombinants.

In generation 3, as many *multex* males carrying the same two-three complement as could be collected were crossed *en masse* with females of the genotype and source shown in Figure 1. The ensuing generation is the first one in which virgins must be selected from each two-three-complement line, rather than from a stock culture, and this represents one of the steps in the procedure limiting the number of complements that can be analyzed simultaneously. It is also the first time that a female carrying a test complement has been used; the autosomes are prevented from recombining however, by the presence of *SM1* and *TM2*. Phenotypically *Cy Ubx e+* flies in generation 4 are of the constitution $SM1/2_i$; $TM2/3_i$, and inbreeding them produces a balanced stock in which the persistence of the majority of 2_i and 3_i is assured, but which may produce homozygotes for either or both of the test autosomes. By choosing appropriate sex-chromosome genotypes for inbreeding in generation 4, the balanced autosomal line may be made to produce, in generation 5, flies homozygous for the test complement and with the appropriate diagnostic complement. In screening for meiotic mutants acting in females, flies of constitution *In(1LR)sc^{V1}, y pn cv m f·y+/y;* $2_i/2_i$; $3_i/3_i$; *spa^{pol}/spa^{pol}* were chosen for crossing. $2_i/2_i$; $TM2/3_i$ and $2_i/SM1$; $3_i/3_i$ females were eschewed on the grounds that heterozygosity for a highly rearranged chromosome was alone sufficient to cause abnormal meiotic behavior of the diagnostic chromosomes. In retrospect, however, the meiotic mutants that were recovered would have been recognized as such in homozygotes in which the other autosome was heterozygous for the balancer; thus, many autosomes which could have been tested successfully were discarded after five generations of crossing owing to the presence of a lethal or sterile mutation in the other member of their two-three complement. The viability and fertility of generation 5 females homozygous for the two-three complements processed are summarized in Table 1. It can be seen that of 470 two-three complements examined, only 171 were lethal free and of these only 118 were also female fertile.

FIGURE 1.—The crossing scheme employed to examine the effects of homozygous two-three complements (2_i; 3_i = i^{th} two-three complement) on the meiotic behavior of the diagnostic complement. Replacement of *y/y* with *C(1)/y+Y* in the female in generation 2 will result in the replacement of Y_i with *y+Y* in all subsequent generations. The symbol, *multex*, in generation 2 represents either *In(1LR)sc^{V1}, y pn cv m f·y+* or *In(1LR)sc^{V1}, y pn v·y+*.

Females of the above constitution were crossed individually to $Y^{S}X{\cdot}Y^{L}$, *In(1)EN, v f B/0; C(4)RM, ci* $ey^{R}/0$ males, where *C(4)RM* designates a reversed-metacentric-compound fourth chromosome. We attempted to make at least five duplicate crosses for each tested two-three complement. One-half the regular maternal fourth-chromosome segregants are recovered as haplo-*4*'s owing to fertilization with nullo-*4* sperm. Haplo-*4*'s are extreme Minute, which causes erratic recovery; consequently, although counted, they have been eliminated from all the data presented; the other half of the regular progeny are *C(4)RM, ci* ey^{R}/spa^{pol}, which are phenotypically normal, triplo-*4* flies. Two types of ova that are exceptional for chromosome *4* are produced: diplo-*4* zygotes, which we presume to be virtually lethal following GRELL (1961), when fertilized by *C(4)RM*-bearing sperm; nullo-*4* ova produce viable *C(4)RM, ci* ey^{R} zygotes when fertilized by *C(4)RM*-bearing sperm but are nullo-*4* and inviable when fertilized by nullo-*4* sperm. Thus half of all maternal fourth-chromosome genotypes, regular and exceptional alike, are recoverable from the cross. Half the maternal *X*-chromosome exceptions are inviable depending on the sex chromosome content of the fertilizing sperm; all regular classes, on the other hand, survive so that the efficiency of recovery of exceptional sex chromosome types is only half that for regular segregants. Progeny phenotypes with respect to *B* are used in scoring for sex-chromosome exceptions; *B*/+ females and + males are the regular, and +/+ females and *B* males are the exceptional classes. The two exceptional gamete types provide information on somewhat different aspects of the meiotic process. Together, they test for homologous recognition and chromosome orientation, while the nullo class, by itself, measures, additionally, the capacity for anaphase movement.

In addition to scoring the progeny of generation 5 females for *X*- and fourth-chromosome exceptions, crossing over in four regions of the *X* chromosome was measured (*pn—cv* = region 1, *cv—m* = region 2, *m—f* = region 3, and *f*—centromere = region 4). Our initial intention was to select for further examination two-three complements which caused abnormal disjunction, or abnormal recombination, or both. We attempted to use a sequential analysis method for early detection of abnormal recombination; unfortunately, recombination was more variable than assumed in designing the sequential analysis scheme so that instead of selecting 10% of the cases for further counting as intended, we were saving the great majority of them. Therefore, abnormal map distance was abandoned as a criterion for selecting presumptive meiotic mutants, although all progenies continued to be scored for recombination. Instead, presumptive mutants were selected on the basis of increased nondisjunction of the *X*'s and the *4*'s alone. All mutants recovered would have been detectable simply on the basis of chromosome-*4* behavior. Also since the two-three complements were homozygous in the test females, the influence of heterozygosity for autosomal inversions on meiotic behavior of the *X*'s and *4*'s is not a factor that need be considered.

$FM6/Y_i$ (or in subsequent generations y/Y_i) males were also tested for the presence of meiotic mutants. Single-autosome homozygotes, in which the other autosome carried either a lethal or a sterile, were also tested since the interchromosomal effect on segregation is inoperative in males. Consequently, many partial two-three complements that were not examined in females were scored in males. The viability and fertility of the homozygous two-three complements examined for the presence of genes affecting fourth-chromosome disjunction in the male are summarized in Table 2. Of 458 two-three complements, 123 were lethal free and male fertile for both 2_i and 3_i, 87 for 2_i but not 3_i, and 90 for 3_i but not 2_i. These 123 full two-three complements and 177 half complements were examined for their effect on fourth-chromosome disjunction.

The combined data for the frequencies of recessive lethal and sterile mutations in both males and females are given in Table 3. Two-three complements causing sterility in either males or females alone were more common than those sterilizing both sexes; the latter are listed both as male steriles and female steriles in the tables.

Since our initial intention was to screen only for mutations affecting meiosis in females, no provision was made to produce males in which sex chromosome nondisjunction could be detected; as pointed out previously, however, it is possible to arrange the cross such that Y_i is replaced by

TABLE 2

Phenotypes of males homozygous for autosomes derived from natural populations at Via Ostiense (VO) and Via Salaria (VS), Rome, Italy. The autosomal pairs are first divided according to whether they carry recessive lethal factors on chromosomes 2 or 3; the data are further subdivided according to the fertility of males homozygous for the nonlethal-bearing chromosomes.

Population	+; +			1(2); +			+; 1(3)			1(2); 1(3)	Σ
	Fertile	Sterile	not tested	Fertile	Sterile	not tested	Fertile	Sterile	not tested		
VO	23	8	3	13	3	2	13	3	4	9	81
VS	100	29	5	77	6	11	74	14	3	58	377
Σ	123	37	8	90	9	13	87	17	7	67	458
ΣΣ	..	168	..	..	112	..	..	111	..	67	458

a marked *Y*, e.g., y^+Y. In the early stages of the experiments presumptive meiotic-mutant-bearing males in generation 5 were crossed to *C(1)RM, y/0; C(4)RM, ci* $ey^R/0$ females taken from the same stock that produced $Y^SX{\cdot}Y^L$, *In(1)EN, v f B/O; C(4)RM, ci* $ey^R/0$ males to which the presumptive meiotic-mutant-bearing females were crossed. Unfortunately, we rediscovered the highly regular segregation of the compound *X* from the compound *4* reported earlier by GRELL (1963) for females of the above genotype. The majority of ova produced were *C(1)RM; 0*, which survive when fertilized by *Y*-bearing diplo-*4* sperm, and *0*; *C(4)RM*, which survive when fertilized by *X*-bearing, haplo-*4* or nullo-*4* sperm. Thus, both regular and exceptional males, but only exceptional females, were recovered with representative frequencies. In later crosses, the sampling was improved by replacing the compound *X* with free *X*'s as indicated in Figure 1; under these conditions, the *X*'s separate and *C(4)RM* passes at random to the poles at the first meiotic division.

The crossing procedure was designed for the detection of recessive mutations on the second or third chromosome that cause abnormal disjunction of either the *X* or the fourth chromosomes or abnormal *X*-chromosome recombination in females or abnormal fourth-chromosome disjunc-

TABLE 3

Summary of viability and fertility characteristics of autosomes derived from data in Tables 1 and 2. Percents of chromosomes 2 and 3 with recessive lethals, male-sterile, and female-sterile factors are listed.

Phenotype	Chromosome	Via Ostiense		Via Salaria	
		♂	♀	♂	♀
Lethal	2	...	39.5	...	39.1
	3	...	35.8	...	43.4
Sterile	2	18.7*	24.0†	7.2*	12.4†
	3	18.7‡	16.0†	15.9‡	14.0†
	2 + 3	25.8§	...	22.5§	...

* Calculated from the +; *l(3)* class in Table 2.
† Calculated from the +; + class in Table 1 by multiplying the percent sterile +; + pairs by the fraction of the tested sterile factors on the chromosome in question.
‡ Calculated from the *l(2)*; + class in Table 2.
§ Calculated from the +; + class in Table 2.

tion in males. Mutants with other meiotic effects that can be imagined would not have been detected by these procedures. For example, mutations that affect the meiotic behavior of only the chromosome on which they are located would have been missed as would mutants affecting *X—Y* disjunction or allowing meiotic recombination in males. The first type of mutant might be detected by crossing test-complement homozygotes with compound-autosome-bearing males in the case of females and perhaps with triploid females in the case of males; this would allow the demonstration and recovery of autosomal alleles causing autosomal nondisjunction. The recovery of recessive genes affecting the linkage relations of the chromosome on which they are carried presents a much more difficult problem whose solution is not clear. The second type of mutant mentioned could be easily detected by replacing Y_i with a marked *Y* as discussed previously in connection with Figure 1. A rather simple modification of the scheme presented in Figure 1 would permit the detection of recessive genes allowing meiotic recombination in males; replacement of *T(2;3)S9, bw e* in generation 3 males and subsequently *SM1; TM2* in generation 4 males with, for example, *S Pin; R Pr* would permit recovery of males of autosomal constitution $2_i/2_i$; $3_i/R$ *Pr* and $2_i/S$ *Pin*; $3_i/3_i$ in which autosomal recombination could be detected.

For every autosomal complement that carried a putative female meiotic mutant, two $SM1/2_i$; $TM2/3_i$; spa^{pol}/spa^{pol} lines were established—one that was *multex/FM6* and one that was *y*. By performing appropriate crosses between these lines it was possible to produce anew females homozygous for 2_i; 3_i and with the diagnostic complement appropriate for retesting the suspected mutant. The same cross also produced (1) $SM1/2_i$; $3_i/3_i$, (2) $2_i/2_i$; $TM2/3_i$, and (3) $SM1/2_i$; $TM2/3_i$, which were also crossed to $Y^SX{\cdot}Y^L$, *In(1)EN, v f B/0; C(4)RM, ci* $ey^R/0$ males to ascertain which chromosome carried the mutant and to detect dominance. Single balanced lines were also established of female-sterile-, male-sterile-, and suspected male-meiotic-mutant-bearing two-three complements. Retests of presumptive male meiotic mutants were carried out in much the same way as for female mutants to confirm the presence of a mutant, to identify its chromosome, and to assess its dominance. Female-sterile and semisterile complements were also retested to examine the possibility that they carried a meiotic mutant so extreme as to virtually sterilize. They were retested both by repeating the original test cross and by crossing them to compound-autosome-bearing males to detect genomes in which sterility was attributable to a high incidence of autosomal nondisjunction. Several of the presumptive female-sterile mutants did in fact produce autosomal-exceptional progeny in such crosses; *mei-T3*, which is discussed in the next section, is such a mutant.

Two-three complements that contained a mutant of interest were carried in stocks segregating for both *SM1* and *TM2*, and, to the extent that these balancer chromosomes improved survival or fertility of the lines, they persisted. However, no balancer is completely effective and the possibility of losing a mutant by recombination between the test autosome and the balancer is a problem. This is true of mutations located in the distal half of *3L* and especially those toward the end of *3R* where the balancing efficiency of *TM2* is low indeed. A number of suspected mutants that disappeared between their initial detection and subsequent retests may have been in chromosomal regions that recombine with the balancers.

Two mutants that were recovered ought perhaps to be mentioned before considering the other meiotic mutants in detail. The first of these was a new occurrence of *SD* (Segregation Distorter). It has been studied by two of us (NICOLETTI 1968, NICOLETTI and TRIPPA 1967; NICOLETTI *et al.* 1967). It maps in the center of chromosome *2* as do other *SD* alleles and exhibits all the segregational properties of other *SD* alleles, but it is unique in that the second chromosome is free of detectable chromosome aberrations.

Females homozygous for the second mutant produce a deficiency of male progeny; the effect of the mutant and its location on the second chromosome are illustrated by the following results: (1) $2_i/2_i$; $3_i/3_i$ females produced 244 ♀ ♀ : 22 ♂ ♂, (2) $SM1/2_i$; $3_i/3_i$ females produced 324 ♀ ♀ : 388 ♂ ♂, (3) $2_i/2_i$; $TM2/3_i$ females produced 240 ♀ ♀ : 65 ♂ ♂, and (4) $SM1/2_i$; $TM2/3_i$ females produced 276 ♀ ♀ : 302 ♂ ♂. Segregation of the maternal *X* chromosome was completely normal. Evidence suggesting that this mutant may have something to do with meiosis, however, is found in the recovery, from the 2_i; 3_i homozygotes, of three products of unreduced eggs.

THE MEIOTIC MUTANTS

In control crosses of females with Canton-S-derived two-three complements and *y/In(1LR)sc^{v1}, y pn cv m f·y$^+$; spa^{pol}/spa^{pol}* diagnostic complements by *Y^{s}X·Y^L, In(1)EN, v f B/O; C(4)RM, ci ey^R/O* males, the combined frequency of *X*- and fourth-chromosome nondisjunction was approximately 1 per 1000 progeny. Consequently, in similar crosses involving the 118 two-three complements tested from the two natural populations, a line was retested if, in all the duplicates examined, two or more exceptional progeny were recovered. After retesting, all but 11 test complements proved not to be detectably different from the controls; these 11 cases, however, showed ten or more times the control frequency of nondisjunction.

In males, four of 123 whole and 177 half complements tested caused high fourth-chromosome nondisjunction and all of these behaved consistently upon retesting. One of these, *mei-S332*, produced high nondisjunction in both sexes and is considered with the female cases. Two cases, *mei-S8* and *mei-O76*, were allelic. It is striking that the two alleles were collected at different times and on opposite sides of Rome. Moreover, the two-three complements differed in that *O76* carried a lethal on chromosome *3* (the meiotic mutant itself is on chromosome *2*) whereas *S8* did not. It seems, therefore, either that the Via Salaria and Via Ostiense populations are related in spite of the distance between the points of collection, or that the meiotic mutant in question is a very common one.

In all, we recovered two different mutants specifically affecting male meiosis, ten affecting female meiosis, and one affecting both sexes. In considering these meiotic mutants, we will discuss first those acting in females, and then those acting in males.

Female meiotic mutants: The segregation data from the tests and retests just described are given in Table 4. The observations made during these tests and retests provided a basis for separating the 11 female cases into two experimentally different categories—those with consistent, easily studied effects (three cases), and those with small, variable effects that may be experimentally intractable (eight cases). The reasons for the intractability are various. (1) The largest category, comprising *mei-O8*, *mei-S10*, *mei-S30*, and *mei-S68*, (a) exhibited high nondisjunction in some generations but not others, and (b) in generations when the phenotype was exhibited, it did not follow either chromosome *2* or *3* (see Table 4). Thus, for *mei-S10*, one generation produced 12/1207 *X* plus *4* exceptions in the $2_i/2_i$; $3_i/3_i$ genotype (where $i = S10$), 2/223 in the $SM1/2_i$; $3_i/3_i$ genotype and 0/646 in the $2_i/2_i$; $TM2/3_i$ genotype. Some generations later, two sublines, both of the constitution $2_i/2_i$; $TM2/3_i$, were tested; one produced 59/181 exceptions, the other 0/161. The high nondisjunction subline was tested two generations later with and without *SM1* and *TM2* and produced: 2/145 in $2_i/2_i$; $3_i/3_i$, 7/63 in $SM1/2_i$; $3_i/3_i$, 3/3062 in $2_i/2_i$; $TM2/3_i$, and 4/2906 in $SM1/2_i$; $TM2/3_i$. Both *mei-O8* and *mei-S30*, initially and in some of the first retests, produced the frequencies of exceptions shown in Table 4, but several generations later gave no evidence of nondisjunction in any genotype. Finally,

TABLE 4

Disjunctional data from the crosses summarized in Tables 5 and 6. All except haplo-4 progeny are recorded.

Line	Maternal constitution X[1]	2[2]	3[3]	Constitution of ova producing recovered progeny: X 4	X 44	X 0	XX 4	XX 44	XX 0	0 4	0 44	0 0	Σ	Frequency of exceptions: X[4]	2[5]	3[5]	4[4]
CS	A	+	+	8307	1	2	1	0	0	3	0	0	8311	0.5	1/7	0/80	0.4
	A	+	+	5112	0	4	0	0	0	0	0	0	5116	0.0			0.8
	B	+	+	14090	1	2	0	0	0	4	1	1	14099	0.4			0.4
	A	SM1	+	4377	2	4	1	1	0	2	1	0	4388	1.1			1.8
	B	SM1	+	15239	4	5	2	0	0	11	1	0	15262	0.8			0.7
	A	+	TM2	5724	6	8	2	0	0	2	0	0	5742	0.7			2.4
	B	+	TM2	16000	10	1	3	0	0	5	0	1	16020	0.6			0.7
	A	SM1	TM2	5455	6	6	2	0	0	1	0	0	5470	0.5			2.2
	B	SM1	TM2	16006	4	4	1	0	0	2	0	0	16015	0.2			0.5
S51	A	+	+	1042	6	2	9	1	1	3	7	0	1071	19.6	158/416	109/430	15.9
	A	+	+	361	2	0	0	0	0	1	0	0	364	1.2			2.3
	B	+	+	414	0	0	1	0	0	1	0	0	416	4.8			0.0
	A	SM1	+	593	0	0	0	0	0	3	0	0	596	5.0			0.0
	A	SM1	+	1999	1	3	0	0	0	2	0	0	2005	1.0			2.0
	B	SM1	+	3133	1	1	0	0	0	4	0	0	3139	1.3			0.6
	A	+	TM2	587	2	1	0	0	0	0	0	0	590	0.0			5.1
	A	+	TM2	2200	3	2	1	0	0	1	0	0	2207	0.9			2.3
	B	+	TM2	2896	1	0	0	0	0	1	0	0	2898	0.3			0.3
	A	SM1	TM2	3258	11	3	0	0	0	0	0	0	3272	0.0			4.3
	B	SM1	TM2	2441	2	1	0	0	0	0	0	0	2444	0.0			1.2
S282	A	+	+	1509	2	3	4	1	0	6	2	1	1528	9.2	4/91	36/95	5.9
	B	+	+	34	1	0	1	0	0	0	0	1	37	54.1			54.1
	A	SM1	+	837	12	6	6	2	4	14	1	1	883	31.7			29.4
	B	SM1	+	862	22	22	12	5	1	12	5	4	945	41.3			62.4
	A	+	TM2	646	0	0	0	0	0	0	0	0	646	0.0			0.0
	B	+	TM2	874	0	0	1	0	0	0	0	0	875	1.1			0.0
	A	SM1	TM2	1548	0	1	1	0	0	0	0	0	1550	0.6			0.6
	B	SM1	TM2	1612	4	2	1	0	0	0	0	0	1619	0.6			3.7
S332	A	+	+	34	14	16	4	1	1	12	2	4	88	272.7	10/92	83/94	431.8
	B	+	+	57	8	18	1	1	2	8	1	6	102	186.3			352.9
	A	SM1	+	204	3	1	6	0	0	2	0	1	217	41.4			23.0
	B	SM1	+	617	2	4	0	0	0	9	0	0	632	14.3			9.5
	A	+	TM2	117	28	28	19	2	4	31	6	11	246	296.7			321.1
	B	+	TM2	62	18	22	2	1	3	15	5	5	133	233.1			406.0
	A	SM1	TM2	1368	12	6	9	0	1	12	0	0	1408	15.6			13.4
	B	SM1	TM2	506	1	1	0	0	0	1	0	0	509	2.0			3.9
O8	A	+	+	684	9	5	4	0	0	1	0	0	703	7.1	1/75	1/62	19.9
S10	A	+	+	1196	1	4	1	0	0	4	1	0	1207	5.0	1/51	1/101	5.0
S30	A	+	+	520	2	0	1	0	0	4	1	0	528	11.4	0/51	0/71	5.7

Line	Maternal constitution X[1]	2[2]	3[3]	Constitution of ova producing recovered progeny: X 4	X 44	X 0	XX 4	XX 44	XX 0	0 4	0 44	0 0	Σ	Frequency of exceptions: X[4]	2[5]	3[5]	4[4]
S68	A	+	+	290	13	21	2	0	1	4	2	0	333	27.0	1/38	2/39	111.1
S82	A	+	+	4	0	1	2	0	0	0	0	0	7	142.9	0/45	0/37	285.7
O89	A	+	+	879	3	0	4	0	0	1	0	0	887	5.6			4.5
S308	A	+	+	289	1	0	1	0	0	4	0	0	295	16.9	0/38	1/21	3.4
S329	A	+	+	167	2	1	0	0	0	0	0	0	170	0	0/17	1/27	17.6

[1] A = *In(1LR)sc^{v1}, y pn cv m f·y$^+$/y*.
B = *In(1LR)sc^{v1}, y pn v·y$^+$/y*.
[2] + = +/+.
SM1 = *In(2LR)SM1, al^2 Cy cn^2 sp^2*/+.
[3] + = +/+.
TM2 = *In(3LR)Ubx^{130}, Ubx^{130} e^s*/+.
[4] Expressed as number of exceptions per 10^3 progeny. For chromosome 4 half of all classes are recoverable; for the *X* half the exceptional and all of the regular progeny are recoverable. Thus the rate of recovery of *X* exceptions is half that of chromosome-4 exceptions.
[5] Expressed as a fraction: The numerator is the number of chromosome-2 (or chromosome-3) exceptional progeny recovered; the denominator is the number of females, when crossed to *C(2L)RM*; *C(2R)RM* [or *C(3L)RM*; *C(3R)RM*] males, yielding the recovered exceptions.

mei-S68 has been examined extensively by Mr. L. ROBBINS, who observed that this appearance and disappearance of the mutant effect has no regular pattern and follows no particular genotype. His results, in fact, suggest that possibly the causal agent is not chromosomal. (2) One case, *mei-S82*, is difficult to study because it is practically sterile. Thus initially, of many matings of $2_i/2_i$; $3_i/3_i$ females, only one produced progeny; she produced only seven offspring, but three were exceptional. (3) The mutant, *mei-O89*, consistently produces about one exception per 100 progeny—a frequency so low as to make analysis exceedingly difficult. Finally (4), two cases, *mei-S308* and *mei-S329* behaved as mutants initially and upon first retesting but subsequently the effect disappeared, apparently permanently. These two may have been cases in which the mutants were lost owing to ineffective balancing, or they may resemble those in category (1) above.

In all cases, males homozygous for these two-three complements behaved normally with respect to sex- and fourth-chromosome segregation. In addition, salivary-gland-chromosome analysis revealed that *mei-S10*, *mei-S68*, and *mei-S329* are cytologically normal; *mei-O8* carries two inversions, *In(3L)P = In(3L)63C;72E1–2* and *In(3R)Mo = In(3R)93D;98F2–6*, both of which are known in other stocks where they are not associated with abnormal meiotic behavior; *mei-S82* carries a small inversion in chromosome 2, *In(2L)35E-F;36C-D*; *mei-S30* and *mei-O89* were not examined.

The three experimentally tractable mutants, *mei-S51*, *mei-S282*, and *mei-S332* were retested in large numbers with and without *SM1* and *TM2* in females with both *multex* chromosomes. The recombination data for all 11 lines with *y pn cv m f·y$^+$* are given in Table 5, and those with *y pn v·y$^+$* in Table 6; the segregation data from all tests are summarized in Table 4. It can be seen from the map lengths

TABLE 5

Recombination data from In(1LR)sc^{V1}, y pn cv m f·y^{+}/y; spa^{pol}/spa^{pol} females X Y^{S}X·Y^{L}, In(1)EN, v f B/O; C(4)RM, ci ey^{R}/O males.

[Maternal + autosomes were derived from an inbred Canton Special stock (control) or from presumptive meiotic-mutant-bearing autosomal pairs. All progeny except exceptions for the sex chromosomes and haplo-4's are included.]

Region	Phenotype	Canton S Controls					Presumptive Meiotic Mutants																					
							S51							S282				S332				08	S10	S30	S68	089	S308	S329
		+ / +	+ / +*	SMI / +*	+ / TM2*	SMI / TM2*	+ / +	+ / +*	SMI / +	SMI / +*	+ / TM2	+ / TM2*	SMI / TM2*	+ / +	SMI / +*	+ / TM2	SMI / TM2*	+ / +	SMI / +	+ / TM2	SMI / TM2	+ / +	+ / +	+ / +	+ / +	+ / +	+ / +	+ / +
All	B/+ ♀	4357	2387	1916	2785	2616	491	169	291	930	293	1060	1568	763	344	316	701	29	99	80	587	356	570	271	172	386	134	93
0	+ pn cv m f ♂	349	574	375	449	243	104	49	21	169	16	144	156	208	126	29	95	6	12	15	69	45	32	19	28	68	22	7
0	y + + + + ♂	1466	779	565	765	526	284	78	110	303	113	307	315	337	168	75	147	6	14	21	91	127	211	64	52	176	50	28
Total noncrossover males		1815	1353	940	1214	769	388	127	131	472	129	451	471	545	394	104	242	12	26	36	160	172	243	83	80	244	72	35
1	y pn + + + ♂	326	139	156	174	206	28	7	19	66	18	65	117	11	24	10	50	1	5	1	35	12	83	14	15	23	7	2
1	+ + cv m f ♂	76	111	122	113	120	15	4	10	32	3	35	60	2	23	5	22	0	5	2	40	7	6	7	2	13	3	1
2	y pn cv + + ♂	335	281	258	321	269	24	11	30	103	29	101	140	31	33	31	78	4	10	12	57	33	41	26	7	45	12	9
2	+ + + m f ♂	505	245	229	286	199	25	11	38	97	35	123	140	38	25	36	56	3	8	7	57	26	101	21	19	49	11	12
3	y pn cv m + ♂	96	138	130	133	141	6	9	6	61	8	70	78	22	13	25	41	1	8	8	27	17	11	9	4	24	8	2
3	+ + + + f ♂	380	173	169	206	217	41	8	28	77	40	87	122	30	33	35	67	1	8	7	62	26	63	27	9	41	15	5
4	y pn cv m f ♂	14	56	71	60	73	5	7	4	25	2	37	58	22	12	10	27	2	4	4	28	7	6	9	6	15	5	6
4	+ + + + + ♂	147	80	82	87	132	22	7	18	46	11	52	91	39	27	15	47	0	7	2	29	11	14	14	7	12	11	1
Total single-crossover males		1879	1223	1217	1380	1357	166	64	153	507	146	570	806	195	190	167	388	12	55	43	335	139	325	127	69	222	72	38
1-2	+ pn + m f ♂	10	1	14	15	36	0	1	2	4	1	2	19	0	1	2	8	1	0	1	13	1	17	1	0	1	0	0
1-2	y + cv + + ♂	7	11	15	17	39	1	0	0	5	2	9	25	0	2	1	12	0	1	2	16	2	4	2	0	2	1	0
1-3	+ pn + + f ♂	64	17	41	46	67	2	0	0	7	7	18	51	0	2	9	27	0	2	2	29	2	14	5	2	3	1	1
1-3	y + cv m + ♂	19	19	39	32	70	0	0	3	8	2	12	39	0	1	1	15	0	1	2	19	4	2	2	1	1	0	0
1-4	+ pn + + + ♂	35	10	41	29	61	1	0	1	8	1	13	37	0	4	8	14	3	3	0	15	3	8	0	2	7	0	0
1-4	y + cv m f ♂	7	10	22	23	50	0	1	0	6	1	8	21	0	0	1	11	0	3	2	14	0	0	0	1	0	1	1
2-3	+ pn cv + f ♂	21	22	26	38	69	0	0	1	11	1	11	33	2	3	4	18	1	5	1	29	1	1	5	3	2	1	0
2-3	y + + m + ♂	48	24	38	52	83	0	1	3	13	1	20	46	3	2	7	22	4	4	2	30	8	5	8	1	6	3	2
2-4	+ pn cv + + ♂	17	13	28	45	64	0	0	4	15	3	14	61	1	4	6	16	0	4	0	28	0	2	3	0	3	2	0
2-4	y + + m f ♂	43	15	28	39	67	1	0	3	14	4	12	40	3	5	15	25	1	0	2	31	6	7	12	1	4	2	0
3-4	+ pn cv m + ♂	0	4	4	3	11	0	0	0	0	0	2	9	0	0	0	7	1	3	0	12	1	0	0	0	0	1	0
3-4	y + + + f ♂	5	3	2	5	22	0	0	0	3	1	2	13	2	2	4	9	0	0	0	12	1	2	1	1	1	0	0
Total double-crossover males		276	149	298	344	639	5	3	17	94	24	123	394	11	26	58	184	11	26	14	248	29	62	39	12	30	12	4
1-2-3	y pn + m + ♂	0	1	1	0	22	0	0	0	0	0	0	4	0	0	0	5	0	0	0	6	0	0	0	0	0	0	0
1-2-3	+ + cv + f ♂	0	1	0	1	10	0	0	1	0	0	0	9	0	0	0	6	0	0	0	6	0	0	0	0	0	0	0
1-2-4	y pn + m f ♂	1	1	5	2	8	0	0	0	0	0	0	3	0	1	0	6	0	0	0	5	0	0	0	0	0	0	0
1-2-4	+ + cv + + ♂	0	0	1	2	11	0	0	0	0	0	0	3	0	0	0	5	0	0	0	9	0	0	0	0	0	0	0
1-3-4	y pn + + f ♂	0	0	1	0	11	0	0	0	0	0	1	2	0	0	0	5	0	0	0	5	0	0	0	0	0	0	0
1-3-4	+ + cv m + ♂	0	0	3	0	2	0	0	0	0	0	0	3	0	0	0	2	0	0	0	6	0	0	0	0	0	0	0
2-3-4	y pn cv + f ♂	0	1	0	6	10	0	0	0	0	0	0	7	0	0	0	0	0	1	0	3	0	0	0	1	0	0	0
2-3-4	+ + + m + ♂	1	0	0	1	6	0	0	0	0	0	0	0	0	0	0	5	0	0	0	4	2	1	0	0	0	0	0
Total triple-crossover males		2	4	11	12	80	0	0	1	0	0	0	31	0	1	0	34	0	1	0	44	2	1	0	1	0	0	0
1-2-3-4	y + cv + f ♂	0	0	0	0	1	0	0	0	0	0	0	2	0	0	1	0	0	0	0	10	0	0	0	0	0	0	0
1-2-3-4	+ pn + m + ♂	0	0	1	3	4	0	0	0	0	0	0	0	0	0	0	0	0	1	0	2	0	0	0	0	0	0	0
Total quadruple-crossover males		0	0	1	3	5	0	0	0	0	0	0	2	0	0	1	0	0	1	0	12	0	0	0	0	0	0	0
Total males		3972	2729	2467	2953	2850	559	194	302	1073	299	1145	1704	751	511	330	848	35	109	93	799	342	631	249	202	496	156	77
Map length		61.4	56.2	75.0	71.7	101.6	31.5	36.1	62.9	63.2	64.9	69.6	91.1	28.9	47.9	87.0	101.2	97.1	104.6	76.3	126.5	59.4	71.6	82.3	47.5	56.9	64.1	59.7

*Data collected in Seattle rather than Rome

TABLE 6

Recombination data from In(1LR)sc^{V1}, y pn v+y^{+}/y; spa^{pol}/spa^{pol} females X Y^{S}X·Y^{L}, In(1)EN, v f B/O; C(4)RM, ci ey^{R}/O males. Maternal autosomal constitutions and classes of progeny recorded as explained in heading of Table 5.

Region	Phenotype	Controls				Presumptive meiotic mutants											
		CS				S51				S282				S332			
		+ + / + +	SM1 + / + +	+ TM2 / + +	SM1 TM2 / + +	+ + / + +	SM1 + / + +	+ TM2 / + +	SM1 TM2 / + +	+ + / + +	SM1 + / + +	+ TM2 / + +	SM1 TM2 / + +	+ + / + +	SM1 + / + +	+ TM2 / + +	SM1 TM2 / + +
all	B/+	5998	6332	7113	6779	169	1359	1263	1016	16	398	88	656	32	232	43	232
0	- pn v	1840	1482	1677	1267	76	317	332	186	2	164	45	131	9	62	9	33
0	y + +	2154	1931	2039	1523	90	453	393	273	7	182	41	158	12	58	12	35
Total noncrossover males		3994	3513	3716	2790	166	770	725	459	9	346	86	289	21	120	21	68
1	y pn -	1136	1277	1282	1287	23	202	192	233	0	34	19	115	9	47	8	27
1	+ - v	916	1101	1057	1093	12	165	164	138	0	35	20	117	7	46	4	35
2	y pn v	837	984	921	1128	27	237	212	178	5	48	17	116	6	46	8	46
2	+ - +	850	990	1000	1136	14	264	207	145	5	43	31	130	2	56	5	38
Total single-crossover males		3739	4352	4260	4644	76	868	775	694	10	160	87	478	24	195	25	146
1-2	- pn +	203	483	452	866	1	63	72	129	0	1	13	96	1	48	5	31
1-2	y - v	159	568	470	933	2	75	62	146	0	1	12	99	5	28	3	31
Total double-crossover males		362	1051	922	1799	3	138	134	275	0	2	25	195	6	76	8	62
Total Males		8095	8916	8898	9233	245	1776	1634	1428	19	508	198	962	51	391	54	276
Map Length		55.1	72.4	68.6	89.3	33.7	64.4	63.8	87.1	52.6	32.3	69.2	90.2	70.6	88.7	75.9	97.8

given in Table 5 that although none of the intractable cases have an appreciable effect on crossing over, the other three do (see also Table 6). Here we might note two points. First, since the Seattle and Rome control crossover data differ slightly, all comparisons to be made are between sets done in the same laboratory. Second, it can be seen in Tables 5 and 6 that reciprocal classes are not recovered equally frequently. We attribute these differences to reduced viability of mutant classes of flies, and have made no attempt to correct the data although, in comparisons among lines differing in intrinsic crossover rates, this is a confounding effect.

In addition to the tests already described, we examined the effects of *mei-S51*, *mei-S282*, *mei-S332* (the tractable meiotic mutants), and *mei-T3* (a case that will be discussed later) on nondisjunction of chromosomes *2* and *3*. This was done by crossing *y*/*y*; *mei-*/*mei-*females with males carrying an *X* chromosome marked with y^{+} and compound autosomal arms [either *C(2L)RM*; *C(2R)RM* or *C(3L)RM*; *C(3L)RM*]. The two compound chromosomes remain univalent in primary spermatocytes; consequently, sperm are formed with neither, one, the other, or both compound chromosomes in roughly equal frequencies. The surviving progeny from a cross between compound-autosome-bearing males and females carrying normal autosomes are derived only from oöcytes and spermatocytes in which the two autosomal elements proceed to the same pole at either meiosis I or II. Since only exceptional products of oögenesis are recoverable from this cross, it is possible to determine that autosomal nondisjunction is occurring, but it is not possible to accurately estimate its frequency.

It is further possible to examine the incidence of *X*-chromosome exceptions among autosomal exceptions obtained from this cross for comparison with that observed in crosses using normal autosomes where autosomal disjunction is

TABLE 7

X-chromosome genotypes of autosomal exceptions produced by crosses of meiotic-mutant-bearing females by males of the following genotypes: (1) C(2L)RM; C(2R)RM, *(2)* C(3L)RM; C(3R)RM, *(3)* C(4)RM/0

		Genotype of primary oocyte with respect to Autosomes Autosomes							
Mother	X Chromosome	22	0	33	0	44	0	ΣAA	Σ0
	X	49	41	28	25	6	2	83	68
mei-S51	XX	4	24	3	12	1	1	8	37
	0	38	2	37	4	7	0	82	6
	X	1	3	12	14	2	3	15	20
mei-S282	XX	0	0	4	1	1	0	5	1
	0	0	0	5	0	2	1	7	1
	X	2	4	43	18	17	28	62	50
mei-S332	XX	0	0	2	1	2	3	4	4
	0	1	3	2	17	2	10	5	30
	X	0	2	15	11	..	..	15	13
mei-T3	XX	0	0	1	0	..	..	1	0
	0	0	0	0	1	..	..	0	1

regular. It is also possible to examine the incidence of *X*-chromosome exceptions among fourth-chromosome exceptions in crosses to *C(4)RM/0* males. The results are presented in Table 7. It can be seen that rather large numbers of autosomal exceptions were recovered from each mutant type; comparable numbers of control matings yielded fewer than 10 autosomal exceptions. These autosomal nondisjunction results, except those from *mei-T3*, have also been summarized in Table 4.

One technical point should be made in interpreting these frequencies. One stock of attached chromosome *3's C(3L)RM, se h rs²; C(3R)RM, sbd gl e⁸*, was used throughout, but two different second chromosome stocks were used. One, *C(2L)RM, b; C(2R)RM, cn*, was used in all tests except some involving *mei-S51* where *C(2L)RM, dp; C(2R)RM, px* was employed. Evidently, segregation in males of these two stocks is different—the *dp*; *px* pair producing potentially recoverable sperm more frequently. Thus the lower frequency of exceptions recorded for chromosome *2* as compared with chromosome *3* almost certainly reflects differences in the tester males and not in the meiotic mutants' effects on the disjunction of the two major autosomes, which, based on the results from *mei-S51*, are probably equivalent.

Before considering the three good female cases in detail, we will consider the case of *mei-T3*. This two-three complement was originally scored as a third-chromosome female sterile. In single-female matings to normal males it is consistently sterile, whereas both $2_i/2_i$; $TM2/3_i$ and $SM1/2_i$; $TM2/3_i$ females are fertile, give large progenies, and produce no excess of exceptions. However, as

shown in Table 7, in mass matings to attached-autosome-bearing males, *T3* homozygotes produce exceptional progeny: two second-chromosome exceptions from 40 matings and 28 third-chromosome exceptions from 65 matings (the difference being a property of the male tester stocks as discussed above). Moreover, the presence of many *X*-chromosome exceptions among the autosomal exceptions indicates that *mei-T3* is a third chromosome recessive meiotic mutant so drastic as to render homozygous females highly infertile.

We now consider the three most extensively tested female meiotic mutants: *mei-S51*, *mei-S282*, and *mei-S332*.

mei-S51: meiotic from Salaria 51. The first effect of *mei-S51* to be noted is that crossing over on the *X* chromosome in females homozygous for the mutant two-three complement is uniformly reduced (with the possible exception of the most proximal region which exhibits a lesser effect) to about one-half the control value. Thus, in the case of *y pn cv m f·y*$^+$ (Table 5), reading the regions from *pn* proximally, the control values versus the experimental values in map units for the Roman data were as follows: region 1—13.7 *vs* 8.4; region 2—24.8 *vs* 9.1; region 3—16.0 *vs* 8.8; and region 4—6.8 *vs* 5.2. For the Seattle data, they were: region 1—11.8 *vs* 6.7; region 2—22.6 *vs* 12.4; region 3—14.8 *vs* 9.3; and region 4—7.1 *vs* 7.7. A similar reduction to about half the control values is evident in the *y pn v·y*$^+$ tests recorded in Table 6.

Although crossing over is uniformly and repeatably reduced in all the tests and genotypes given in Tables 5 and 6, it is not evident which major autosome carries the meiotic mutant. In all cases, crossing over is slightly reduced in both *SM1/2*$_i$; *3*$_i$*/3*$_i$ and *2*$_i$*/2*$_i$; *TM2/3*$_i$ and perhaps even in *SM1/2*$_i$; *TM2/3*$_i$ females. If the last result is real, then *mei-S51* is somewhat dominant; in any event the main, recessive, effect appears to be synthetic—that is, it requires recessive factors carried on both chromosomes *2* and *3*. Alternatively, it may be that *mei-S51* is dominant but relatively ineffective in reducing exchange in the presence of heterozygous inversions causing increased crossing over.

The segregational behavior of *mei-S51* is still more puzzling. At first, the line exhibited both abnormal segregation and abnormal crossing over. Subsequently, the segregational behavior became normal, although the crossover effect remained unchanged. Autosomal nondisjunction, however, was subsequently found to occur in one subline. It seems, therefore, that the disjunctional anomaly in *mei-S51* is genetically separable from the crossover effect, but whether or not the mutant crossover behavior is necessary for nondisjunction requires further study.

Although the genetic basis for the abnormal segregation in *mei-S51* is obscure, the pattern of segregation is clear and repeatable: (1) there is a positive correlation in the probability of nondisjunction of nonhomologous chromosomes; (2) nondisjoining nonhomologs tend to separate from each other; (3) the nondisjunction occurs at the first meiotic division as evidenced by the genotypes of the *X*-exceptional females. Thus, in tests in which the *X* and *4* were followed, progeny were recovered from eight oöcytes in which the two *X*'s separated from the two *4*'s, and from only one in which all four elements went to the same pole.

Moreover, among autosomal exceptions produced by *mei-S51*, there were 47% (133/284) *X*-chromosome exceptions compared with 1% (12/1058) from oöcytes with regular autosomal disjunction. Thus, disjunctional behavior of the *X*'s and the autosomes within a cell are strongly correlated. Furthermore, in simultaneous *X* and autosomal exceptions, the two *X* chromosomes separate from the two autosomes 90% (119/133) of the time. These observations suggest that in oöcytes of *mei-S51* females, chromosomes may pair nonhomologously and separate from each other at the first meiotic division.

Segregation of the sex and fourth chromosomes is normal in *mei-S51* males. Salivary analysis revealed no anomalies on either the second or third chromosomes.

In summary, the simplest interpretation is that the *S51* two-three complement appears to carry either a dominant gene or recessive factors on chromosomes *2* and *3* which cause a uniform reduction in crossing over to about one-half the control value. There appears to be another factor causing a high probability of nondisjunction for all chromosomes owing to the tendency of nonhomologs to separate from one another at the first meiotic division. This mutant is being studied further by Mr. L. ROBBINS.

mei-S282: meiotic from Salaria 282: The first effect to be noted is that crossing over is reduced to about one-half the control value in $2_i/2_i$; $3_i/3_i$ and $SM1/2_i$; $3_i/3_i$ females, but is normal in *TM2* heterozygotes. There is, therefore, a recessive crossover mutant on chromosome *3*. This reduction in crossing over, unlike that of *mei-S51*, is not uniform along the chromosome, but is polarized; the reduction being most pronounced distally. Thus, we observe from the data in Table 5 that the map lengths (control *versus* experimental) were as follows: region 1—13.7 *vs* 1.7; region 2—24.8 *vs* 10.4; region 3—16.0 *vs* 7.9; and region 4—6.8 *vs* 8.9. This same polarized effect, less striking owing to the interchromosomal effect, is also evident in the data from *SM1* heterozygotes recorded in Tables 5 and 6.

The third chromosome recessive, *mei-S282*, also causes an elevated frequency of nondisjunction of all the chromosomes (see Table 4). As in the case of *mei-S51*, the nondisjunction occurs at the first meiotic division as indicated by the *X*-chromosome constitution of *X*-exceptional females, and nondisjunction of the different chromosome pairs is highly correlated. This correlation is illustrated by the following observations: (1) In the absence of *SM1*, the number of *X*-chromosome exceptions was 15 and of fourth-chromosome exceptions 11 in a total of 1565 flies; on the basis of independence, the expected number of double exceptions is $15 \times 11 \div 1565 = 0.1$, whereas the observed number was five. In *SM1* heterozygotes, the expected number of double exceptions is $67 \times 85 \div 1828 = 3.1$ as compared with an observed number of 23. These calculations are from the summed A and B sets in Table 4. (2) Although not recorded in the table, there were also two intersexes from ova with two *X* chromosomes and two sets of autosomes. (3) There were approximately 30% (14/49) *X*-exceptions among autosomal exceptions (Table 7) compared with less than 1% (11/1554) among regular autosomal segregants (Table 4).

Different nondisjoining chromosome pairs assort independently. Thus, in total, there were eight diplo-*4* and 5 nullo-*4* exceptions among two-*X* exceptions, and eight diplo-*4* and seven nullo-*4* exceptions among nullo-*X* exceptions (Table 4). In the double exceptions recorded in Table 7 the two *X*'s went to the same pole as the two autosomes six times and to the opposite pole eight times.

The results agree with expectations based on random recovery of *X* chromosomes among autosomal exceptions and suggest complete failure of synapsis of the entire complement in a fraction of cells followed by random assortment to the poles. Two other observations must be considered in connection with the idea of random assortment in a subset of cells. First, in the absence of *SM1*, two fourth-chromosome exceptions were recovered in males—both from 543 noncrossover males, none from the 196 crossover males. With *SM1*, 18 fourth-chromosome exceptions were recovered from 640 noncrossover males; only four were recovered from 375 recombinant males, but this is still ten times the frequency observed in *SM1* control crosses (18/19650). Thus, nondisjunction of the fourth chromosomes implies a lack of crossing over in the *X*'s, which tends to support the notion of a subset of cells with no pairing; there were four exceptional chromosome-*4* cases in crossover males, however. Second, if segregation is random when nondisjunction occurs, then there should be *X* exceptions: chromosome-4 exceptions: double exceptions in the ratio of 1:2:1 (owing to the fact that for chromosome *4*, half of all classes are recoverable, while for the *X*, half of the exceptional, but all of the regular, classes are recovered). The observed classes in the first test (Table 4) were 10:5:4; with *SM1* they were: 20:19:8; with *SM1* and *y pn v y*$^+$ they were 24:44:15. These ratios are evidently variable, but the latest, largest test agrees with the 1:2:1 expectation, and results of a still larger experiment, performed by Miss Dilys Parry, also agree with expectation (36:77:30).

Segregation of the sex and fourth chromosomes is normal in *mei-S282* males. Salivary analysis revealed no anomalies on either the second or the third chromosome.

Thus we tentatively conclude that *mei-S282* is a recessive on chromosome *3* that causes (1) failure of pairing in a fraction of cells and (2) a polarized reduction in crossing over (most pronounced distally) among regularly disjoining chromosomes. This mutant is being studied further by Miss Parry.

mei-S332: meiotic from Salaria 332: Salivary analysis revealed no anomalies on either chromosome *2* or *3*. Nondisjunction in *mei-S332* homozygotes or with *TM2* is extremely high for both the *X* and fourth chromosomes (Table 4). With *SM1*, segregation is much more regular but nondisjunction is nevertheless higher than normal. Thus, it appears that a partially dominant nondisjunction-producing mutant is located on chromosome *2*. That the effect of *mei-S332* on segregation extends to the sex and fourth chromosomes in males is shown later in Table 8. Two important points may be made about the abnormal segregation caused by *mei-S332*. First, the incidence of nondisjunction in males and females is approximately the same and nonhomologs are independent. Thus summing the *SM1*$^+$ data (Table 4), we see that in females the frequency of *X*-chromosome exceptions

TABLE 8

Segregation data from FM6/y^+Y; spa^{pol}/spa^{pol} males X y pn; C(4)RM, ci ey^R females. Paternal autosomes were derived from an inbred Canton Special stock (control) or from presumptive meiotic-mutant-bearing autosomal pairs. All progeny except haplo-4's are included.

Sperm Constitution	Phenotype	Controls				Meiotic Mutants										
		CS				S8				081			S332			
		+ +	Cy +	+ Ubx	Cy Ubx	+ +	Cy +	+ Ubx	Cy Ubx	Cy +	+ Ubx	Cy Ubx	+ +	Cy +	+ Ubx	Cy Ubx
X; 4	y^2 B ♀♀	5448	8380	6968	8618	176	502	349	1544	302	84	1381	49	268	61	298
Y; 4	pn ♂♂	5121	7908	6677	7340	135	420	294	1247	262	93	1101	57	285	87	273
X/Y; 4	B ♀♀	5	17	4	9	0	0	0	1	9	0	1	1	3	8	3
0; 4	y pn ♂♂	19	33	14	14	0	1	2	10	18	0	2	30	5	82	5
X; 4/4	y^2 B pol ♀♀	1	1	1	1	22	0	71	3	5	0	0	12	0	27	0
X; 0	y^2 B ci ey ♀♀	2	2	3	7	88	0	122	1	14	0	0	13	0	25	0
Y; 4/4	pn pol ♂♂	1	2	1	1	29	0	85	5	17	1	1	18	0	20	0
Y; 0	pn ci ey ♂♂	1	2	2	0	68	1	135	1	9	0	1	12	0	28	1
X/Y; 4/4	B pol ♀♀	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
X/Y; 0	B ci ey ♀♀	0	0	1	1	0	0	0	1	1	0	0	1	0	4	0
0; 4/4	y pn pol ♂♂	2	0	0	1	0	0	0	0	0	0	1	8	0	18	0
0; 0	y pn ci ey ♂♂	0	0	0	0	0	0	0	0	4	0	0	14	0	34	0

is 25.8%, of chromosome *4* exceptions is 36.4%, and of double exceptions is 9.7% compared with an expectation of 9.4% on the assumption of independence. This agreement with expectations on the basis of independence extends to the relationships among the various exceptional classes. Further, the attached autosome results given in Table 7 show that in *mei-S332* females, the frequency of *X*-chromosome exceptions among autosomal exceptions ($43/155 = 28\%$) is approximately the same as among regular autosomal segregants ($23/105 = 22\%$). Thus the *X* chromosomes and the autosomes appear to behave independently in all tests. In males (see Table 8), comparable frequencies of nondisjunction and chromosomal independence are exhibited. Summing the *SM1*$^+$ data in Table 8 shows that the total frequency of sex-chromosome exceptions is 33.0%, of chrosome-*4* exceptions is 38.5%, and of double exceptions is 13.2% compared with an expectation based on independence of 12.7%. Thus, in males, frequencies of nondisjunction similar to those observed in females are found as is chromosomal independence. However, although the various classes are in agreement with the expectations based on independence, there are some unexplained differences between the tests with and those without *TM2*, and a curious deficiency of certain nullo-chromosome gamete types.

The second important point about the segregation in *mei-S332* homozygotes of both sexes is that the nondisjunction occurs predominantly, at the second meiotic division. The evidence for this is that among 47 female *X*-exceptions recovered from *y/y pn cv m f·y*$^+$ females (Table 4), 35 were *y* (i.e., received sister *X* centromeres) and therefore must have been the result of second division nondisjunction, while only 12 were *y*$^+$. Of the latter, four were tested; three were sterile and the fourth was homozygous for the centromere marked by *y*$^+$ and, therefore, also must have been from second division nondisjunction (the ratio of 35:12 probably reflects a reduced viability of homozygous sc^{v1}). However,

among 20 progeny from diplo-3 ova recovered from crosses of *mei-S332/mei-S332; TM2/3$_i$* females to *C(3L)RM; C(3R)RM* males, 5 were *Ubx* (i.e., *TM2/+*) indicating that approximately 15% of autosomal exceptions result from nondisjunction in the first meiotic division. The evidence that the nondisjunction in males takes place predominantly at the second division comes from the sex-chromosome exceptions. First division nondisjunction produces *X/Y*- and nullo-*X*-nullo-*Y* sperm as complementary products leading to the formation of *B* female and *y pn* male exceptions in the crosses recorded in Table 8. Nondisjunction at the second division, on the other hand, leads to *FM6/FM6*-bearing sperm, y^+Y/y^+Y-bearing sperm, and nullo-*X*-nullo-*Y* sperm which produce lethal metafemales, apparently regular *pn* males, and exceptional *y pn* males respectively. Thus, second division nondisjunction is distinguished from first division nondisjunction by the deficiency of exceptional *B* females expected from the latter. The results in Table 8 show 52 *y pn* male exceptions and only two *B* females in the absence of *TM2* and 134 *y pn* ♂♂:13 *B*♀♀ in the presence of *TM2*. Thus, it is clear that most of the nondisjunction in males occurs at meiosis II; whether the few female exceptions result from first division nondisjunction or from regular disjunction in *XYY* products of second division nondisjunction in the preceding generation, remains to be determined.

There is a second meiotic effect of the *S332* two-three complement. Crossing over is increased in all autosomal genotypes as shown in the "map length" row of Tables 5 and 6. In the tests recorded in both tables, the crossover effect is consistent and is most pronounced in the $2_i/2_i$; $3_i/3_i$ and $SM1/2_i$; $3_i/3_i$ genotypes. Thus it appears that the *S332* two-three complement carries a dominant crossover enhancer, possibly on chromosome 3. Tentatively we symbolize the disjunctional mutant on chromosome 2, *mei-S332a*, and the crossover mutant, *mei-S332b*.

While the crossover-enhancing effect of *mei-S332b* is clear, it is difficult, from the available data, to specify the pattern of the increase. The *y pn cv m f·y*$^+$*/y* data (Table 5) indicate no regular polarization of the enhancement, but in all cases the most proximal region shows the most pronounced effect. The *y pn v·y*$^+$*/y* data (Table 6) however, show a reverse polarity without heterozygous inversions, but a larger proximal increase similar to that observed previously, in the other three genotypes.

In summary, we tentatively conclude that *mei-S332a* is a partial dominant on chromosome 2 that causes second meiotic division nondisjunction in both males and females with a fixed probability for each chromosome pair and with the different pairs assorting independently. This implies that the second meiotic division is at least partially under common genetic control in the two sexes. Further, *mei-S332b* is a dominant, possibly on chromosome 3, that increases recombination along the chromosome in an, as yet, undetermined pattern. These mutants are being studied further by MR. B. DAVIS.

Male meiotic mutants: Of the four male meiotic mutants found, one was *mei-S332* (just discussed), two were allelic and will be referred to as *mei-S8*, and the last is *mei-O81*. Data on the segregation of the sex and fourth chromosomes for

these cases are shown in Table 8. Salivary analysis revealed no abnormalities in any of these lines.

mei-S8: meiotic from Salaria 8: This is a recessive mapping at 79.7 on chromosome *2* that causes high nondisjunction of chromosome *4*, but has no effect on the sex chromosomes. Nondisjunction of chromosome *4* takes place in primary spermatocytes in cytological preparations. A clear and consistent excess of nullo-*4* over diplo-*4* sperm suggests chromosome loss concomitant with the abnormal segregation. *mei-S8* may be a gene that specifically controls the meiotic behavior of some chromosome pairs in the complement, but not others. For example, the sex chromosomes might be insensitive to the meiotic mutant, or, perhaps, chromosome *4* is special because of its small size.

mei-O81: meiotic from Ostiense 81: Evidently this mutant is a recessive on chromosome *3*, which affects the behavior of all the chromosomes. Failure of homologous pairing can be observed in cytological preparations of primary spermatocytes. Although the data are few, it seems most reasonable to imagine that all of the chromosomes are nondisjoining independently at the same rate. The overall frequency of sex-chromosome nondisjunction was 5.0%, of chromosome-*4* nondisjunction was 7.8%, and of double nondisjunction was 0.78%, compared with an expectation based on independence of 0.39%.

The male meiotic mutants are being studied further by DRS. B. NICOLETTI and G. TRIPPA.

GENIC EFFECTS ON CROSSING OVER

In addition to the detection and isolation of meiotic mutants of relatively drastic effect, the experimental design employed here allows a more general analysis of the total effect on crossing over, between a pair of stock—and therefore standard —*X* chromosomes, of genetic differences segregating in these populations. A number of duplicate determinations of *X*-chromosome recombination was made for each two-three complement. Thus it is possible to determine the variance in crossing over that may be ascribed to differences among two-three complements.

First, there are a number of general considerations. (1) The statistic used to measure crossing over is map length, which is the mean number of crossovers per chromosome ($\sum_i ir_i / \sum_i r_i$, where r_i is the number of i-recombinant strands). (2) To minimize the error owing to differences in the number of duplicates tested per two-three complement and to differences in fecundity among two-three complements, cultures producing fewer than 15 male offspring were not included in the analysis, and only two-three complements with at least two acceptable duplicates and only the first five of these were included. (3) The variation attributable to error (that is, the mean squares among duplicate cultures about the mean of each two-three complement), s^2, and the mean squares due to variation among two-three complements about the mean for all two-three complements, s_g^2, were estimated by computer. The results are given in the left-hand section of Table 9 along with the fraction, $s_g^2/(s^2 + s_g^2)$, which is the proportion of the total variance

TABLE 9

Estimates of the contribution of differences among homozygous two-three complements to the total variability in the map distance between pn *and the centromere of the X chromosome. Model I treats the variance among duplicates and Model II the variance among chromosomes as discussed in the text*

Population	Number of complements tested	Map length	Model I			Model II		
			s^2	s^2_g	$s^2_g/s^2+s^2_g$	s^{2*}	s^2_g	$s^2_g/s^2+s^2_g$
Canton Special	41	61.48	116.20	2.3	.019	3779	8	.002
Via Ostiense	16	61.35	184.18	81.2	.306	3949	62	.016
Via Salaria	78	62.53	206.79	80.9	.281	3956	111	.027

* For all experiments the additional contribution to the variance attributable to duplicates was not significantly different from zero. The error mean square (s^2) was therefore estimated by pooling the sum of squares owing to duplicates with that ascribable to error.

in crossing over on the *X* chromosome that can be attributed to differences among two-three complements.

These results may be checked in another way. Each chromosome recovered in these crossover experiments will have 0, 1, 2, or 3 crossovers; that is, map lengths of 0, 100, 200, or 300 units, and a group of chromosomes will have a mean map length. Variances can be computed as the squared deviations of each strand from a mean (either the overall mean, or the mean of a particular two-three complement, as before). Such an analysis has been done; the results are given in the right-hand portion of Table 9.

The two analyses differ in that, in the first procedure, the metric employed was conventional map distance which, being a mean, is normally distributed and thus satisfies one of the basic variance-analysis assumptions. However, it does not weight the accuracy of each crossover determination according to the number of progeny per duplicate. The second procedure, on the other hand, does not deal with a normally distributed variable, but does give each strand equal weight. The fact that both methods lead to similar estimates of s_g^2 suggests that the general conclusions to be drawn are correct.

The map length is the same for Canton-S and the two natural populations. However, the most striking feature of this analysis is that the variance attributable to differences among two-three complements is not significantly different from zero for the Canton-S controls, but is significantly greater than zero and similar (i.e., ca. 80 cM^2) for the two different natural populations. The genetic interpretation of this component of the variance in crossing over is not immediately obvious. The most reasonable interpretation is that in natural populations many genes that affect crossing over are segregating (and, incidentally, therefore, that natural populations harbor many potentially-resolvable meiotic mutants). However, two ambiguities exist. First, the number of gene differences involved, as contrasted to their effect, is not resolved by this analysis. Second, the variance measured was the variance in recovery of crossover classes which need not be wholly a reflection of variance in the rate of crossing over. For example, viability

differences among the phenotypic classes, if correlated with the maternal genotype, could have contributed to the variance. Nevertheless, it seems most probable that there are many genes segregating in natural populations that affect the rate of recombination.

A similar conclusion has been reached by LEVINE and LEVINE (1954, 1955) who demonstrated an effect of genes on chromosome 3 on *X*-chromosome recombination in *Drosophila pseudoobscura*, and by LAWRENCE (1958, 1963) who found significant effects of the parental genotype on *X*-chromosome crossing over in *D. melanogaster*. However, in Drosophila, selection for high or low recombination rate has met with dubious success (see, e.g., PARSONS 1958, and ACTON 1961).

ON THE COEFFICIENT OF COINCIDENCE

The probability of observing a chromosome recombinant in a particular genetic interval is the product of the probability that the preconditions for exchange in that interval (e.g., pairing) will be satisfied and the probability that an exchange will in fact occur. Altering either of these probabilities changes the observed frequency of crossing over. A still useful way of making the distinction between these two components of recombination was proposed in 1915 by BRIDGES. He imagined that homologous chromosomes twisted about one another to form rather widely spaced *nodes*, or points at which exchange is possible, and that there is a fixed probability that, given a node, an exchange will occur. He also suggested that chiasma interference could be considered the consequence of the spacing of the nodes (i.e., that the distribution of the number of nodes per chromosome or chromosome segment was not Poisson). Reading "the set of all chromosomal preconditions for exchange" for "nodes" yields a still valid way to make a first separation among the causes of changes in recombination rates and, in particular, to inquire whether a meiotic mutant that affects recombination does so by changing the probability either that the preconditions are satisfied or of the exchange event itself.

A mutant that affects the probability of exchange given the preconditions, without affecting the preconditions themselves, should not influence the intensity of interference. This can be seen as follows. Consider a length of chromosome, divided into two marked regions, each sufficiently small so that at most one node per region is possible. Let a be the probability of a node in only one region, b be the probability of a node in only the other, and d be the probability of two nodes, one in each region. Let the probability of an exchange, given a node, be x. Then the coefficient of coincidence, C, is

$$C = \frac{x^2 d}{x(a+d)x(b+d)} = \frac{d}{(a+d)(b+d)},$$

which is independent of x. Thus variation in x, and hence in map length $= x(a+b+2d)$, will not change C.

On the other hand, meiotic mutants that affect the rate of recombination by influencing node distribution (i.e., have their effect on any one of the set of pre-

conditions for exchange) will likely change both crossing over and interference since the intensity of interference is a function of *a*, *b*, and *d* or, following BRIDGES 1915, the consequence of the spacing of the nodes.

In this connection, from all of the crossover data given here, a rather interesting situation presents itself. The entire *X* chromosome (from *pn* to the centromere) is followed as two adjacent equal-sized regions (directly in those crosses involving the *y pn v·y*$^+$ chromosome, but also in the crosses with the *y pn cv m f·y*$^+$ chromosome if *cv* and *f* are ignored). The map length of this chromosome varies from about 30 units under the influence of homozygous *mei-S51* to over 90 units in the presence of *mei-S332a/SM1*; *mei-S332b/mei-S332b*. Map lengths intermediate between these extremes are provided by the control crosses and crossover-affecting meiotic mutants with and without autosomal inversion heterozygosity. The physical structure of the *X* chromosome is, of course, identical in all cases.

Thus it is possible to inquire about the relation between map length and coefficient of coincidence in a situation in which map distance varies but the physical structure and the regions studied remain invariant. This relation is shown in Figure 2. The data for the points in the plot are in Tables 5 and 6. The 95% confidence limits for the estimates of *C* on the points closest to the origin are quite wide (e.g., 0.25 and 0.86 for *mei-S282* where $C = 0.61$) owing to the low numbers of recovered double recombinants; nevertheless, the estimates of *C* are apparently reproducible as evidenced by the fact that replicate tests (or tests of the same autosomal constitution, but with the two differently marked *X* chromosomes) give similar estimates. The only exceptions are one test with *mei-S282* with only two double crossovers, and one test of *mei-S332* involving only 35 male progeny.

With the exception of *mei-S282*, a regular, and approximately linear, relationship between map length and the coefficient of coincidence obtains for the points shown (with, of course, the constraint that as map length approaches 100 units with just two regions, the coefficient of coincidence necessarily, making the usual assumptions about exchange, approaches 1.0). This result is consistent with the hypothesis that both the meiotic mutants *mei-S332b* and *mei-S51* affect crossing over by altering one or more of the preconditions of exchange and, not directly, the probability of exchange. This is evidently also the case for the interchromosomal effect. This latter is in agreement with the results of interchromosomal effect tests generally (see, e.g., RENDEL 1957, 1958).

If the preliminary estimates of *C* are confirmed by further testing, then homozygous *mei-S282* reduces crossing over without reducing coincidence both in structurally normal and *SM1* females and appears to be a mutant affecting the probability of exchange itself. It is significant that *TM2/mei-S282* females, either with or without *SM1*, behave like the controls. The observation, that *mei-S282* reduces crossing over in a polarized manner, does not affect this argument. However, the segregation data taken in conjunction with the recombination results indicate that there is a subset of cells in which there is no pairing. If this cellular heterogeneity extends to partially paired chromosomes—which could, of course, explain the polarized effect—then the coefficient of coincidence would be inflated.

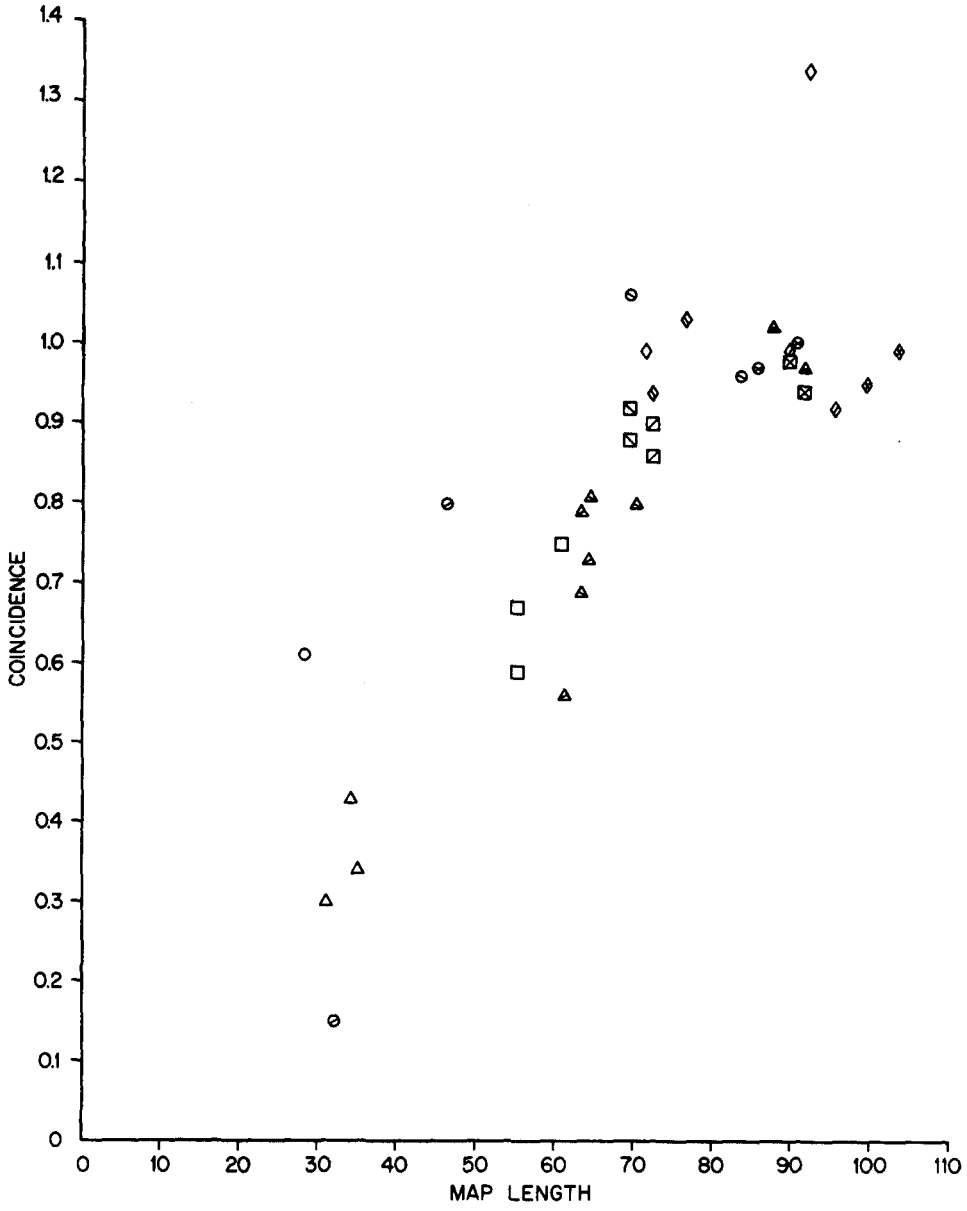

FIGURE 2.—A plot of the coefficient of coincidence against map length for all control crosses and meiotic mutants with an effect on crossing over. The points are calculated from the data given in Tables 5 and 6; in those from Table 5, however, the markers *cv* and *f* have been ignored. The genotypes with respect to meiotic mutants are represented by the following symbols: □ = normal; △ = *mei-S51*; ◇ = *mei-S332b*; ○ = *mei-S282*. Where a symbol is crossed from the upper right to lower left, the females were heterozygous for *SM1*, and where crossed from the upper left to lower right, heterozygous for *TM2*.

Thus, until the mechanism of *mei-S282* is understood, this result cannot properly be used to position the place in the meiotic cycle at which *mei-S282* acts.

From the suggestion that neither the mutants, *mei-S51* or *mei-S332b*, nor the interchromosomal effect act by affecting the probability of an exchange given the preconditions, and from the uncertainty surrounding *mei-S282*, it might be imagined that the probability of exchange is always unity once the preconditions are satisfied; that is, that exchange cannot usefully be thought of as a two-step process as we have been doing here. The resolution of this problem will rest with the discovery of either conditions (see, for a possibility, HAYMAN and PARSONS 1961) or meiotic mutants that affect recombination rate, but leave coincidence unchanged.

ON THE GENETIC CONTROL OF MEIOTIC CHROMOSOME BEHAVIOR

It is likely from the results of the variance analysis on crossing over given above, from the number of genes affecting meiosis previously known, and, most importantly, from the frequency of meiotic mutants segregating in the natural populations we have studied, that many—and conceivably most—steps in the meiotic process are under cytogenetically resolvable genic control. It seems worthwhile, therefore, even though our information on the control processes of meiosis is fragmentary, to consider some generalized theoretical framework within which the control system may be studied. To this end we may regard the continuity of the germ line as being composed of a cycle of chromosome behavior consisting of the two meiotic divisions and a number of mitotic divisions; in the latter are included incidentally the formation of the soma and importantly the gonial mitoses. We consider initially two such control cycles—one in each sex. We recognize, moreover, four *genetic landmarks* (i.e., processes with genetic consequences) in the female cycle: mitotic exchange and segregation, exchange in meiosis I, disjunction in meiosis I, and disjunction in meiosis II. In the male cycle there are only three genetic landmarks owing to the absence of meiotic exchange.

At this juncture, two points should be made. First, the sequences being considered here are concerned solely with the genetic control of chromosome behavior; they are not to be taken as indicating, except incidentally, anything about the cells in which the meiotic phenomena occur, nor are these primarily temporal sequences. Second, there are two conceptually different kinds of mutations that could alter the meiotic behavior of a mutant individual. These are: (1) mutations that alter a control step in meiosis such that some normal process of meiosis does not occur, is abnormal, or occurs at the wrong time, and (2) mutations, if such exist, that affect the ability of one or more of the chromosomes to respond to one or some of the normal meiotic control steps. Most often it would be expected that the first type of meiotic mutant would affect the behavior of chromosomes other than, or in addition to, the chromosome on which the mutant itself is located, whereas the second type of mutation is most likely to affect only the chromosome on which it is carried. Therefore, it is the first type of mutant that we selected

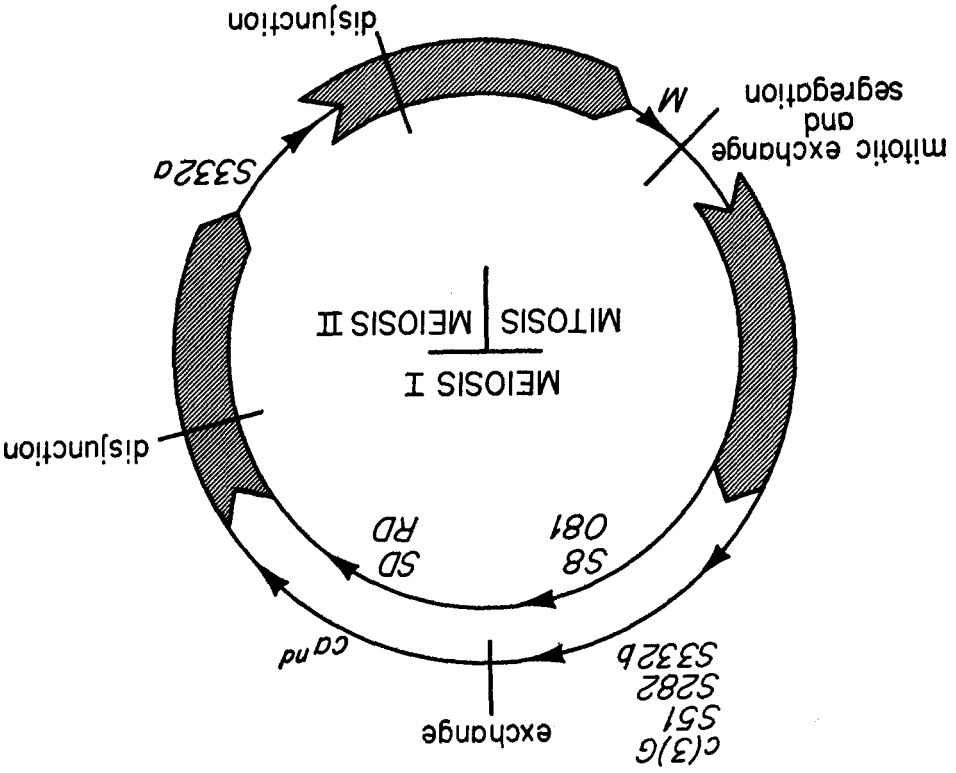

FIGURE 3.—A schematic representation of the germinal cycle of chromosome behavior. *Landmarks* are indicated by radial lines and inferred *control points* by arrows. When under separate genetic control the outer circle represents the female cycle and the inner circle, the male cycle; a single segment indicates common control in the two sexes, while in shadowed segments, information on the sexual specificity of the control system is lacking. The division of the cycle into its two successive meiotic and intervening mitotic components is indicated in the center of the circle.

and will use to infer *control points*—that is, points at which a genetic effect is necessary for the normal process of meiosis to continue.

From the analysis of meiotic mutants already considered we can tentatively draw certain inferences about the nature of the sequence of events in the genetic control of the chromosomes during the germinal cycle (see Figure 3). Since mitosis in general and, more importantly, the genetic control of mitotic exchange and segregation are apparently identical in the two sexes, it seems a fair inference that the control mechanisms are the same for some portion (and possibly all) of the events succeeding gamete maturation but preceding the first meiotic division. Although it is clear that cytodifferentiation of the gametes is different in the two sexes, it is not known whether there are differences in the chromosome control systems during gamete maturation or, for that matter, during any stage in the mitotic part of the cycle. The control systems in the two sexes diverge at first

meiosis as evidenced by: (1) the absence of exchange in the male, (2) the meiotic mutants, *c(3)G*, *mei-S51*, *mei-S282*, *mei-S332b* and ca^{nd}, all of which affect the first meiotic division and all of which have an effect only in the female, and (3) the meiotic mutants *mei-O81*, *mei-S8*, *RD*, and *SD* which act only in the male and affect meiosis I. The control systems converge again sometime during the second division as evidenced by *mei-S332a*, which acts during the second division and in a similar manner in both sexes. The evidence for identical control of at least a portion of second meiosis in the two sexes provided by *mei-S332a* allows the possibility that the system controlling chromosome behavior is identical in the two sexes except for the first meiotic division where, in Drosophila, the unusual situation of no meiotic exchange in the male exists, and thus allows the hope that the female cycle in the genetic control flow chart we are developing applies to forms other than Drosophila.

The resolving power of this conceptualization is determined by the number of landmarks and by the number of control points known. Thus in the female we can resolve four control points, $c(3)G^+$, $mei\text{-}S51^+$, $mei\text{-}S282^+$, and $mei\text{-}S332b^+$, that occur before the exchange process is completed and one control point, ca^+, that has its effect after exchange, but before first division disjunction is over. In both the female and the male, $mei\text{-}S332a^+$ has its effect before second division disjunction is completed. The meiotic mutants with effects on male first division are also noted in the diagram; *mei-S8* and *mei-O81* are placed before *RD* and *SD* because the former cause nondisjunction and, therefore, may interfere with pairing whereas *SD* and *RD* probably manifest themselves only after pairing.

This visualization has the very useful property that the analysis of a meiotic mutant implies from the mutant effect, a control point and, from the inferred wild-type action, one or more landmarks. To illustrate this we will consider the behavior of *mei-S282*. We would like to emphasize that the discussion to follow is for illustrative purposes only and is not meant primarily as an hypothesis about *mei-S282* and, owing to the virtual absence of analysis to date, is most certainly not an accurate description of the behavior of the mutant. For this purpose only, then, we accept that in females homozygous for *mei-S282*, there is a fraction of cells in which all of the chromosomes, both homologs and nonhomologs, assort at random at the first division and in which there is no recombination, while in the rest of the cells, segregation of homologs is regular. We accept, further, that in the cells in which disjunction is normal, recombination is abnormal in all the chromosomes in that there is a polarized reduction in crossing over, least near the centromere and becoming more extreme proceeding distally on the chromosome. This reduction is such that many regular products come from no-exchange tetrads. To explain this, we imagine that, at some moment in meiosis I in normal females, the chromosomes are disposed at random in the cell. At a particular time, homologous chromosomes begin to search for each other, the initial recognition point being near the centromere. When centromere regions become associated, the homologs can disjoin. Pairing proceeds from the centromeres distally. During this period, exchange may take place. At or near the end of pairing, there is a

genetic signal to stop exchange, and it is this signal that is provided by the normal allele of *mei-S282*. The mutant produces the same signal but at any time after the search process has started rather than after pairing has been completed. It is obvious that there are many other working models consistent with the few results obtained to date, but the predictions of this model are fairly rigorously testable. Again solely for purposes of this discussion, we suppose that this model proves to be correct. In that case, it would not only be possible to place the control point of *mei-S282* on Figure 3 (that is *mei-S282*$^+$ would be an arrow marking the termination of exchange in the first division of the female cycle), but also to add, as landmarks, the sequence of normal events inferred from the abnormal behavior of the mutant.

This type of analysis can be extended to hypotheses concerning the relations between different control points inferred from different mutant loci. For example, the meiotic mutant, *c(3)G*, has two drastic effects on meiosis: exchange is eliminated and nondisjunction is very high for all chromosome pairs. From these results only, it is natural to imagine that the abnormal segregation is a consequence of the absence of exchange. However, since according to the model for *mei-S282* just presented, disjunction is assured before pairing occurs and therefore before exchange is possible (that is, a pattern of regular disjunction is fixed even though exchange has not yet occurred), *c(3)G*$^+$ would necessarily affect meiosis before the onset of pairing. Moreover, although there is a very high rate of nondisjunction in *c(3)G* homozygotes, there is a tendency for homologs to separate. Therefore *c(3)G*$^+$ must act after the establishment of homologous recognition. Thus *c(3)G*$^+$ in this model must act after centromere association but before the initiation of pairing—perhaps functioning to stabilize centromere association. This hypothetical sequence of events is shown in Figure 4. Thus the analysis of each meiotic mutant will increase the precision with which other meiotic mutants can be placed in the control cycle and hence will increase the information provided by each new mutant.

The authors are extremely grateful for the indispensable assistance of Mr. B. DAVIS, Mr. A. MICHELI, Mr. J. OREM, Miss D. PARRY, Mr. L. ROBBINS, Mrs. A. ROSENFELD, Mrs. D. SMITH, and Mrs. M. UZIEL.

We also especially thank Dr. M. KASTENBAUM for his help with the statistical analysis of the population results on crossing over.

Finally, LINDSLEY and SANDLER wish to extend their appreciation to Professor G. MONTA-

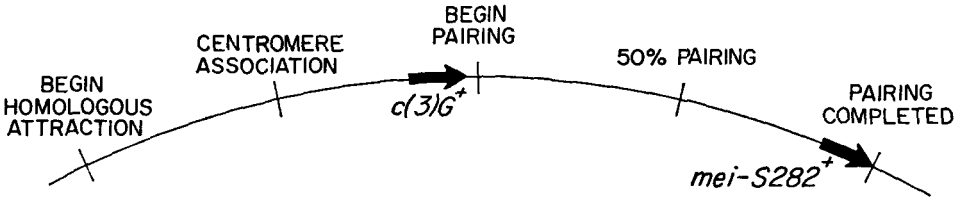

FIGURE 4.—An arc of the germinal cycle illustrating the new landmarks and control points inferred from the analysis of *mei-S282*. (See text for discussion).

LENTI for his hospitality during their sojourn as National Science Foundation Senior Postdoctoral Fellows in the Institute of Genetics at the University of Rome where much of the work reported here was performed.

SUMMARY

From two natural populations near Rome, Italy, 118 sets of major autosomes (chromosomes *2* and *3*) that were viable and fertile in females were extracted and made homozygous in females carrying pairs of standard, marked, *X* and *4* chromosomes. Crossing over on the *X* chromosome and segregation of the *X*'s and *4*'s were measured for the purpose of discovering *meiotic mutants* on the chromosomes from nature; that is, mutations affecting one or more of the meiotic processes. In addition to detecting meiotic mutants that affect females, we examined 123 major autosomal sets and 177 single major autosomes (either chromosome *2* or *3*) for their homozygous effects on fourth-chromosome segregation in males.—The following mutants were found: 1) Eight mutants that resulted in irregular segregation of the sex and fourth chromosomes in females; they were not studied further. 2) Two different mutants that caused, in females, correlated nondisjunction of all of the chromosomes and a fifty percent reduction in recombination; in one case the reduction was uniform, and in the other it was more extreme distally than proximally. 3) Two different mutants that produced high nondisjunction of the fourth chromosome in males were found. One of these also caused *X-Y* nondisjunction; the other did not affect the sex chromosomes. 4) One mutant was recovered that caused very high nondisjunction at the second meiotic division in both sexes. It also enhanced crossing over in females. 5) A new example of the *SD* gene was found.—A comparison of the variances in *X*-chromosome recombination among females carrying the various autosomal sets from the natural populations with that of a group carrying control, Canton-S autosomal sets, revealed that in these experiments a significant fraction of the total variance in crossing over was attributable to genetic differences among the autosomal sets from nature.—From these results it is concluded that there are many meiotic mutants segregating in natural populations.—Data on the segregation and recombinational phenotypes of the meiotic mutants recovered are presented, and a tentative schematic cycle of chromosome behavior in the germ line is presented. This cycle reveals that, in Drosophila, the activity of mutants that affect the first division is confined to one sex indicating separate genetic control of the first division in the two sexes. A mutant affecting the second meiotic division has a similar effect in both sexes indicating common genetic control of the second division. Procedures for the further elucidation of the genetic control of chromosome behavior are discussed.

LITERATURE CITED

ACTON, A. B., 1961 An unsuccessful attempt to reduce recombination by selection. Am. Naturalist **95**: 119–120.

BRIDGES, C. B., 1915 A linkage variation in Drosophila. J. Exptl. Zool. **19**: 1–21.

COOPER, K. W., 1950 Normal spermatogenesis in Drosophila. pp. 1–61. In: *Biology of Drosophila.* Edited by M. DEMEREC. Wiley, New York.

DARLINGTON, C. D., 1932 The control of the chromosomes by the genotype and its bearing on some evolutionary problems. Am. Naturalist **56:** 25–51.

DAVIS, G. D., 1963 The effects of claret-nondisjunctional on chromosome behavior in *Drosophila melanogaster.* Ph.D. Thesis, University of Georgia.

DUNN, L. C., and D. BENNETT, 1967 Sex differences in recombinations of linked genes in animals. Genet. Res. **9:** 211–221.

EMERSON, S., 1967 Fungal genetics. Ann. Rev. Genet. **1:** 201–220.

ERICKSON, J., 1965 Meiotic drive in Drosophila involving chromosome breakage. Genetics **51:** 557–571.

FAULHABER, S. H., 1967 An abnormal sex ratio in *Drosophila simulans.* Genetics **56:** 189–213.

GERSHENSON, S., 1928 A new sex-ratio abnormality in *Drosophila obscura.* Genetics **13:** 488–507.

GOWEN, J. W., 1928 Mutation, chromosome nondisjunction and the gene. Science **68:** 211–212. —— 1933 Meiosis as a genetic character in *Drosophila melanogaster.* J. Exptl. Zool. **65:** 83–106.

GOWEN, M. S., and J. W. GOWEN, 1922 Complete linkage in *Drosophila melanogaster.* Am. Naturalist **56:** 286–288.

GRELL, E. H., 1961 The tetrasomic for chromosome *4* in *Drosophila melanogaster.* Genetics **46:** 1177–1183. —— 1963 Distributive pairing of compound chromosomes in females of *Drosophila melanogaster.* Genetics **48:** 1217–1229.

GRELL, R. F., 1967 Pairing at the chromosomal level. J. Cellular Physiol. (Suppl.): **70** 1: 89–112.

HANKS, G. D., 1964 The analysis of a case of meiotic drive in *Drosophila melanogaster.* Genetics **50:** 123–130.

HARTL, D. L., Y. HIRAIZUMI, and J. F. CROW, 1967 Evidence for sperm dysfunction as the mechanism of segregation distortion in *Drosophila melanogaster.* Proc. Natl. Acad. Sci. U.S. **58:** 2240–2245.

HAYMAN, D. L., and P. A. PARSONS, 1961 The effect of temperature, age and an inversion on recombination values and interference in the *X*-chromosome of *Drosophila melanogaster.* Genetica **32:** 74–88.

HINTON, C. W., 1966 Enhancement of recombination associated with the *c(3)G* mutant of *Drosophila melanogaster.* Genetics **53:** 157–164. —— 1967 Genic modifiers of recombination in *Drosophila melanogaster.* Can. J. Genet. Cytol. **9:** 711–716.

KAPLAN, W. D., 1953 The influence of Minutes upon somatic crossing over in *Drosophila melanogaster.* Genetics **38:** 630–651.

LAWRENCE, M. J., 1958 Genotypic control of crossing over on the first chromosome of *Drosophila melanogaster.* Nature **182:** 889–890. —— 1963 The control of crossing over in the *X* chromosome of *Drosophila melanogaster.* Heredity **18:** 27–46.

LE CLERC, G., 1946 Occurrence of mitotic crossing over without meiotic crossing over. Science **103:** 553–554.

LEVINE, R. P., and E. E. LEVINE, 1954 The genotypic control of crossing over in *D. pseudoobscura.* Genetics **39:** 677–691. —— 1955 Variable crossing over arising in different strains of *Drosophila pseudoobscura.* Genetics **40:** 399–405.

LEWIS, E. B., and W. GENCARELLA, 1952 Claret and nondisjunction in *Drosophila melanogaster*. Genetics **37**: 600–601.

LINDSLEY, D. L., L. SANDLER, B. NICOLETTI, and G. TRIPPA, 1967 The genetic control of recombination in Drosophila. Australian Conf. Replication and Recombination Genet. Material (in press).

MEYER, G., 1964 A possible correlation between submicroscopic structure of meiotic chromosomes and crossing over. Prague, Publishing House Czechoslovak Acad. Sci., pp. 461–462.

MORGAN, T. H., 1912 Complete linkage in the second chromosome of the male Drosophila. Science **36**: 719–720.

MORIWAKI, D., 1937 A high ratio of crossing over in *Drosophila ananassae*. Z. Ind. Abst. Vererb. **74**: 17–23.

NICOLETTI, B., 1968 Il controllo genetico della meiosi. Atti Assoc. Ital. Genetica **13** (in press).

NICOLETTI, B., and G. TRIPPA, 1967 Osservazioni citogenetiche su di un nuovo caso di "Segregation Distortion" (*SD*) rinvenuto in una popolazione naturale di *Drosophila melanogaster*. Atti Assoc. Ital. Genetica **12**: 361–365.

NICOLETTI, B., G. TRIPPA, and A. DE MARCO, 1967 Reduced fertility in *SD* males and its bearing on segregation distortion in *Drosophila melanogaster*. Atti Accad. Naz. Lincei, Rend. Classe Sci. Fis. Mat. Nat. **43**: 383–392.

NOVITSKI, E., 1947 Genetic analysis of an anomalous sex-ratio condition in *Drosophila affinis*. Genetics **32**: 526–534.

NOVITSKI, E., and G. D. HANKS, 1961 The analysis of irradiated Drosophila populations for instances of meiotic drive. Nature **190**: 989–990.

PARSONS, P. A., 1958 Selection for increased recombination in *Drosophila melanogaster*. Am. Naturalist **92**: 255–256.

PEACOCK, W. J., and J. ERICKSON, 1965 Segregation distortion and regularly nonfunctional products of spermatogenesis in *Drosophila melanogaster*. Genetics **51**: 313–328.

RENDEL, J. M., 1957 Relationship between coincidence and crossing over in Drosophila. J. Genet. **55**: 95–99. —— 1958 The effect of age on the relationship between coincidence and crossing over in *Drosophila melanogaster*. Genetics **43**: 207–214.

RHOADES, M. M., 1941 Different rates of crossing over in male and female gametes of maize. J. Am. Soc. Agron. **33**: 603–615.

ROBERTS, P., 1962 Autonomy of a claret nondisjunctional ovarian transplant in *Drosophila melanogaster*. Drosophila Inform. Serv. **36**: 112.

RONEN, A., 1964 Interchromosomal effects on somatic recombination in *Drosophila melanogaster*. Genetics **50**: 649–658.

SANDLER, L., Y. HIRAIZUMI, and I. SANDLER, 1957 Meiotic drive in natural populations of *Drosophila melanogaster*. I. The cytogenetic basis of segregation distortion. Genetics **44**: 233–250.

SCHULTZ, J., 1934 Report on equational. Carnegie Inst. Wash. Yearbook **33**: 280.

SCHULTZ, J., and H. REDFIELD, 1951 Interchromosomal effect on crossing over in Drosophila. Cold Spring Harbor Symp. Quant. Biol. **16**: 175–197.

SLIZYNSKI, B. M., 1960 Sexual dimorphism in mouse gametogenesis. Genet. Res. **1**: 477.

SMITH, P. A., and R. C. KING, 1967 The ovarian morphology of *Drosophila melanogaster* homozygous for *c(3)G*. (Abstr.) Genetics **56**: 590–591.

STALKER, H. D., 1961 The genetic systems modifying meiotic drive in *Drosophila paramelanica*. Genetics **46**: 177–202.

STERN, C., 1936 Somatic crossing over and segregation in *Drosophila melanogaster*. Genetics **21**: 625–730.

STURTEVANT, A. H., 1929 The claret mutant type of *Drosophila simulans*; a study of chromosome elimination and cell lineage. Z. Wiss. Zool. **135**: 323–356.

STURTEVANT, A. H., and G. W. BEADLE, 1936 The relations of inversions in the *X* chromosome in *Drosophila melanogaster* to crossing over and disjunction. Genetics **21**: 554–604.

STURTEVANT, A. H., 1956 Failure of *w* or *cn bw* to suppress the nondisjunctional effects of ca^{nd}. Drosophila Inform. Serv. **29**: 166.

TANAKA, Y., 1913 Gametic coupling and repulsion in the silkworm, *Bombyx mori*. J. Coll. Agric., Sapporo **5**: 115–148.

WEAVER, E. C., 1960 Somatic crossing over and its genetic control in Drosophila. Genetics **45**: 345–357.