DYSFUNCTIONAL SPERM PRODUCTION IN DROSOPHILA MELANOGASTER MALES HOMOZYGOUS FOR THE SEGREGATION DISTORTER ELEMENTS*

BY DANIEL L. HARTL†

DEPARTMENT OF GENETICS, UNIVERSITY OF WISCONSIN, MADISON

Communicated by James F. Crow, April 15, 1969

Abstract.—Drosophila males heterozygous for the segregation distorter chromosome show a reduction in fecundity which is correlated with the degree of distortion of their segregation ratio. When males are made homozygous for the segregation distorter elements, their fecundity is lowered to just that extent expected if each SD were independently causing the sperms carrying the other to dysfunction. In three cases tested, Sd Ac/Ac, Sd Ac/Sd Ac, and Sd Ac St/ Sd Ac St, the fecundity of the males is consistent with the dysfunction model, whereas the females are normal.

The Sd Ac St/Sd Ac St males are almost completely sterile. They do produce sperms, however, which are motile and which look morphologically normal in the phase contrast microscope. They are transferred to the female during copulation and are stored in apparently normal numbers in the seminal receptacle and spermathecae.

When Drosophila melanogaster males are heterozygous for the segregation distorter (SD) second chromosome, they produce mostly SD-bearing progeny. The time of action of segregation distorter is known to be prezygotic. That segregation distortion is sensitive both to temperature and irradiation in or near meiosis I suggests that its mechanism might have important meiotic or even premeiotic components.

Beyond that, its precise mechanism of action is unknown, although two general alternatives have been suggested. The functional pole model is actually two hypotheses. It assumes first that all Drosophila primary spermatocytes (including those of normal males) have two different Anaphase I poles, one of which differentiates into two normal, functional sperms, the other of which gives rise to two morphologically normal, fully motile, but nonfunctional sperms. The model then proposes that the segregation distorter simply orients the SD/+ bivalent at Metaphase I so as to consign the +−-bearing dyad to the nonfunctional pole. The experiments to be reported in this paper provide no information about whether or not the meiocytes are normally polarized, but they do bear on the hypothesis of nonrandom orientation.

The hypothesis of sperm dysfunction, in contrast to the above model, proposes that the Metaphase I orientation of the SD/+ bivalent is random. The action of the segregation distorter is to render the +−-bearing sperms incapable of fertilization. The dysfunction model is entirely independent of any normal functional−nonfunctional polarity that might exist: if normal meiocytes are polarized, then the mechanism of the segregation distorter is an imposed dysfunction over and above that; if they are not polarized, then the action of the
segregation distorter is simply to predispose the +−-bearing sperms to function abnormally.

Peacock and Erickson⁴ have compared the number of sperms stored in females with the number of progeny obtained from comparable females inseminated by SD/+ and +/+ males. They have found, both in SD and controls, that only one half of the stored sperms appear to be capable of fertilization, a result which clearly argues for the functional pole hypothesis.

On the other hand, SD/+ males seem to have their fecundity reduced in proportion to their degree of segregation distortion; when the segregation distorter is suppressed, the fecundity of SD/+ males is normal.⁵ This result is consistent only with the hypothesis of sperm dysfunction.

A third discrimination between the two hypotheses can be based on the fecundity of SD/SD genotypes. If the functional pole hypothesis is correct, then the fecundity of SD/SD males should be normal. The sperm dysfunction hypothesis, on the contrary, predicts a severe reduction in the fecundity of SD/SD males which should be correlated with the activity of the SD chromosomes in the genotype.

This article reports experiments which measure the fecundity of SD/SD males. The results agree quantitatively with the expectations of the dysfunction hypothesis. The dysfunctional sperms themselves seem in all respects to be normal (to the point of resolution in the phase contrast microscope), but they are unable to fertilize eggs. The results are so similar to those on t-allele distortion in the house mouse⁶ that sperm dysfunction is also proposed as the mechanism in that case.

Materials.—The chromosomes used in this study are denoted by their genotypes rather than by their technical names. Different chromosomes carrying the same mutant genes are distinguished by numbers written in parentheses after the genotypes. The technical nomenclature of the segregation distorter chromosomes, their composition, degree of distortion, and origin, is presented in Table 1.

Table 1 also presents the control chromosomes. Both the SD's and the controls have been backcrossed to the standard cn bw strain for over 100 generations and are therefore virtually isogenic for all but the second chromosome.

Methods.—The measurement of fecundity, which here means the number of adult progeny produced under some specified mating regime, closely follows that outlined in an earlier report.⁵ Males a few hours old (usually 5 hr) were placed individually in vials with single cn bw females for 17 to 19 hr, after which the males were removed. The fertilized females were transferred to fresh medium every 3 or 4 days until they no longer laid fertilized eggs. This procedure tends to measure, to some extent, the speed of maturation as well as the fecundity. Because only highly inbred strains are used, however, the developmental time component is minimized. It has been shown with this material that the results of these “early sperm” experiments parallel those measuring total productivity.⁵

Genetics of the segregation distorters: The segregation distorter chromosomes discovered in nature are inversion-linked complexes of at least three distinct genetic elements. The segregation distorter locus itself, Sd, is located somewhere in or near the centric heterochromatin of chromosome II.⁶ (The symbol Sd will be used for the segregation distorter locus; SD will denote any combination of segregation distorter elements on one chromosome. This departure from previous literature will hopefully prevent confusion between the segregation distorter locus and a segregation distorter chromosome.) Alone, Sd is a segregation distorter of little potency; the standard testcross for SD activity (SD/cn
TABLE 1. List of chromosomes used.*

<table>
<thead>
<tr>
<th>SD chromosome</th>
<th>Genotype</th>
<th>k-value</th>
<th>Origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cy SD(NH)-2</td>
<td>Cy Sd Ac St</td>
<td>1.00</td>
<td>SD(NH)-2 (Japan)</td>
</tr>
<tr>
<td>SD-72</td>
<td>Sd Ac St (1)</td>
<td>0.99</td>
<td>Madison</td>
</tr>
<tr>
<td>SD(B)-54</td>
<td>Sd Ac St (2)</td>
<td>0.99</td>
<td>U.S., but not Madison</td>
</tr>
<tr>
<td>R(R-1)-cn14</td>
<td>Sd Ac cn</td>
<td>0.96</td>
<td>SD-56 (Madison)</td>
</tr>
<tr>
<td>R(SD-86)-1bw</td>
<td>Sd Ac bw (1)</td>
<td>0.87</td>
<td>SD-86 (Madison)</td>
</tr>
<tr>
<td>R(SD(NH)-1)-1bw</td>
<td>Sd Ac bw (2)</td>
<td>0.96</td>
<td>SD(NH)-1 (Japan)</td>
</tr>
<tr>
<td>R(pr)-7</td>
<td>Ac bw</td>
<td>0.54</td>
<td>SD-86 (Madison)</td>
</tr>
</tbody>
</table>

Control chromosomes

cn bw

Comments

Recessives cn (cinnabar eyes) and bw (brown eyes). Together they produce white eyes. Standard stock, egg hatchability about 50%.

cn
Recessive cn, carried as cn/cn bw c c × cn bw/cn bw c c. Second chromosome from wild-type Tokyo stock, carried as +/cn bw.

+ +

Same as +, except the dominant gene Cy (Curly wings) has been inserted into the left arm.

* The k-value is the proportion of SD progeny from the cross SD/cn bw c c × cn bw/cn bw c c.

bw c c × cn bw/cn bw c c; see Table I for definitions of the gene symbols) with Sd alone produces a segregation ratio (called the k-value) of about 0.6.7

A second element, called Activator of Sd (symbol: Ac), is located in the heterochromatin to the right of the centromere.8 By itself, Ac is a nondistorter (k = 0.5), but it enhances the distortion of the Sd element. When Sd and Ac are in coupling, the k-value of Sd Ac/cn bw males is about 0.85.

There is another modifier, or group of modifiers, located in the right arm of chromosome II, called Stabilizer of Sd (symbol: St).9 St alone shows no distortion. In either coupling or repulsion with a coupled Sd Ac region, however, it enhances the distortion to give a segregation ratio of 0.99 or more.

With these three elements, seven different SD chromosomes can be constructed: Sd Ac St, Sd Ac, Sd St, Ac St, Sd, Ac, St. There are, therefore, 28 different SD/SD genotypes; only the three most critical ones are examined here.

Results and Interpretation.—The functional pole hypothesis predicts that the fecundity of SD/SD genotypes will be normal, because the only effect of SD is to orient its own bivalent nonrandomly and not to predispose some kinds of sperms to function abnormally.

The dysfunction hypothesis makes quite a different prediction. If the mechanism of SD action is the production of dysfunctional sperms, then in an SD1/SD2 genotype, if (1) the SD's distort each other as efficiently as they distort cn bw, and if (2) the SD's act independently of one another, then it can be shown10 that the fecundity of SD1/SD2 males is proportional to 1/(2k1) + 1/(2k2) − 1, where k1 and k2 are the segregation ratios of SD1/cn bw and SD2/cn bw, respectively. The proportionality constant is just the fecundity of normal males. Hence, the ratio of the fecundity of SD1/SD2 males to the fecundity of normal males should be 1/(2k1) + 1/(2k2) − 1.

The assumption that the SD's are as effective against each other as they are against cn bw is gratuitous but, as will be seen, it seems to fit the fecundity results quite well. That need not always be the case, however. Some SD combinations might show mutual suppression or enhancement, as is observed in the house mouse at the t-locus. There, some t/t combinations are sterile; others show apparently normal fecundity.6
Table 2. Fecundity and degree of segregation distortion of young SD/SD males.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Male genotype</th>
<th>Number of males tested</th>
<th>Number of fertile males</th>
<th>Per cent of fertile males</th>
<th>Age of male during mating period</th>
<th>Segregation ratio (chrom-1/ chrom-1 + chrom-2)</th>
<th>Total progeny per fertile male and standard error</th>
<th>Fecundity ratio (A/B)</th>
<th>Predicted ratio (A/B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>cn/ Ac bw</td>
<td>13/11</td>
<td>84.6</td>
<td>6-22 hr</td>
<td>0.477</td>
<td>232.2 ± 43.3 (B)</td>
<td>137.6 ± 17.0 (A)</td>
<td>0.593</td>
<td>0.548</td>
</tr>
<tr>
<td></td>
<td>Sd Ac cn/ Ac bw</td>
<td>19/17</td>
<td>89.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sd Ac cn/cn bw</td>
<td>84/63</td>
<td>75.0</td>
<td>5-24 hr</td>
<td>0.963</td>
<td>116.3 ± 12.3</td>
<td>77.4 ± 12.6</td>
<td>0.516</td>
<td>0.585</td>
</tr>
<tr>
<td></td>
<td>Sd Ac bw (1)/ Ac bw</td>
<td>7/5</td>
<td>71.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sd Ac cn/ Sd Ac bw (1)</td>
<td>29/4</td>
<td>13.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sd Ac cn/ Sd Ac bw (2)</td>
<td>27/19</td>
<td>70.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (pooled)</td>
<td>Sd Ac/cn bw</td>
<td>91/68</td>
<td>74.8</td>
<td>5-24 hr</td>
<td>0.961</td>
<td>113.5 ± 11.8</td>
<td>18.4 ± 4.4 (A)</td>
<td>0.162</td>
<td>0.187</td>
</tr>
<tr>
<td></td>
<td>Sd Ac cn/ Sd Ac bw</td>
<td>56/23</td>
<td>41.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>+/ cn bw</td>
<td>13/10</td>
<td>77.0</td>
<td>5-28 hr</td>
<td>0.500</td>
<td>167.5 ± 22.8</td>
<td>90.6 ± 27.0 (A)</td>
<td>0.541</td>
<td>0.503</td>
</tr>
<tr>
<td></td>
<td>Sd Ac St (1)/ Cy +</td>
<td>8/7</td>
<td>87.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sd Ac St (1)/ Cy Sd Ac St</td>
<td>29/0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sd Ac St (1)/ Cy Sd Ac St</td>
<td>15/1</td>
<td>6.7</td>
<td>1-6 days</td>
<td>0.500</td>
<td>2.0 ± 0.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>+/ cn bw</td>
<td>7/7</td>
<td>100.0</td>
<td>1-8 days</td>
<td>0.518</td>
<td>1961 ± 313 (B)</td>
<td>6.8 ± 3.4 (A)</td>
<td>0.004</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Sd Ac St (1)/ Cy Sd Ac St</td>
<td>6/5</td>
<td>83.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sd Ac St (2)/ Cy Sd Ac St</td>
<td>4/2</td>
<td>50.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2 presents the results of experiments testing three different SD1/SD2 combinations. The observed fecundity ratios correspond satisfactorily with the predictions of the dysfunction hypothesis.

Experiment 1 compares Sd Ac cn/Ac bw males with cn/Ac bw. The fecundity of the Sd Ac cn/Ac bw males is only 59.3 per cent as large as that of cn/Ac bw males, and the cn/Ac bw genotype has been shown to have a fecundity very close to that of normal males. If the segregation ratio of Sd Ac cn/cn bw is taken as 0.845 (this is the mean of several experiments involving young Sd Ac cn/cn bw males), and if the segregation ratio of Ac bw/cn bw is taken as 0.523 (the value observed for Ac bw/cn), then the ratio of the observed fecundities is expected to be 1/[2(0.845)] + 1/[2(0.523)] — 1 = 0.548. From the results of Table 2, the true fecundity ratio can be estimated to be between 0.519 and 0.666, within one standard error.11

Although the estimate of the fecundity ratio of Sd Ac cn/Ac bw males agrees with that expected if the Sd Ac cn chromosome were still causing sperm dysfunction, the variance in the fecundities of the two genotypic classes are very large, and the low fecundity ratio could possibly be a statistical accident. Moreover, the segregation ratio from the Sd Ac cn/Ac bw males is normal, which would not be expected on the basis of a simple mutual dysfunction model.

On the other hand, if Sd were the element primarily responsible for producing whatever it is that predisposes a spermatocyte to give rise to dysfunctional sperms, and if Ac were the element which was responsible for determining which specific chromosome in a male would be rendered dysfunctional by the action of Sd, then with two Ac's of equal "strength" in a genotype, the segregation ratio would be expected to be normal, whereas the fecundity ratio would still be reduced in accordance with the mutual dysfunction model. The results of Table 2 agree remarkably well with this hypothesis.

The specific gene that directs the action of Sd in the above hypothesis need not be Ac, although that is the simplest suggestion. The positions of the crossovers in the synthesis of the Ac bw and the Cy Sd Ac St chromosomes imply that the position of the directing element, if there is one, must be on chromosome II between Cy on the left arm (6.1 on the genetic map) and cn (57.5) on the right. This does include the Ac region, which is near 55.1.16

Experiment 2 measures the fecundity of Sd Ac cn/Sd Ac bw. The segregation ratios of the Sd Ac cn/bw genotypes are higher than the standard values of Table 1, but that is probably of little significance since such variations are by no means unusual even in well-controlled SD experiments.

What does seem to be significant is the low proportion of fertile males within the Sd Ac cn/Sd Ac bw (1) genotype, which is in fact a corollary of the dysfunction hypothesis. The probability that a specific sperm dysfunction in an SD1/SD2 genotype is 2 — 1/(2k1) — 1/(2k2), which in this case turns out to be about 0.95; hence, some excess sterility is understandable when only a small number of sperms per male are sampled. Judging from the proportion of fertile males, evidently more sperms per male were sampled from Sd Ac cn/Sd Ac bw (2) than from Sd Ac cn/Sd Ac bw (1).

The fecundity ratio is estimated from the pooled results to be 0.123–0.201
within one standard error.\textsuperscript{11} The relation for predicting the fecundity ratio from the dysfunction hypothesis must be modified in this case, because here the ratio has been measured relative to \textit{SD/+} and not \textit{+/-}. Since the model implies that the fecundity of \textit{SD/+} is \(1/(2k)\) as large as that of \textit{+/-}, the appropriate formula becomes \(1 + (k_1/k_2) - 2k_1\). When \(k_1\) for \textit{Sd Ac cn/cn bw} equals 0.845, as before, and \(k_2 = 0.964\) for \textit{Sd Ac bw (2)/cn bw} (this value was determined from an independent experiment), then the expected ratio is 0.187, which is close to the observed.

Alternatively, suppose \(k_1 = k_2\). Then in order for the fecundity ratio to be 0.162, \(k_1\) would have to be 0.92 with a standard error of 0.02. This value is reasonably close to 0.96, the pooled segregation ratio.

Experiment 3 tests the prediction that when both chromosomes in an \textit{SD/SD} genotype have \(k\)-values against \textit{cn bw} of near 1.0, then the males should be nearly sterile. In experiment 3\textit{a}, \textit{Sd Ac St (1)/Cy Sd Ac St} males were compared with \textit{Sd Ac St (1)/Cy +} and with \textit{+/-cn bw}. The \textit{Sd Ac St (1)/Cy +} males were generated by the same mating scheme as the \textit{Sd Ac St (1)/Cy Sd Ac St} males in order to rule out any extraneous sterility factors that might have been present in the stocks.

The experiment provides two values with which to test the hypothesis. In the \textit{Sd Ac St (1)/Cy +} genotype, since \(k_2 = 0.5\) for \textit{Cy +/cn bw}, the fecundity ratio should be just \(1/(2k_1)\), where \(k_1\) is the segregation ratio of \textit{Sd Ac St (1)/cn bw}. Letting \(k_1 = 0.995\), the predicted fecundity ratio is 0.503, which is satisfactorily close to the observed value of 0.541.

The \textit{Sd Ac St (1)/Cy Sd Ac St} males are nearly sterile, as expected.\textsuperscript{†} Their \textit{Sd Ac St (1)/Cy Sd Ac St} female siblings are highly productive, however, but only when mated with normal males. When they are mated with their brothers, few offspring are produced.

Matings of \textit{Sd Ac St (1)/Cy Sd Ac St} males by their \textit{Sd Ac St (1)/Cy Sd Ac St} siblings were observed and, when each mating was completed, the male and female were dissected in Ringer’s solution and the testes of the male and the seminal receptacle and spermathecae of the female were examined in a phase contrast microscope. A similar experiment was performed with \textit{cn bw} females. The males all showed great masses of morphologically normal, motile sperms. Furthermore, as dissections of females at intervals after mating revealed, the sperms are transferred during copulation and are stored in large numbers in the females’ seminal receptacles and spermathecae. Dissections of still older (and still sterile) females suggested that eventually all the sperms disappear from the females. The females do lay eggs, more than 50 per female, in fact, but whether these eggs represent inviable zygotes or not is an unresolved question, since Drosophila virgin females do lay unfertilized eggs. Since the hatchability of eggs laid by females mated with \textit{Sd Ac St/+} males is normal,\textsuperscript{1} then true dysfunctional sperms must not cause egg lethality, and it would follow that the eggs laid by females mated with \textit{Sd Ac St/Sd Ac St} males are the same eggs they would have laid had they remained unmated. Furthermore, if polyspermy occurs with as low a frequency in \textit{cn bw} females as it does in \textit{Drosophila melanogaster} in general,\textsuperscript{12} then dysfunctional sperms must not even penetrate the eggs. Therefore, if the \textit{Sd Ac St (1)/}
Cy Sd Ac St males are sterile because they produce only dysfunctional sperms, then those sperms also do not penetrate the eggs. Where they go is unknown, but an earlier hypothesis that they are never even ejaculated is evidently incorrect.

A repetition of this experiment is tabulated as experiment 3b. This time the males were allowed to remain with cn bw females for eight days, which probably accounts for the slightly greater fecundity than in the previous case. Hiraizumi and Watanabe have described an aging effect on SD in which the degree of segregation distortion of an SD/+ male decreases as he ages, as if the SD were somehow becoming "weaker." The apparent increase in fecundity with male age observed in the homozygous SD's above might also be caused by this aging effect.

A total of 14 mated pairs were dissected in this experiment, six from matings of Sd Ac St (1)/Cy Sd Ac St and eight from Sd Ac St (2)/Cy Sd Ac St. Without exception, the testes showed motile sperms; without exception, the females' seminal receptacles and spermathecae revealed large numbers of apparently normal, motile sperms.

Some of the Sd Ac St/cn bw offspring of the males in experiment 3b were tested to see if the distorting ability of an SD chromosome is changed by passage through an Sd Ac St/Sd Ac St genotype. No change was detected: Sd Ac St (1)/cn bw males gave a mean segregation ratio of 0.995 (five tested), Sd Ac St (2)/cn bw gave 0.991 (seven tested), and Cy Sd Ac St/cn bw gave 1.00 (two tested).

Discussion.—Although the results of Table 2 support the dysfunction hypothesis, not every observation is consistent with the model. Sandler, Hiraizumi, and Sandler have reported that SD-5/SD-72 males are fertile; Nicoletti and Trippa have made a similar observation on SD(NC)-1/SD-72 males. In neither case, however, has the fecundity been quantitatively determined. Even the Sd Ac St homozygotes in this study are not completely sterile. Conceivably, old males kept for four or five days with several females might produce enough offspring to make their low productivity look as if it were caused by the culture conditions and not by their relative infertility. On the other hand, the fertility of these males might also be accounted for by some degree of mutual suppression of their SD chromosomes.

Mange has also reported an SD/SD combination which is fertile, but its fecundity was not determined precisely. Since one of the segregation distorters that she used was a recombinant carrying bw, moreover, the male genotype was probably Sd Ac St/Sd Ac, and hence some fertility is understandable.

Although the ineffective sperms produced by the Sd Ac St/Sd Ac St males in this study have been assumed to be dysfunctional, they might originate in another way. If normal Drosophila meiocytes are polarized to produce functional and nonfunctional sperms, then an Sd1/Sd2 male produces four classes of sperms: functional (carrying Sd1), functional (carrying Sd2), nonfunctional (carrying Sd1), and nonfunctional (carrying Sd2). The near-sterility of the Sd Ac St/Sd Ac St males shows that both of the first two classes are dysfunctional. If they degenerate, say, then all of the ejaculated sperms would be from the last two classes. Assuming that these sperms do not degenerate even though they carry
chromosomes that have been acted upon by SD, the ejaculated sperms would be expected to show the same morphology and behavior as "pure" Peacock-Erickson nonfunctional sperms. And they do.

On the other hand, it seems unlikely that the dysfunctional sperms do degenerate, because mature sperm bundles from heterozygous SD males have 64 sperms each, the same as normal males.\(^4\)

Therefore, either (1) nonfunctional sperms and dysfunctional sperms have a similar morphology and behavior, on a light microscopic level, even though the former are a normal feature of Drosophila reproduction and the latter are caused specifically by the action of SD, or (2) nonfunctional sperms, in the Peacock-Erickson sense, do not exist (which questions neither Peacock’s and Erickson’s adroitness nor their accuracy but only the interpretations placed on some otherwise beautifully executed experiments). This second hypothesis does not preclude the possibility that normal Drosophila males do regularly produce some nonfunctional sperms, as suggested by Novitski and Sandler;\(^7\) it does imply, however, that a detailed description of the origin, morphology, and behavior of the nonfunctional sperms—if they exist—is as yet unavailable.

I should like to thank Professor J. F. Crow for his stimulating encouragement of this work, Professor Yuichiro Hiraizumi for his helpful discussions, Mrs. Umetani for her technical aid, and Professors S. W. Brown and C. Stern for their comments on the manuscript.

* This is paper 1301 from the laboratory of Genetics. Work supported by NIH grant number GM15422 and by NASA Traineeship NSG(T)-23.
† Present address: Department of Genetics, University of Minnesota, Saint Paul.
‡ Note added in proof: Drs. John Erickson and Eleanor Markowitz have recently obtained both cytological and genetic evidence which indicates that there is normal disjunction of the second chromosomes in the nearly sterile Sd Ac St/Sd Ac St males.
\(^1\) Sandler, L., Y. Hiraizumi, and Iris Sandler, Genetics, 44, 233–250 (1969).
\(^2\) Mange, Elaine, Genetics, 58, 399–413 (1968).
\(^4\) Peacock, W. J., and J. Erickson, Genetics, 51, 313–328 (1965).
\(^5\) Hartl, D. L., Y. Hiraizumi, and J. F. Crow, these PROCEEDINGS, 58, 2240–2245 (1967).
\(^7\) Hiraizumi, Y., and K. Nakazima, Genetics, 55, 681–697 (1967).
\(^8\) Sandler, L., and Y. Haraizumi, Genetics, 45, 1671–1689 (1960).
\(^10\) If \(k_1\) is the proportion of SD\(_b\)-bearing offspring among the progeny of an SD\(_b\)/cn bw male, and if \(p_1\) is the fraction of his \(cn\) bw-bearing sperms that function normally, then \(p_1 = (1/k_1) - 1\). Similarly for an SD\(_b\)/cn bw male, \(p_2 = (1/k_2) - 1\). In an SD\(_b\)/SD\(_b\) genotype, if both SD's act in the same way toward each other as they do against \(cn\) bw, then the probability that any sperm functions normally is \(1/(2k_1) + 1/(2k_2) - 1\), which is a measure of fecundity when sperm number limits progeny production.
\(^11\) This value is obtained by allowing the numerator to vary within one standard error of its mean while the denominator is treated as a known constant.
\(^13\) Hiraizumi, Y., and S. Watanabe, Genetics, in press.
\(^16\) Hartl, D. L., unpublished.
\(^17\) Novitski, E., and I. Sandler, these PROCEEDINGS, 43, 318–324 (1957).