Novitski, E. University of Oregon, Eugene. The concept of gamete dysfunction.

Recent interest in gamete dysfunction impels me to make some comments about the history of the term in Drosophila genetics. It first appeared in print, along with a detailed discussion of its possible importance, in a paper by Lindsley and Sandler (1957); this work, however, seems not to be generally appreciated, judging by the number of instances where reference to it would have been appropriate but was not made.

The initial observation of Iris Sandler, in her master's thesis, that the various segregation products from the Bar Stone translocation in the male were recovered with grossly disparate (but repeatable) frequencies, was moved from the level of a puzzling curiosity to an intriguing observation when it was realized, during a joint conference with Larry and Iris Sandler, that a remarkable mathematical relation obtained among the various classes. For the reader not familiar with this argument, a simple analogy will make the point clear. Take one set of alleles, A and A', which depress viability to a and a' respectively, and an independent set of alleles B and B', which depress viability to b and b', respectively. One would hardly expect in a cross where all four are present, and where the four combinations AB, AB', A'B and A'B' should be found equally frequently that they would appear in the arithmetical proportions ab, ab', a'b, a'b' with a precision to the fraction of a percent. For one thing, the synergistic interactions of viability effects should lead to gross departures from precise mathematical expectations. For another, there is no reason to postulate that viability effects are strictly multiplicative, as opposed to additive. A more rational guess might be that the net effect of two deleterious causes might depend on their interaction during development. Nevertheless, such mathematical agreement between the observed and calculated frequencies did exist, and has been later obtained repeatedly by Zimmering (1960), and Zimmering and Barbour (1961).

During discussions on this point during 1956 and 1957, I maintained that such precision must arise in some geometrical circumstance in gametogenesis, and was not likely to be caused by some biological malfunctioning, as inviability, infertility, dysfunctionality, unfertilizability, etc. In a paper that Iris Sandler and I published in 1957 we presented this argument and suggested further that if the available cytological evidence were correct, then the actual time of the effect would have to come after the spermatocyte divisions and during the spermatozoal stage. Another point of view (gamete dysfunction) proposed by Lindsley and Sandler during these discussions was that perhaps each sperm produced could be assigned a probability of functioning, p_1, determined by some one aspect of the chromosome complement, and that any other similar but independent aspect could be assigned another probability of functioning, p_2. The joint probability of survival would then be simply $p_1 p_2$. Considerations which seemed to me to argue against this proposal included the fact that in all cases where there was established an unequal recovery of two homologs that differed in size, it was the smaller that was more frequently recovered, independent of genetic constitution, and that when combinations of independent chromosomes were considered, the least frequently recovered were in some instances those that had the most balanced and complete, or normal, genomes. Irrespective of the specific point of view, however, perhaps the most significant feature of both ideas is that they unequivocally discarded the more trivial explanations based on zygote inviability, experimental error, etc., and pinpointed the basis of the phenomenon to the meiotic and prezygotic stages.

Some years later Peacock and Erickson (1965) concluded, from a comparison of the number of sperm stored and available for fertilization in a female with the actual number of progeny produced by sisters of such females, that only half as many progeny were produced as there were sperm present. This lead to the suggestion that half of the sperm were functional, and half non-functional, a positive answer to the question, "are all products of meiosis regularly functional?". This latter point has recently been questioned by Zimmering and Fowler (1968), and Fowler (in press), who find in experiments patterned after those of Peacock and Erickson that in some cases as many as 75% of the sperm present in one group of females may be represented by progeny from their sisters, and that, furthermore, the results from their tests appear to be subject to such great variability as to make any conclusions from such experiments suspect. In any case, the hypothesis of the regular non-functioning of a fraction of the products of meiosis has been consistent with the observations of Peacock that there were no gross cytological abnormalities at any stage in the meiosis of segregation distorter males, that the sc^4-sc^8 chromosome shows no meiotic loss, but is recovered with frequencies deviating from expectation, that sex-ratio in D. pseudoobscura does not exhibit any gross meiotic abnormality (like a precocious replication of the X

chromosome) as was previously thought, and that the distribution of "granules" (micro-organisms) is non-random with the segregation of the sc^4-sc^8 chromosomes amoung the secondary spermatocytes.

Within the past several years the question of dysfunction has been reopened by the work of Hartl, Hiraizumi and Crow (1968), in which they show that there is an initial decreased fertility of segregation distorter males, roughly proportional to the excess recovery of the SD chromosome over its normal homolog, and interpret this, as well as the decreased lifetime productivity of SD males, as manifestations of sperm dysfunction. In view of this, the reappraisal of the behavior of the Bar Stone translocation becomes of considerable interest.

The fertility of B^S males cannot readily be compared with their wild-type sibs because of the profound difference that might be based in the different phenotypes. Preliminary comparisons of wild type males and Bar males, both with B^S males, raised in complete darkness, except for the few minutes necessary for daily remating, indicated that the translocations males were quite infertile.

The mutational occurrence of a phenotypically normal eye in a Bar^S stock has made it possible to compare the fertility of translocation and non-translocation-bearing males independent of the usual phenotypic manifestation of Bar eyes. Translocation males were mated to Oregon-R females; F_1 females were mated again to Oregon-R males. Their progeny should consist of two types of males, translocation and non-translocation, phenotypically indistinguishable. These males were mated to six or seven cn bw ♀♀ each day for a total of 27 days, (subcultures after the first were assigned the letters of the alphabet, necessitating the termination of the experiment after twenty-six-plus-one days). To obviate any complications arising from hidden defects in the vision of the Bar Stone reverted males, all cultures were kept in complete darkness, except for the short period when the females were changed each day.

		Age of male in days					
		1-5	6-10	11-15	16-20	21-25	26-27
Total Progeny	+	26,942	20,875	7,469	2,403	1,554	742
	B^S	1,705	1,142	199	36	0	0
Fertile ♂ days	+	83	70	41	18	11	6
	B^S	54	37	6	4	0	0
Progeny/♂/day	+	325	298	182	133	141	124
	B^S	32	31	33	9	0	0

For ease of presentation the data are clumped into five day periods, except for the last two. Fertile ♂ days refers to the number of fertile ♂♂ times the number of days the males produced offspring during the five day period in question. The significant rows are, of course, the last two, which give the average number of progeny per fertile male per day.

The table shows a great difference between the fertility of the translocation male and its wild type sib, a difference much too great to be accounted for by the production of inviable aneuploid zygotes. While it cannot be denied categorically that the translocation males are less fertile because the translocation has accumulated sterility factors independent of the translocation itself, it seems much more likely that a phenomenon like sperm dysfunction is responsible for the low fertility. It should be noted, however, that the pattern of infertility is strikingly different from that of segregation distorter, since the latter appears to be of normal fertility during most of its fertile period.

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