

not to fragments after chemical degradation of the tritiated molecules.

The findings in the rat material may appear less conclusive. Also here very few grains were located outside the tissue in the sections. The background label over the sections, however, was significant in all experiments, probably indicating binding of 5-HT to tissue components. The fibroblasts were easily identified. However, only ca. 3–5% of the fibroblasts possessed increased numbers of grains, and then mostly over the nuclei. Figure 2 shows labelled fibroblasts from subcutaneous tissue, and Figure 3 one from a tendon.

In the Atlantic hagfish, most fibroblasts evidently actively concentrate 5-HT, and the 5-HT rapidly accumulates in their nuclei. In the rat, however, only comparatively few fibroblasts (and nuclei) appear to take up 5-HT. This may be due to real species differences. Another possibility is that the ability to accumulate 5-HT is associated with one certain phase of the cell cycle, which is shorter in rat fibroblasts than in those of hagfish. Still another explanation is that a postulated transport mechanism of

5-HT into fibroblasts and their nuclei in the rat material has remained largely saturated with non-radioactive 5-HT during the incubation.

Although many aspects thus need further analysis, the present preliminary findings indicate that fibroblast nuclei may take up 5-HT. Also steroid hormones (see O'MALLEY and MEANS⁷) appear to mediate their effect on proliferation and division of target cells by direct action on nuclei. A similar mechanism for the action of 5-HT on fibroblasts may explain the observed effect on the growth of cultured fibroblasts^{4,5}. Such a mechanism of action of 5-HT in the organism may attribute an important additional role to the large amounts of 5-HT being present normally. In addition, it points at possible roles for 5-HT from mast cells and blood platelets, for instance during hemostasis and in healing of wounds and scar formation.

⁷ B. W. O'MALLEY and A. R. MEANS, in *The Cell Nucleus* (Ed. H. BUSCH; Academic Press, New York 1974), p. 379.

Sterility and Lethality in Crosses Involving Two Translocation Heterozygotes of the German Cockroach, *Blattella germanica* (L.)¹

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Summary. Productivity in crosses involving two independent reciprocal translocations in *Blattella germanica* are reported. Lethal effects alone could not account for the reductions in hatch since completely unproductive crosses occurred frequently. The latter are attributed to the inability of reduced numbers of viable embryos to force open the egg case. The implications for genetic control of the joint dominant effects from embryonic trapping and translocation semisterility are discussed.

The possibility of using reciprocal translocations for control of the German cockroach, *Blattella germanica* (L.), is under investigation in our laboratories². Introduction of a single translocation into laboratory populations effectively retards population growth^{3,4}. However, a much greater inhibition is expected from the use of double translocation stocks⁵. A first measure of productivity in crosses involving two translocations has been obtained using T(2;11) *Cu* in combination with 2 other stocks: T(3;12) and that identified previously as T(9;11)^{3,6}. The latter is referred to throughout this paper as 'T(9;?)', for reasons explained below. High lethality was associated with the double translocations and resulted in striking reductions in the numbers of progeny. The combined lethal effects of 2 translocations could not account for the sterility (non-hatch), which reached 94% in one set of crosses, and an additional mortality-causing factor is reported here.

Each of the translocations noted above has somewhat different characteristics. Briefly, metaphase I chromosome disjunction is random in heterozygous T(2;11) *Cu* males and, presumably, in (T9;?) females since hatch averages in crosses to wild type are close to the expected 50%⁶. T(2;11) *Cu* females are sterile. Alternate disjunction occurs in about 60% of the cells from T(9;?) males⁶. This agrees with an average hatch of 58%. Hatch in T(3;12) males and females is estimated at 60–62%, but disjunction is alternate in more than 70% of the cells in heterozygous males⁷. These differences account for some of the results presented from crosses involving 2 translocations.

T(9;?) and T(3;12) are maintained in backcross systems to the closely-linked markers ruby eye (*ru*) and hooded pronotum (*hd*), respectively^{6,7}. In these systems, > 98% of the phenotypically normal progeny are translocation heterozygotes (T/+). T(2;11) *Cu* is identified by its curly-wing phenotype⁸. In order to obtain phenotypically distinct double heterozygotes, 2 stocks of T(2;11) *Cu*, one homozygous for *ru* and the other for *hd*, were developed. From the former, *Cu* males were selected and crossed to T(9;?) females (T +/+ *ru*). Progeny with normal eye color and curly wings were assumed to be double translocation heterozygotes. T(2;11) *Cu*; T(3;12) double heterozygotes were developed similarly, using the T(2;11) *Cu*, *hd*/*hd* stock.

Cytological examination of male progeny was made to verify the presence of both translocations. As expected, T(2;11) *Cu*; T(3;12) pachytene cells showed 2 separate

¹ Acknowledgment. This research was supported in part by Naval Facilities Engineering Command Contract No. N00025-74-C-0014 and a grant from Johnson's Wax Fund, Inc. The data on the translocation heterozygote and the wild-type matings were obtained by NANCY L. ROSS, and their use is gratefully acknowledged.

² M. H. ROSS and D. G. COCHRAN, *Patna J. Med.* 47, 325 (1973).

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⁴ I. HUBER, *Bull. New Jersey Acad. Sci.* 19, 27 (1974).

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⁶ D. G. COCHRAN and M. H. ROSS, *Can. J. Genet. Cytol.* 16, 639 (1974).

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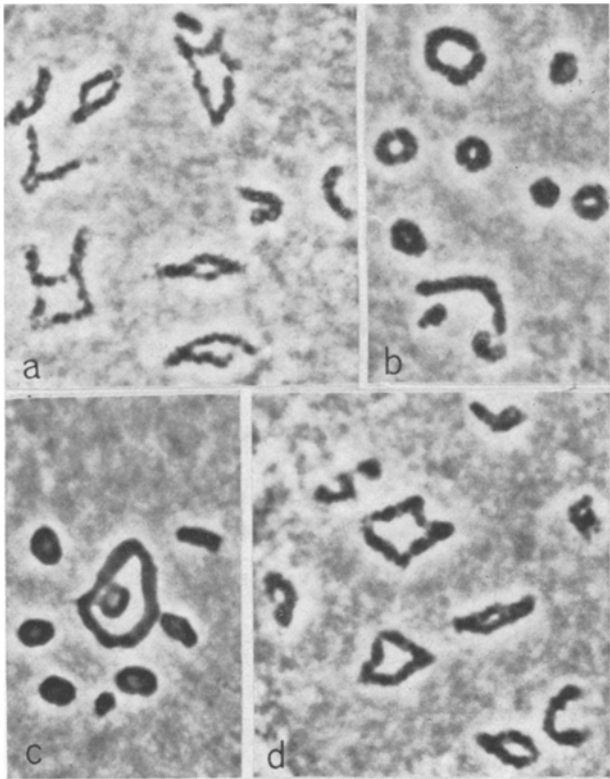
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Hatch data from crosses involving one or two translocations

Parental cross	No. of matings	No sterile matings ^a	Sterility (%)	Avg. prog./ productive pair	Lethality (%)	Avg. prog./ total pair
a) T(2;11)Cu ♂ X +/+ ♀	12	6	50	19.9 ± 1.5	50	10.0
b) T(2;11)Cu ♂ X T(3;12) ♀	27	17	63	10.9 ± 1.4	73	4.0
c) T(2;11)Cu; T(3;12) ♂ X +/+ ♀	42	24	57	11.9 ± 0.8	70	5.5
d) T(2;11)Cu ♂ X T(9;?) ♀	38	26	68	6.8 ± 0.9	82	2.1
e) T(2;11)Cu; T(9;?) ♂ X +/+ ♀	18	17	94	4.0 ^b	90	0.2
f) +/+ ♂ X +/+ ♀ (control)	12	0	0	40.0 ± 0.7	0	40.0

^aCrosses with no hatch due to lethality and embryonic trapping. ^bProgeny from a single pair.

cross configurations (Figure a). Characteristics of the single stocks^{6,7}, were evident in that the configuration was maintained as a ring in T(3;12) but separated frequently into chains-of-four in T(2;11)Cu (Figure b). Two aberrant cells were observed in which the chromosomes formed a ring-of-eight (Figure c). Apparently each translocation formed a chain-of-four which subsequently joined at the ends, possibly due to chromosome stickiness. In the double stock with T(2;11)Cu and T(9;?), common involvement of chromosome 11 should have resulted in formation of a ring-of-six. Instead, 2 separate ring configurations were observed (Figure d). Apparently, the identification of chromosome 11 in 'T(9;11)' was incorrect. Therefore, the designation 'T(9;?)' is used herein, pending definitive identification, of the second chromosome.



Testes squash preparation from nymphal German cockroaches. a) Pachytene cell showing separate T(2;11)Cu and T(3;12) cross configurations. b) Same at diplotene with T(2;11)Cu showing a chain-of-four. c) Aberrant cell with a ring-of-eight. d) Cell with separate rings-of-four from T(2;11)Cu and T(9;?). × 1000.

The data reported here are from first oothecae only, because wild-type females crossed to T(2;11)Cu males did not produce second oothecae. Dissections revealed that further egg maturation did not occur. This is especially noteworthy since sterility in Cu females is also associated with immature ovaries.

The crosses in which productivity was measured are listed in the Table, col. 1. Oothecae from unproductive matings were examined for fertilization and lethal effects, i.e., for embryonic development and the presence of dead embryos. Progeny were averaged both with respect to the total number of parental pairs used and the number of productive pairs. This distinction is very important, and its explanation involves the additional mortality-causing factor mentioned above. High lethality has a secondary effect which is that small numbers of viable embryos in an ootheca are often trapped inside and cannot escape. This is apparently the result of the reduced number of viable embryos which are unable to generate enough pressure to force open the keel of the egg case^{7,9}. Because of this factor, large numbers of matings may be completely unproductive. Thus, embryonic trapping exerts a dominant effect on productivity, augmenting the semi-sterility of translocation heterozygotes. Since this effect has not previously been measured in crosses with either single or double heterozygote, the crosses listed were made to evaluate its significance in both situations.

The data on non-hatch due to embryonic trapping are shown in the Table, cols. 3 and 4. Crosses of the single stock (a) suggest that a lethality of 50% may result in complete sterility in approximately one-half of the matings. Of course, this estimate must be substantiated by comparative data from other stocks with random disjunction. However, the frequency of sterile matings evident in crosses involving 2 interchanges (b-e) leaves no question as to the importance of the embryonic trapping effect to genetic control measures. It is responsible for the marked differences between the two progeny averages in the translocation crosses (cols. 5 and 7, a-e).

Progeny averages based on productive pairs provide an estimate of the actual translocation lethal effects, i.e., those due to unbalanced gametes (Table, cols. 5 and 6). Lethality in crosses of the single stock, T(2;11)Cu⁶ (a), was close to the 50% typical of this interchange. Lethality in crosses involving T(3;12) (b and c) were markedly less than in the T(9;?) crosses (d and e), reflecting the higher frequency of alternate disjunction in T(3;12). Calculations based on earlier hatch data for T(3;12) indicated that 1. crosses b and c would give similar results and 2. progeny averages based on productive pairs would reach ca. 12-13 nymphs/ootheca. Actual

⁹ L. M. Roth, Ann. ent. Soc. Am. 67, 215 (1974).

progeny averages (Table, b and c) were slightly lower than predicted, but it is likely that some trapping of viable embryos occurred in oothecae counted as 'productive'. This could also account for the average of 6.8 offspring in d, in which crosses between interchanges with random disjunction were expected to average ca. 9–10 nymphs/ootheca. Also this for reason, it seems likely the lethality estimate of 82% is somewhat high. The lethality expected from crosses between 2 translocations with random disjunction is 75%.

We cannot yet account for the lack of productivity and apparent high lethality in crosses of the double heterozygote of $T(2;11)Cu; T(9;?)$ (Table, e). The data suggest an unexpectedly low production of balanced gametes although, in the single stock of $T(9;?)$, alternate disjunction is favored in the males. From the data presented it appears that disjunction and lethality in the $T(3;12)$ double could be predicted on the basis of the characteristics of the single stocks, but this is not true for the $T(9;?)$ crosses.

From the standpoint of genetic control, the most important estimate is the average replacement per pair based on the total parental group (Table, col. 7). It appears that the maximum effect possible from initial releases of $T(2;11)Cu; T(3;12)$ males (c) would be a significant retardation of population growth. Alternatively, the double heterozygote $T(2;11)Cu; T(9;?)$ (e) could cause nearly complete population suppression. Both the

higher lethality and sterility from embryonic trapping would enhance the effects of introducing such double heterozygous stocks over those using single translocations, and may thereby partially overcome the lack of fit translocation homozygotes. The effectiveness of this approach would vary according to the particular stocks involved. From the present data, it appears that population suppression could be achieved by using stocks combining two interchanges with little or no directed disjunction in males, provided they prove to be competitive.

A second type of combination from which unique advantages might be derived is the double heterozygote of translocations having one chromosome in common (3-chromosome doubles). Viable gametes formed following disjunction in the ring-of-six configurations would carry one or the other parental interchange¹⁰. Thus, matings would be similar to those of translocation homozygotes in that all offspring would be heterozygotes, although the latter would be divided between the 2 parental types. Our first attempt to develop a 3-chromosome double, using $T(2;11)Cu$ with $T(9;?)$, failed due to chromosome misidentification. Nevertheless, the principle is valid and stocks are on hand which can be used to test it¹¹.

¹⁰ C. R. BURNHAM, *Discussion in Cytogenetics* (Burgess Publ. Co., Minneapolis 1962), p. 1–375.

¹¹ M. H. ROSS and D. G. COCHRAN, in *Handbook of Genetics* (Ed. R. C. KING; Plenum Publ. Co., New York 1975), vol. 3, p. 35.

Differential Effects of Lipids on the Osmotic Fragility of Lysosomes

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Summary. The effect of a wide range of concentrations of oleic acid, oleyl alcohol and oleic acid methyl ester on lysosomal stability has been studied under both hypotonic and isosmotic medium conditions. Both oleic acid and oleyl alcohol exhibited a biphasic interaction pattern with lysosomes; stabilizing at low concentrations and labilizing at high concentrations. Lysosome labilization by the ester required an initial lag period.

Membrane protection by lipid-soluble drugs has been observed in erythrocytes, lysosomes and catecholamine granules^{2–7}. The study of lysosomal stabilization by anti-inflammatory drugs is of special interest, since lysosomal labilization and leakage of lysosomal enzymes are implicated as important factors in many inflammatory con-

ditions. Assessment of lysosomal stabilization by drugs has usually been carried out under isosmotic medium conditions. In order to have a meaningful degree of damage to lysosomal latency in control lysosomal suspensions, the suspensions had to be exposed to unfavourable conditions, i.e. prolonged incubation at 37°C or 45°C^{6–8} or acid pH^{5–7}. Under these conditions, extensive damage to membrane structural components might be brought about as a result of hydrolysis by the lysosomal enzyme composite.

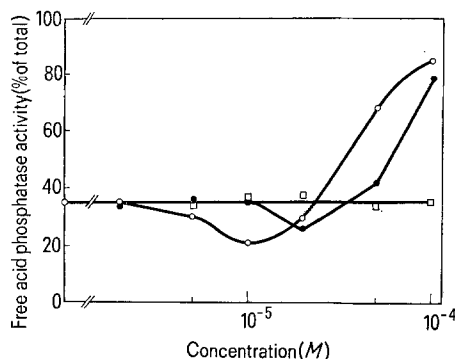


Fig. 1. Effect of oleic acid (○—○), oleyl alcohol (●—●) and oleic acid methyl ester (□—□) on the release of acid phosphatase from a lysosome-rich suspension. Lysosomes were incubated in 0.1 M sucrose, 0.01 M Na-Hepes buffer, pH 7, for 15 min at 37°C.

¹ Acknowledgment. We should like to thank Mr. DAVID GINZBURG for the assistance he gave us during the 3 months he spent at our department as a summer student.

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