Insecticide Resistance: Effects of WARF Antiresistant on Toxicity of DDT to Adult Houseflies

Abstract. *Addition of* N,N-*dibutyl*-p-*chlorobenzene sulphonamide (Antiresistant/DDT) in amounts equal to one fifth the dose of DDT increased the toxicity of DDT to the DDT-resistant portion of a housefly population. Full susceptibility was not regained. There was no increase in toxicity to the DDT-susceptible portion.*

The chemical, *N,N*-dibutyl-*p*-chlorobenzene sulphonamide, sometimes referred to as WARF/AR and officially designated Antiresistant/DDT, has been claimed (*1–5*) to act as an effective synergist of DDT in DDT-resistant houseflies. Many other effective synergists are known, but WARF/AR is of special interest because it appears to be an exception to the general rule (*6, 7*) that most effective synergists of DDT are structurally related to it.

Reports of laboratory trials (*2, 3*) indicate that WARF/AR greatly increases the effectiveness of DDT to resistant strains of housefly and also effects some reduction in the LD_{50} of the susceptible strain (*3*). Field trials (*1, 4, 5*) with DDT-resistant populations of houseflies have shown that residual deposits of WARF/AR plus DDT kill a larger proportion of the population initially and give longer lasting control than residual deposits of DDT alone. Initial results (*4*) indicate that neither treatment gives the four weeks of control that has been suggested as the criterion of practical effectiveness (*8*). More recent results (*5*) indicate that residual deposits of WARF/AR plus DDT may control houseflies successfully for periods of 12 weeks or longer.

In laboratory tests with houseflies, the effectiveness of DDT plus WARF/AR was compared with the effectiveness of DDT alone using a series of doses providing from negligible to complete kill of both sexes. The results are of particular interest because the strain of housefly used exhibits a balance polymorphism for DDT resistance, susceptible and resistant flies appearing in approximately constant proportions in each generation. Because of this polymorphism it was possible to compare susceptible and resistant flies which had been reared together and which presumably had the same genetic background but differed in the presence or absence of resistance mechanisms. Strains of houseflies that are heterogeneous for insecticide-susceptible and resistant phenotypes are well known (*9, 10*), but research workers do not appear to have realized that these strains are suitable for investigating resistance mechanisms and especially for comparing susceptible and resistant phenotypes against an identical genic background. The strain of houseflies used, which has never knowingly been selected with insecticide, originated from the Canberra line, the particular subline supplied being designated ES, meaning that it was selected in Australia for both early emergence and for susceptibility to DDT. When received, it was homogeneous for DDT susceptibility (LD_{50} for males, 0.026 μg, and for females, 0.049 μg) (*13*), but it has now developed a balanced polymorphism for resistance (Figs. 1 and 2), about two thirds of the test flies being DDT-susceptible and one third DDT-resistant. The portions have approximate LD_{50}'s shown in Table 1.

Flies were reared on a medium consisting of dried whole milk, yeast, and ground paper (*12*) at 25°C and were tested 5 to 7 days after emergence.

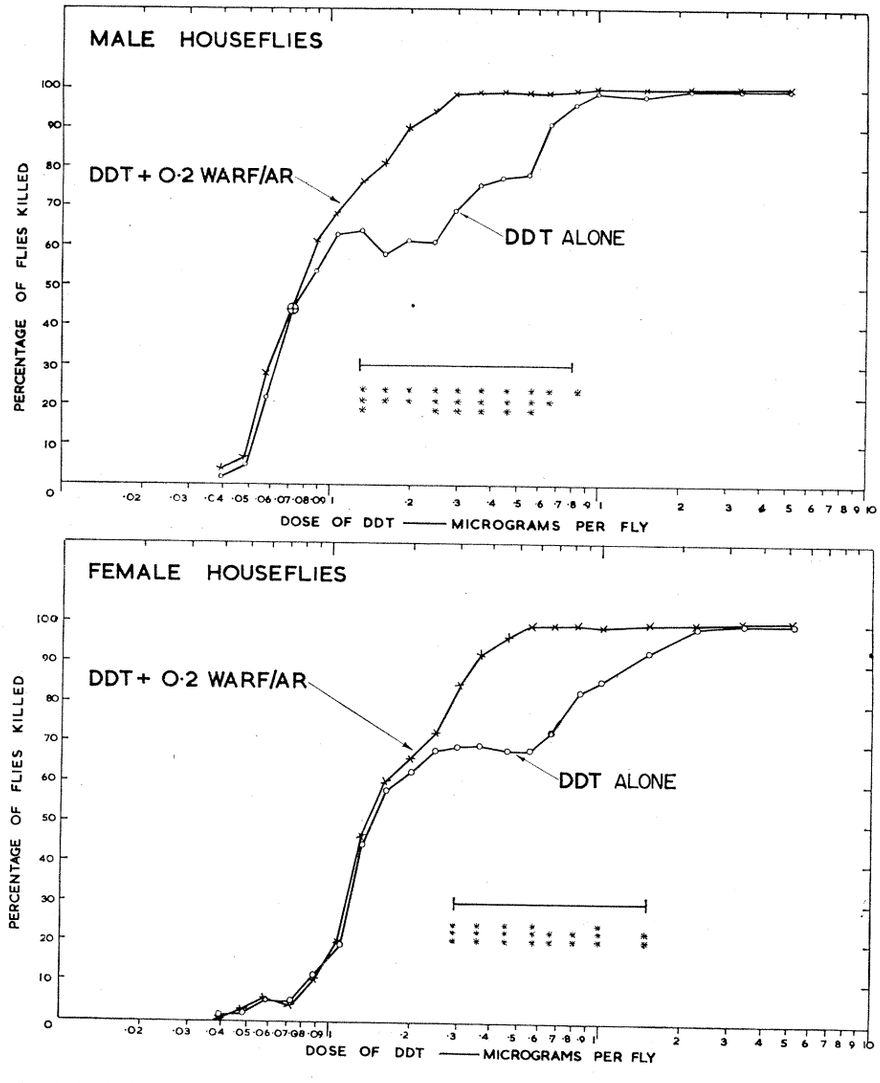

Fig. 1. Relationships between percentage of adult houseflies killed with measured doses of DDT and with the same doses of DDT plus WARF/AR in proportions of 5 to 1. Within the indicated range of doses (males above, females below) there are statistically significant differences between the kills with DDT alone and the kill with the same doses of DDT plus WARF/AR. The probability levels are indicated at each dose: * 0.05, ** 0.01, *** 0.001. Other differences are not statistically significant.

Table 1. Differing LD_{50}'s (the dose which is lethal to half the flies) of the four portions of the housefly population used for comparing the effectiveness of WARF/AR plus DDT with the effectiveness of DDT alone.

Sex of flies	LD_{50} for DDT (μg/fly)	
	DDT-susceptible portion	DDT-resistant portion
Males	0.064	0.58
Females	0.12	0.85

Early emerging and late emerging flies were discarded, only those emerging during a 24-hour period being retained for testing. Flies were treated individually on the mesonotum with a 1 μl droplet of an acetone solution containing the required amount of either DDT or DDT plus WARF/AR. Control flies were treated with acetone alone. Flies were anesthetized with carbon dioxide during treatment. Groups of ten sequentially treated flies were kept at 25°C in petri dishes 4.5 cm in diameter, each containing a paper strip to which a mixture of honey, sugar, and dried milk had been applied. At each concentration of DDT, or DDT plus WARF/AR, there were from three to eight independent tests, 100 flies being used for each test. The values shown are average values of these tests.

Throughout the tests the proportion of WARF/AR to DDT was 1 to 5, as recommended by the manufacturers. It is not known whether this proportion produces the maximum effects.

In Fig. 1 (male flies) and Fig. 2 (female flies) the percentage of flies killed at each dose of either DDT or DDT plus WARF/AR is plotted against the logarithm of the weight of DDT applied to each fly (*13*).

The plateau in the dosage-mortality relationship for DDT alone, in both males and females, indicates that the test flies are not homogeneous for DDT susceptibility. One portion (about 62 percent of males and 68 percent of females) is susceptible to relatively small doses of DDT, the LD_{50}'s being shown in Table 1. These values are within the upper range of normally DDT-susceptible strains, but both are 2.5 times the 1959 LD_{50}'s of the parent ES strain (*11*), possibly indicating that in the emergence of the polymorphism for resistance, all individuals have become less susceptible. The other portions of the population (being 38 percent of males and 32 percent of females) have LD_{50}'s (Table 1) arithmetically times 9 and times 7 of the LD_{50}'s of the susceptible portions. These values are beyond the upper range for DDT-susceptible flies and therefore this portion of the population must be regarded as resistant. In this respect it resembles latter generations of the Canberra strain from which it was derived. The original Canberra line appeared homogeneous for DDT susceptibility during 1952 (*9*) but was markedly heterogenous in 1960 with 17 percent resistant males and 19 percent resistant females (*10*).

In the susceptible portion of the population there are no real differences in the percentages of flies killed with DDT or with DDT plus WARF/AR. Thus this synergist conforms with those previously investigated, most if not all (*6, 7*) of which are ineffective in increasing the kill of DDT-susceptible insects. The effects of added WARF/AR are marked in the resistant portion of the population, almost complete kill being achieved at DDT concentrations (0.291 μg males, 0.543 μg females) insufficient to kill more than a small percentage of the resistant portions of the population. The estimated LD_{50}'s of DDT plus WARF/AR to these resistant portions are, males 0.16 μg DDT/fly and females 0.30 μg DDT/fly. Thus at the LD_{50}'s the effects of added WARF/AR were to improve the effectiveness of the DDT to males by 3.6 times and to females by 2.8 times. Alternatively, it may be considered that the added WARF/AR reduced the level of resistance from times 9 for males and times 7 for females to times 2.5 for both sexes. This is a large reduction, but the failure of the synergist to convert resistant flies to fully susceptible flies conforms with the pattern of other synergists (*6*), full susceptibility never being regained (*14*).

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13. Plotting the results of the more widely used probit mortality against logarithmic dose transforms did not clarify the relationship between dose and kill. Only the plot for females treated with DDT plus WARF/AR could be regarded as a reasonable fit to a straight line; similar plots for males suggested two lines of poor fit, intersecting at about probit five, convex upward. As is to be expected from Figs. 1 and 2, the data for DDT alone plot as three intersecting lines of moderate fit. There are no indications of parallelism.
14. The sample of WARF/AR was obtained from Allied Chemical Corporation, New Jersey, through the World Health Organization, Geneva. Their assistance is gratefully acknowledged.

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Cortico-Subcortical Homeostasis in the Cat's Brain

Abstract. *Transcortical polarization of one cerebral hemisphere, while producing the well-known changes in the amplitude of the evoked potentials in the ipsilateral cortex, induced opposite behavior of these indicators in the contralateral cortex. With the corpus callosum sectioned, the reciprocal relationship was enhanced. Anesthetic doses of barbiturates not only eliminated reciprocity but made the potentials on both sides react in unison to unilateral polarization. These findings suggest the existence of a negative feedback system between the cerebral cortex and the subcortex and the existence of a "left-right equalizing" mechanism carried by pathways in the corpus callosum.*

Small amounts of Pentothal or Nembutal injected into the carotid artery of nonanesthetized, curarized cats produce a temporary reduction of the amplitude of the potentials evoked by electrical stimulation of the chiasma and recorded in the ipsilateral visual area I. In contrast, the signals recorded from the hemisphere opposite to the side of injection are enhanced after a latency of 30 to 120 seconds (Fig. 1, top). The magnitude changes last for several minutes, and both sides return to the pre-injection levels at about the same time. The depression by anesthetics in the injected side is a well-known phenomenon; however, to the best of our knowledge, potentiation of evoked responses contralaterally to the