

CROSS AND MULTIPLE RESISTANCE IN MOSQUITOES *

par

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General principles.

There exists some confusion on this subject owing to inadequate definition of terms. This confusion is not merely an academic inconvenience, since a clear understanding of the basis of resistance to alternative insecticides is essential, in order to cope with resistance in practice. It is convenient to define *cross-resistance* to a group of poisons as that which depends on a single defence mechanism. Clearly, any one of the group of insecticides to which this mechanism gives protection, will select out a strain resistant to all the group. It may happen that the mechanism is more or less efficient in protecting the insects from one member of the group than the others. But the relative levels of resistance to the group (i.e. the « *resistance spectrum* ») will not depend on which member has been used for selection. Thus, a single mechanism seems to be responsible for resistance to γ -BHC and the dieldrin analogues ; and it is usually more effective against the latter. Thus, even when resistance arises following the use of γ -BHC in the field, the strain will be found to have higher resistance to dieldrin, chlordane, etc. It is worth mentioning here that the particular form of the resistance spectrum is helpful in identifying a given mechanism ; and it may even give a clue to the nature of the defence system involved.

Another, quite different reason for resistance of two insecticides, is *double-resistance*. This is due to the simultaneous presence of two quite separate defence mechanisms, giving protection against two groups of poisons. Thus, strains of insects can become resistant to D.D.T. (and analogous compounds) and subsequently resistant to γ -BHC and the cyclodiene compounds. Finally a strain can also acquire resistance to yet more groups, resulting in *triple* — or *multiple-resistance*.

It is evident that double, triple or multiple resistance in a strain is not invariable ; normally it arises in several stages according to the field pressure by different groups of insecticide. In the laboratory, the various mechanisms can generally be separated by appropriate genetical manipulations. This is clearly not the case with cross-resistance which, due to its nature, must always give protection against a certain group of poisons.

A third entity, which ought to be recognized, is one which I describe as *duplicate* - or *triplicate* or even *multiply* - resistance. This describes the situation where two or more mechanisms exist, in the same insect, to protect it from the same poison.

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An example of this is D.D.T.-resistance in the housefly, which has been shown to depend on three, genetically and biochemically distinct, protective mechanisms. The practical importance of recognizing the existence of duplicate resistance is that a method of countering a given mechanism will not achieve a full return to susceptibility. This probably explains why the use of synergists (such as D.M.C., for D.D.T.-resistance) are not entirely successful, since they only eliminate one of the causes of resistance (in this case, dehydrochlorination).

Situation in anopheline mosquitoes.

Very little information on cross-resistance of D.D.T.-resistant anophelines is available. Dr George DAVIDSON has shown that resistant *Anopheles albimanus* (5), *A. quadrimaculatus* (6), *A. stephensi* (8), and *A. sudaicus* (4) all show cross-resistance to D.D.D., methoxychlor and diethyl diphenyl-trichlorethane. The data are not sufficient for delineation of resistance spectra, however, and give no clues as to the mechanism responsible. Results of later workers indicate that cross resistance to Deutero-D.D.T. is less than to D.D.T. in *A. quadrimaculatus*, suggesting that dehydrochlorination is partially responsible (10).

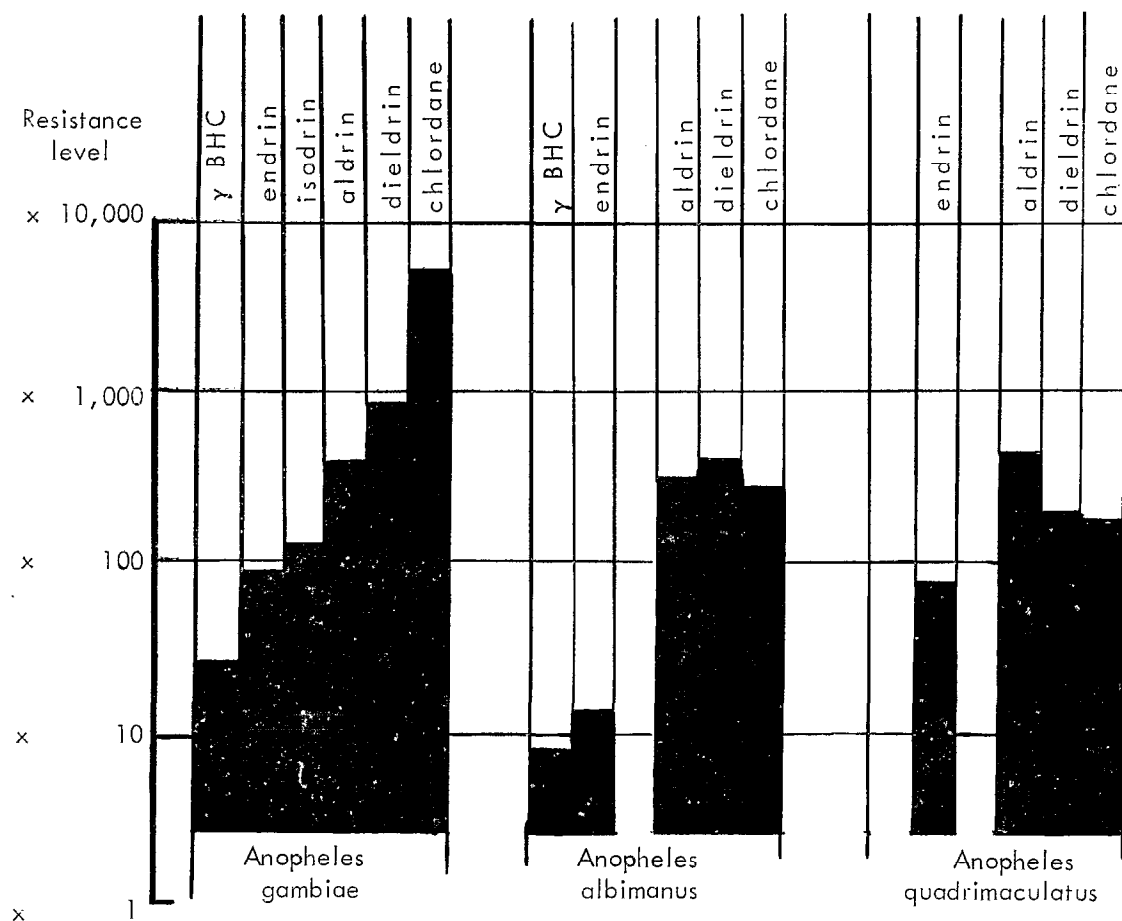


FIG. 1. — Resistance spectra of strains of *Anopheles gambiae*, *A. albimanus* and *A. quadrimaculatus* based on data of Davidson (3, 5, 6). These spectra are typical of dieldrin-resistance (1).

Other work by DAVIDSON has more completely defined the cross-resistant patterns of dieldrin-resistant strains of *Anopheles gambiae* (3), *A. albimanus* (5), and *A. quadrimaculatus* (6) (fig. 1). The spectra constructed from his data are typical of this type of resistance, showing lowest resistance to γ -BHC, intermediate tolerance of endrin and isodrin and highest resistance to dieldrin, aldrin and chlordane (1).

Double resistance, both to D.D.T. and the B.H.C.-dieldrin series, has been demonstrated in *Anopheles albimanus*, *A. aconitus*, *A. culicifacies*, *A. gambiae*, *A. pharoensis*, *A. quadrimaculatus*, *A. sacharovi*, and *A. stephensi*. Both types of resistance can develop in *A. sundanicus* and *A. pseudopunctipennis*; but the double resistant form does not seem to have arisen in the field. Where double resistance occurs, it raises considerable difficulties in control and in malaria eradication. The alternative is to change to an organophosphorus insecticide or a carbamate. So far, no resistance in anophelines has been reported for these two types of compound.

Situation in culicine mosquitoes.

Cross-resistance to D.D.T.-analogues has been studied in *Culex fatigans*, (12), *C. tarsalis* (16) and *Aedes aegypti* (15, 14). The results indicate that dehydrochlorination is not the sole means of defence in these resistance strains (except, perhaps, in

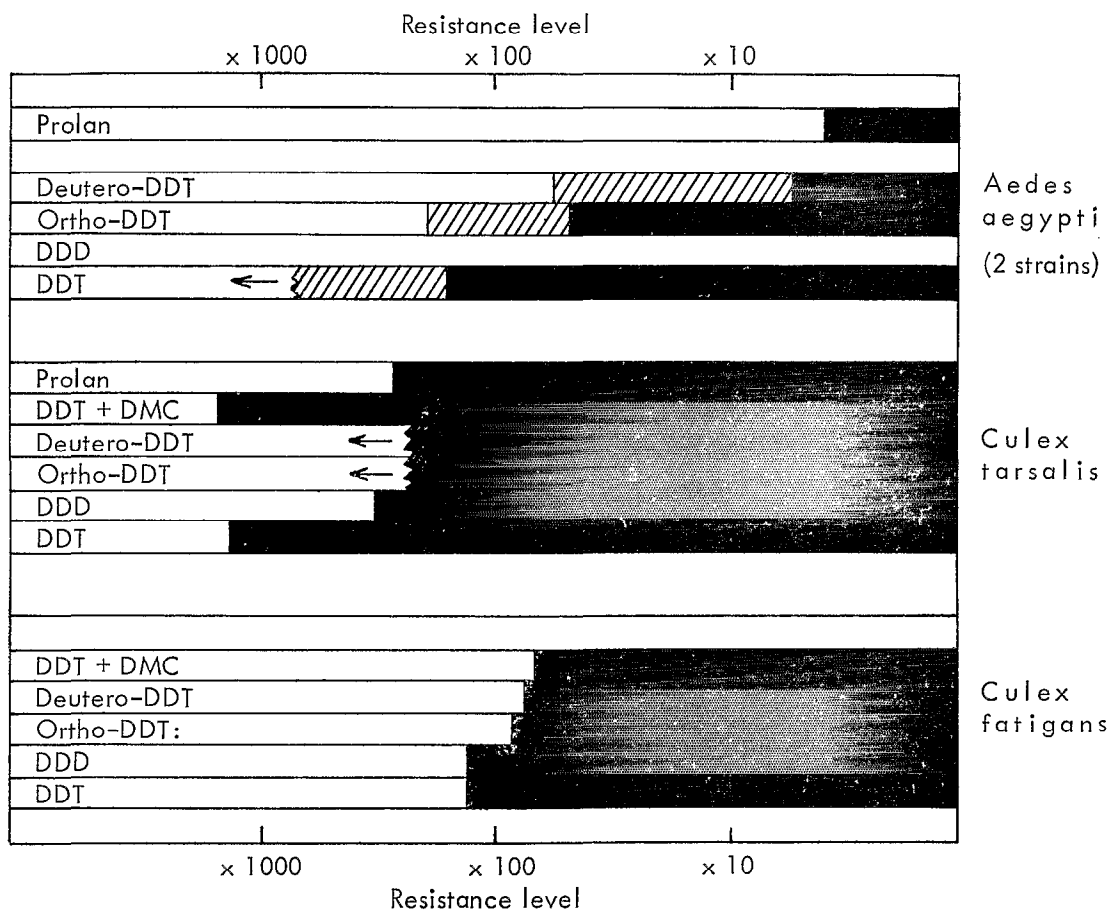


FIG. 2. — Resistance spectra of D.D.T.-resistant strains of *Culex fatigans* (12), *C. tarsalis* (16) and *Aedes aegypti* (14, 15). Ortho-D.D.T., Deutero-D.D.T. and Prolan are difficult or impossible to degrade by dehydrochlorination; while D.M.C. generally suppresses this mechanism.

Aedes aegypti), since there is cross resistance to analogues difficult or impossible to degrade in this way (fig. 2). Also, addition of the synergist D.M.C. does not suppress resistance in *C. tarsalis*. Biochemical studies, on the other hand, show that the dehydrochlorination mechanism is enhanced in the resistant strains (12, 13, 14). The probability is that more than one mechanism of defence to D.D.T. can develop in culicine mosquitoes (11).

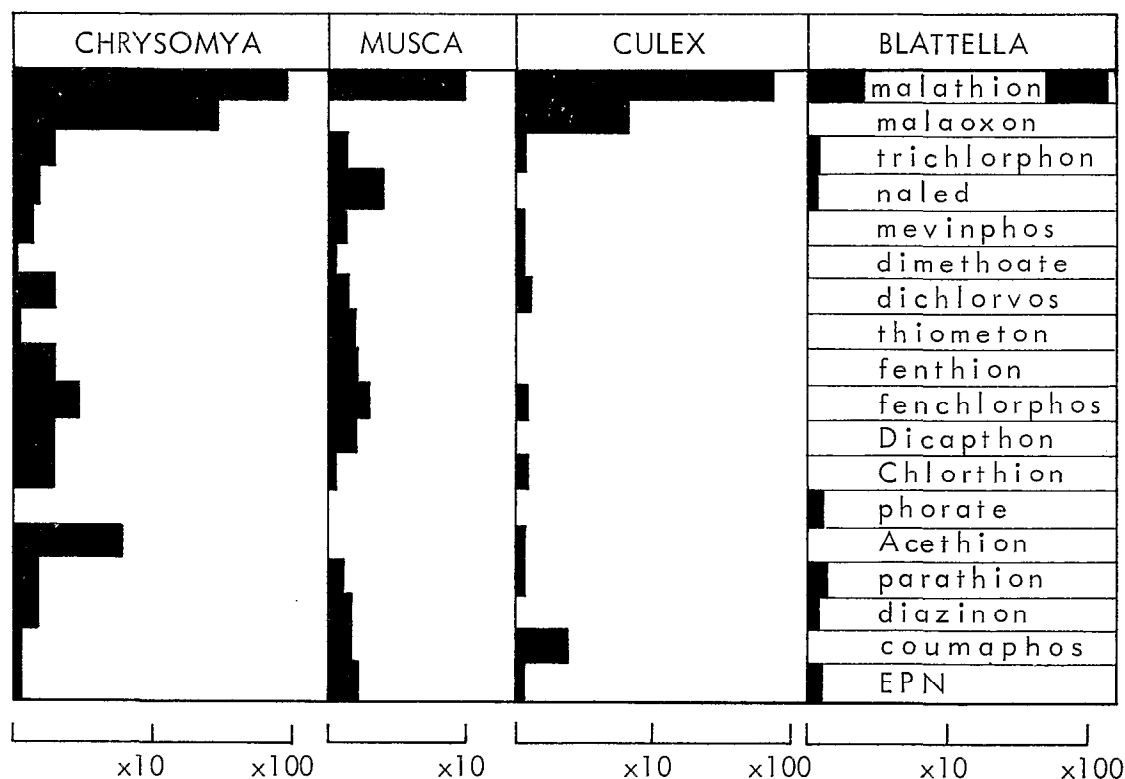


FIG. 3. — Resistance spectra of a malathion-resistant strain of *Culex tarsalis* (2) compared to spectra of malathion-resistant strains of other insects.

The dieldrin-resistance spectrum of *Aedes aegypti* is the only relevant example among culicines ; it is of the characteristic type mentioned earlier (8).

Organophosphorus resistance is known in a few culicines, including *Culex tarsalis*, *Aedes nigromaculis*, and *A. taeniorhynchus*. A cross-resistance spectrum for *C. tarsalis* (larvae) can be drawn from the results of F.W. PLAPP and co-workers (2). The strain investigated had high and very specific resistance to malathion and somewhat less to mala oxon, which is characteristic of several insects which have developed malathion resistance (fig. 3). The specific nature of this resistance (as compared to that affecting other phosphorus compounds) is due to the defence mechanism which depends on detoxication by a carboxyesterase system.

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