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GENETIC CONSIDERATION IN THE CHOICE OF INSECTICIDE

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Resistance to the chlorinated hydrocarbon insecticides in anopheline mosquitos is an inherent feature dependent, in all the cases so far fully studied, on two single, independent, genetic factors (Davidson & Mason, 1963). Table 1 lists the species studied and the types of inheritance involved.

The speed of selection of resistance will depend primarily on three things:

(1) the original frequency of the resistance gene;

(2) the nature of the gene; and

(3) the exerted pressure of the selecting agent, viz. the insecticide.

There are, unfortunately, no records of the frequency of DDT resistance in unselected mosquito populations, but from the fact that, where this resistance has appeared, it has usually only done so after several years of the use of DDT, it is concluded that it is quite rare. Two records exist of the frequency of dieldrin resistance in unsprayed areas. One is from the town of Sokoto in Northern Nigeria where 6% of the A. gambiae showed resistance, almost certainly of the heterozygous type (Armstrong et al., 1958), and one from the Bobo-Dioulasso area of the Upper Volta where some 5-12% of the same species were resistant (Hamon et al., 1958).

The relative survival values of the heterozygous and homozygous resistant mosquitos in the presence of the selecting agent will depend on the degree of resistance conferred by the resistance gene and its degree of dominance. Dieldrin-resistant mosquitos, having a high degree of resistance and in which the gene is always either dominant or semi-dominant, will thus show a greater survival in the presence of the insecticide than DDT-resistant mosquitos, in which the degree of resistance is low and the gene expression often recessive.

TABLE 1. TYPES OF INHERITANCE OF INSECTICIDE RESISTANCE IN ANOPHELINE MOSQUITOS

Dieldrin resistance		DDT resistance		
Dominant	Semi-dominant	Dominant	Semi-dominant	Recessive
A. gambiae	*A. gambiae*	*A. stephensi*	*A. stephensi*	*A. sundaicus*
Ivory Coast Upper Volta Cameroon Liberia	Nigeria Upper Volta Ivory Coast	Iran	Iraq	Indonesia (Java)
	A. albimanus		*A. pharoensis*	*A. albimanus*
	El Salvador		Egypt	El Salvador
	A. quadrimaculatus			*A. quadrimaculatus*
	USA			USA
	A. stephensi			
	Iran			
	A. sundaicus			
	Indonesia (Java)			
	A. pharoensis			
	Egypt			

The activity of the selecting agent will depend on a number of factors:

(a) its inherent toxicity;

(b) the efficiency with which it is applied;

(c) the proportion of the mosquito population coming under its influence; and

(d) the behaviour of the mosquito.

The insecticides of proven value in the control of mosquitos are the three chlorinated hydrocarbons: DDT, gamma-BHC and dieldrin. The first of these is irritating to mosquitos and seldom, if ever, achieves a complete mortality. The other two produce high mortalities but with differing persistences, gamma-BHC being the shorter-lived. The proportion of the mosquito population coming under the influence of the insecticide will depend on the efficiency of application and whether or not the attack is against the larval or adult stage, or both. Where directed against both stages a more rigorous selection must result and, if resistance is present, it will predominate more rapidly. Where the spraying of human habitations is the line of attack, the rate of selection will depend to an important extent on the behaviour of the adult mosquito. A man-biting, house-resting mosquito population will obviously be subjected to a higher selection pressure than a predominantly animal-biting, outside-resting population.

It follows from all this that dieldrin resistance will be rapidly selected by dieldrin. Macdonald (1959) calculates that if the resistant individual should have 10 times the survival value of the susceptible (which might be an underestimate), an original frequency of 1% could become 75% in five generations, i.e. some two or three months after spraying. Examples of the rapid selection of dieldrin resistance in the field are too numerous to mention. Where it has not occurred in areas where this insecticide has been used on a large scale, it seems safe to assume in fact that the genetic factor for dieldrin resistance is absent from the mosquito population, e.g. in parts of East Africa.

Because cross-resistance to gamma-BHC in dieldrin-resistant mosquitos is of a comparatively low order, selection by BHC would be expected to be slower. This is borne out by field experience in Northern Nigeria (Hamon & Garrett-Jones, 1963).

A change of insecticide to DDT in areas where dieldrin resistance has appeared will be initially successful and will remain so providing the genetic factor for DDT resistance is not also present. Dieldrin-resistant A. gambiae have thus been successfully controlled in the Western Sokoto region of Northern Nigeria since 1957 without the appearance of DDT resistance though indications of slightly increased tolerance to DDT are apparent. Further, when A. gambiae from this area were tested on dieldrin in 1961 they were found to be completely susceptible, i.e. the dieldrin resistance had disappeared.

Because of its low degree and often recessive expression, DDT resistance is usually only slowly selected. Macdonald (1959) calculates that for a recessive factor and a similar degree of selection to that considered in relation to dieldrin resistance, 1000 generations would elapse before the gene frequency increased from

0.01 to 0.1%, and another 100 generations before it increased to 1.0%. After this, the increase would be quite rapid and a further 15 generations of selection would produce nearly 100% resistant individuals.

Examples of this slow selection by DDT in the field are to be found in A. stephensi in Saudi Arabia and A. sundaicus in Indonesia (Java). Both were originally successfully controlled by a change of insecticide to dieldrin, but now resistance has appeared to this insecticide in both species (though not in areas where DDT resistance was present in the case of A. sundaicus).

It seems logical, therefore, to recommend DDT as the insecticide of first choice for the control of anopheline mosquitos, unless the absence of dieldrin resistance from the population in question can be guaranteed. Moreover, because of the slow selection of DDT resistance, it may be possible to eradicate malaria before resistance in the vector interferes. Further, the low degree of resistance imparted implies that some resistant individuals will actually be killed by DDT (and this has been shown to be the case in the laboratory with DDT-resistant A. stephensi and A. sundaicus exposed to field dosages of DDT on mud surfaces). Thus higher dosages and more frequent applications of DDT are now being advocated, and in some areas actually being applied, where DDT resistance is already apparent in the mosquito population, e.g. A. culicifacies in India and A. stephensi in Iran. (In Iran dieldrin resistance is present in addition to DDT resistance and various organic phosphates are being tried out on the prevailing mud surfaces.)

There are indications that DDT with its incomplete kill may not produce a mortality sufficient to intercept malaria transmission by highly efficient vectors, even though these are susceptible to the insecticide, e.g. A. gambiae in the Cameroons (Cavalié & Mouchet, 1961). Under these conditions and where dieldrin-BHC resistance prohibits the alternative use of these insecticides, some of the organic phosphates, e.g. fenthion or carbamates, for example U.C. 10854 (Hadaway & Barlow, 1963), may prove more efficient than DDT, even on mud walls, provided that their use for residual spraying of human habitations presents no risks of toxicity to man.

Although mixtures of antibiotics and other drugs have been in general use for some considerable time for combating bacterial resistance, little consideration has been given to the use of mixtures of insecticides for insect control. In the DDT and dieldrin groups of chlorinated hydrocarbons and in the organic phosphates we have groups showing what appears to be independent action and, what is more, laboratory investigations have shown that mixtures of DDT and dieldrin, for example, at slightly above the LC_{50} levels of each, give near 100% mortalities of susceptible anophelines (Macdonald, 1959).

It was with these ideas in mind that an investigation of the potentialities of mixtures was started in Indonesia in 1961 in an area where the A. sundaicus population showed some 10% dieldrin-resistant individuals. Paired mixtures of DDT, BHC, dieldrin and malathion were used in experimental huts fitted with window-traps. Any mosquitos surviving passage through these huts and a subsequent holding period were tested on the lower discriminating dosage of dieldrin, known to distinguish between susceptible and heterozygous resistant individuals. It was shown that BHC and dieldrin by themselves and mixtures of DDT and BHC or DDT and dieldrin all selected in favour of dieldrin resistance, though the mixtures showed less selection than the single insecticides. Mixtures of BHC and malathion or dieldrin and malathion, on the other hand, did not select in favour of dieldrin resistance, but then neither did malathion and this insecticide on the prevalent non-absorbent surface give as high and long-lasting kills as did mixtures of it with BHC and dieldrin. Mixtures of DDT and malathion gave incomplete kills at a significantly lower level than malathion alone and little better than DDT alone, although no selection in favour of dieldrin resistance occurred.

In spite of these somewhat disappointing results it is considered that further trials are worth while both with other dosages and other insecticides and on other types of surfaces.

It has long been the hope that truly negatively-correlated insecticides, i.e. those insecticides to which resistant insects are more susceptible than susceptible ones, might be found and might be used in practice. Cetyl bromoacetate and phenylthiurea were two such compounds showing evidence of negative correlation in the laboratory, but did not prove effective in the field. Hopes have now been revived by the recent work of Georghiou & Metcalf (1963) with m-isopropylphenyl methylcarbamate. Laboratory selection with this compound of a strain of A. albimanus containing both DDT- and dieldrin-resistant individuals has resulted in a marked reduction of the proportion of these individuals without any enhanced tolerance to the carbamate appearing.

SUMMARY

The various factors affecting the speed of selection of resistance to the chlorinated hydrocarbon insecticides in anopheline mosquitos are discussed in the light of the knowledge that two single, independent, genetic factors are involved, one conferring a high degree of resistance to dieldrin and related compounds and in which the genetic factor is either dominant or partially dominant, and the other conferring a low degree of resistance to DDT and related compounds and in which the genetic factor is often recessive or only partially dominant.

DDT is considered to be the logical first choice of insecticide unless the absence of dieldrin resistance can be guaranteed. Where DDT cannot be used and where dieldrin resistance is present, organic phosphates or carbamates might be useful alternatives on some surfaces. A plea for more field studies on the potentialities of mixtures of the two groups of chlorinated hydrocarbons or of chlorinated hydrocarbon and organic phosphate for the prevention of the appearance of resistance is made.

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