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THE PRESENT STATUS OF INSECTICIDE RESISTANCE IN ANOPHELINE MOSQUITOS

by

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ABSTRACT

The problem of insecticide resistance in anopheline mosquitos has created more concern and repercussion than any other problem in applied medical entomology during the last quarter of a century. This concern stems from the serious challenge that the phenomenon of resistance now poses to man's first attempt to eradicate an insect-borne disease, such as malaria, on a world-wide basis. The number of anopheline species resistant to insecticides are enumerated and in one important malaria vector, An. albimanus, resistance has appeared to all the three groups of insecticides i.e. chlorinated hydrocarbon, OP (malathion) and carbamate (propoxur) in some countries in Central America. Since resistance to chlorinated hydrocarbon insecticides in anopheline mosquitos has been well covered in the literature, special emphasis has been placed in this paper on two aspects: (a) the progression or regression of resistance in some anopheline species to DDT; and (b) the development of resistance in some anopheline species to OP and carbamate insecticides. The data received by WHO up to 1972 have been analysed. In addition, the determination of LT50 values and interpretation of results based on time - mortality regression lines are discussed. The implication of resistance in principal malaria vectors is also reviewed.

1. INTRODUCTION

The problem of insecticide resistance in anopheline mosquitos has created more concern and repercussion than any other problem in applied medical entomology during the last quarter of a century. This concern stems from the serious challenge that the phenomenon of resistance now poses to man's first attempt to eradicate an insect-borne disease, such as malaria, on a world-wide basis. Seventeen species of malaria vectors are resistant to both DDT and dieldrin insecticides, two to DDT alone and nine to dieldrin alone. In one important malaria vector species, An. albimanus, resistance has appeared to all the three groups of insecticides, i.e. chlorinated hydrocarbon, OP (malathion) and carbamate (propoxur) insecticides.[1]

The resistance picture of malaria vectors to chlorinated hydrocarbon has not changed radically during the past three years, as reported by Busvine (1969). Busvine & Pal (1969) and Brown & Pal (1971), except for the development of resistance of anopheline mosquitos to OP and carbamate insecticides. During the period under review, WHO has received results of susceptibility tests pertaining to about 40 anopheline species from different parts of the world, which have been included in the WHO Information Circular on Insecticide Resistance, Insect Behaviour and Vector Genetics and summaries released by the WHO Malaria Eradication Division. As mentioned above, special emphasis has been placed in this paper on two aspects:

(a) the progression or regression of resistance in some anopheline species to DDT;

(b) the development of resistance in some anopheline species to OP and carbamate insecticides.

One observation which stands out is that most instances of OP and carbamate resistance in mosquitos have not occurred because of the use of these compounds in operational public health programmes, but are due to indirect selection exerted by the extensive use of these compounds for the control of agricultural pests. The recent WHO Malaria Conference in Brazzaville (1972) considered this problem and stated that "the extensive use of organic pesticides in agriculture, especially on cotton and rice, has been associated with the development of resistance in malaria vectors to these insecticides. All the above elements will have to be taken into account by the malariologist in deciding on the extent and duration of the use of insecticides."

2. METHODS USED IN DETECTION AND MEASUREMENT OF RESISTANCE AND INTERPRETATION OF RESULTS

WHO recognized at an early stage the importance of developing standard test methods for detecting and measuring the level of resistance in vector populations. The resistance test kits for mosquitos and other vector species have proved very valuable and an impressive amount of data has thereby been obtained throughout the world. The larval test method has the advantage that a series of concentrations of insecticides in ethanol can be used to obtain concentration - mortality regression lines to determine LC50 or LC95 values. In the standard test for susceptibility of adult mosquitos to organochlorine insecticides, DDT and dieldrin,

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[1] It will not be out of place to mention that the resistance problem is continuing to affect the control of some other species of mosquitos, the encephalitis vector, Culex tarsalis, and the pest mosquito Aedes nigromaculis, both in California (Womeldorf et al., 1972). In many areas of that state, these species have now developed resistance to all the organochlorine and organophosphorus insecticides available. By the end of 1970, approximately twice the normal operational dosages of malathion, parathion, parathion methyl, fenthion, EPN, difenphos and chlorpyrifos had failed to give satisfactory control of C. tarsalis larvae. As a consequence, control of adult mosquitos by means of propoxur applied by the ultra-low-volume (ULV) air-spray method has been adopted to meet emergencies involving this vector, together with source reduction through environmental control measures. Aedes nigromaculis has also developed resistance to all available organochlorine and organophosphorus insecticides in certain mosquito abatement districts in California. Moreover, this species shows some tolerance to carbamates; control failures have been encountered when adulticide sprays with propoxur have been applied. Therefore, the control may once again come to depend upon the use of petroleum oils, fortified oils and larvivorous fish.

mosquitos are exposed to a series of concentrations of impregnated papers for one hour. As in the case of larval tests, a concentration - mortality regression line is obtained to determine LC50 or LC95 values.

The WHO Expert Committee on Insecticides (1970) recommended that in view of the impossibility of supplying a full range of concentrations of impregnated papers for all OP and carbamate insecticides,[1,2] only two concentrations of each may be provided, and to make up for the reduction in the range of concentrations supplied, tests should be done using different exposure times, in addition to the standard one-hour period. The Committee recognized that this procedure will alter the basis of detection and measurement of resistance, since mortalities will be related to exposure times (rather than to concentrations) and from the regression lines, the LT50 and LT95 values can be calculated. The Committee felt that this was justified on two grounds: "(a) that investigations have shown, at least with organochlorine compounds, that there is a close relationship between exposure time and the dose of insecticide picked up: (Busvine 1958, Pennell et al., 1964, Ariaratnam & Brown 1969). A close watch should, however, be kept that with the newer compounds, the close relationship between concentrations and time does, in fact, obtain particularly with carbamates; and, (b) that change in the method of detecting resistance is not so serious with newer compounds, since there is not a large body of comparative data already available." In view of the above recommendation, the following OP and carbamate impregnated papers are supplied with mosquito test kits: malathion 0.5 and 5.0%, fenthion 0.25 and 2.5%, fenitrothion 0.1 and 1.0%, propoxur 0.01 and 1.0%. A full series of concentrations of the above insecticides was also available for special research investigations.

LC50 vs LT50

Hamon & Sales (1970) carried out a series of tests with Ae. aegypti, An. gambiae A and Culex pipiens fatigans by the method recommended by the Expert Committee, and obtained a straight exposure mortality relationship (see Fig. 1). Sales & Mouchet (1972) also obtained similar results with propoxur, fenitrothion, fenthion and malathion with C.p. fatigans and Ae. aegypti.

In addition, Rongsriyam & Busvine (1973) have indicated that it is possible to calculate Ct values in two ways, from LT50 x concentration or from LC50 x time, and their tests have shown "that the values estimated in these two different ways are not substantially different" (see Table 3).[3] A computer programme on the same lines as LC50 and LC95 has been developed to deal with time exposure mortality data and a few of the results obtained with anopheline species are given in Table 2.

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[1] The detection of resistance to OP and carbamate insecticides is complicated: whereas only two types of impregnated papers (DDT and dieldrin) were quite adequate to detect resistance to organochlorine insecticides, it is not possible to choose one or two OP or carbamate compounds which will unequivocally indicate resistance to other members of the group concerned.

[2] The greatly increased cost would be aggravated by the more rapid deterioration of impregnated papers of these insecticides in storage.

[3] Babione, R. (personal communication, 1968) has indicated that LT50 determinations give a valid measure of resistance to OP compounds, but with carbamates, the lethal effect is not enhanced by increase in exposure time as much as by increases in insecticide concentrations.

Discriminating dosages

Busvine (1973) has summed up the question of discriminatory dosages as follows:-

In many resistance investigations it is useful to employ a dose level which will be expected to kill all individuals in a population sample. In this way resistant individuals will be discovered in "monitoring" tests at a single dose level. The problem exists in choosing the appropriate level which must be done after extensive tests at several partially lethal levels with the normal population, in order to define its response characteristics. The difficulty is that, on theoretical grounds, it is impossible to determine an "LD100" from a probability dose regression line. As a working approximation, the WHO Expert Committee on Resistance in 1963 adopted as a criterion a dose level double that which had killed all insects in the experiments used to delineate the base line for a susceptible strain.

This criterion is likely to work well with a test which gives a steep regression line for susceptible populations. It is evident, however, that no indication of the probability of chance inclusion of a normal survivor can be estimated from a dose level, without information on the regression slope. Therefore, it is sounder to choose the discriminating level by a mortality probability. This criterion was, in fact, adopted in 1970 by FAO in the standardized test for resistance in red flour beetles, for which a 99.9% kill was selected (Plant Prot. Bull., 18, 107, 1970). If a discriminating dose is chosen on this basis, there is 0.001 probability of a normal insect surviving, so that in a batch of 100, there is 0.1 chance. One would then expect one survivor in each 10 tests, but for a single survivor in repeated tests, the chance markedly declines, 0.1, 0.01, 0.001, etc. Therefore, persistent survivors in successive tests are fairly good proof of true resistance.

Discriminating doses in genetical investigations

One of the first uses of discriminating doses was the special case of distinguishing genotypes segregating in genetical investigations (by Davidson, 1958, Bull. WHO 18, 759).[1] The principles are similar, except that, in addition to the objective of killing all susceptible individuals, one is faced with the problem of selecting doses which have a low probability of killing heterozygotes but no resistant genotypes.

Dr Davidson has suggested the following discriminating doses for anopheline mosquitos:

0.4% dieldrin for one hour killing all susceptibles;
4.0% dieldrin for two hours killing all heterozygotes;
4.0% DDT for one hour killing most susceptibles.

Brown & Pal (1971), have suggested the following disseminating concentrations for some of the insecticides:

DDT		Dieldrin		Malathion	
SI	IR	SI	IR	SI	IR
0.4	4.0	0.4	4.0	1.6	3.2

S = susceptible I = intermediate R = resistant

Zahar & Davidson (1973) observed that one-hour exposure to the following concentrations gives nearly 100% kill, when susceptible populations of three anopheline species were tested.

[1] Personal communication.

	An. albimanus	A. stephensi	A. gambiae
Malathion	3.2%	5.0%	3.2%
Fenthion	2.5%	2.5%	2.5%
Fenitrothion	1.0%	1.0%	1.0%
Propoxur	0.1%	-	-

Georghiou (1972) in his larval tests used two discriminating dosages of the three insecticides as follows:

	Low dosages	High dosages
Propoxur	10 ppm	100 ppm
Malathion	0.5 ppm	2.0 ppm
Parathion	0.03 ppm	0.1 ppm

and used the following levels of mortalities obtained with these dosages for determining the frequency of occurrence of resistance in An. albimanus.

Insecticide	% Mortality		Frequency of resistance
	Low Dosage	High Dosage	
Malathion or parathion	95 - 100	100	S (none; susceptible)
	75 - 94	95 - 100	L (low)
	25 - 74	50 - 94	M (moderate)
	0 - 24	0 - 49	H (high)
Propoxur	95 - 100	100	S (none; susceptible)
	75 - 94	75 - 100	L (low)
	25 - 74	25 - 74	M (moderate)
	0 - 24	0 - 24	H (high)

Before a final decision is taken with regard to diagnostic dosages of OP and carbamates, it is essential to obtain further data from well separated areas on different species and also on the genetics of resistance and the nature of genes and their inheritance.

3. FIELD OCCURRENCE OF DDT AND DIELDRIN RESISTANCE

As indicated in Table 1, 17 species of anopheline mosquitos have developed resistance to both DDT and dieldrin, two to DDT and nine to dieldrin. While the resistance to dieldrin was generally absolute and irreversible, during the attack phase of malaria eradication programmes there has been a gradual increase in the level of resistance in anopheline mosquitos to DDT and when the insecticide was withdrawn, a reversion to susceptibility was observed in a number of instances. Two examples are cited.

An. culicifacies: the first report of increased tolerance in A. culicifacies to DDT in India came from two villages of Panch Mahal District of Gujarat in September 1959 after about five to seven years of spraying of DDT in this area (Rehman et al., 1959). Subsequent tests indicated that DDT resistance had increased by three to 11 times during 1959 and 1961.

In Maharashtra, where DDT had been withdrawn due to the entry of National Malaria Eradication Units into consolidation/maintenance phase, or where DDT had been replaced by HCH due to very high resistance in A. culicifacies, systematic observations on the susceptibility level revealed a significant reversal to normal susceptibility. It was observed that within one or two years of withdrawal of DDT spray from areas where no mortality was recorded in A. culicifacies when exposed to 4.0% DDT impregnated papers, mortalities as high as 70% were obtained with the same dosage (see Table 4, Raghvan et al., 1967). This finding is significant from the point of view of control of this species where resistance to HCH has been encountered simultaneously.

An. stephensi: resistance to DDT was first observed in Erode (Madra State) in 1956 (Rajagopalan et al.). Since then, resistance in this species to DDT and gamma HCH or DDT alone has been recorded from many localities in the States of Adhra Pradesh, Gujerat, Madras, Mysor and Rajasthan. In Salem, DDT and HCH were applied both as adulticide and larvicide. After the development of a high degree of resistance, the main weapon for malaria control in this area has been anti-larval operation either by application of lead-free aviation gasoline or Aromex or biological control by the release of Gambusia fish. After six years, the population reverted to susceptibility as the mortality with 4% DDT impregnated papers rose from 12.2 to 46.6%.

RESULTS OF SUSCEPTIBILITY TESTS AGAINST DDT, A. STEPHENSI FROM SALEM TOWN

Year	Period	No. tested	% Mortality with 4% DDT papers
1964	Nov.	100	12.2
1966	Sept.	50	2.5
1967	May	80	15.0
1970	Sept.	160	46.6

(after Srivastava & Roy 1972)

An. albimanus: extensive series of tests are being carried out with this species in Central America. Some of the results obtained during 1970-71 are summarized below.

	Mortality after exposure to 4% DDT	
Costa Rica	Side 1	10 - 34% (1 hour)
"	Side 2	36 - 74% (1 hour)
Dominican Republic	Side 1	62 - 88% (2 hour exp.)
" "	Side 2	97% (1 hour)
" "	Side 3	100% (2 hours)
El Salvador		
San Salvador		37 - 74% (1 hour)
San Miguel		1% (1 hour)
Guatemala		
Escuintla		13 - 28% (1 hour)
"		31 - 60% (1 hour)

	Mortality after exposure to 4% DDT (continued)
Retalhuleu	16 - 30% (1 hour)
"	33 - 70% (1 hour)
Nicaragua	
Matagalpa	homozygous resistant

It would seem that this species is resistant to DDT in most of the areas tested.

Anopheles maculipennis sacharovi: Drobozina et al. (1972) have reported resistance to DDT in this species in Azerbaijan (USSR).

The results of susceptibility tests with DDT with different anopheline species in various countries where this insecticide is still being used for malaria programmes should be carefully watched to determine the degree of progression or regression of resistance to this insecticide. It must be repeated here that a moderate degree of resistance to DDT does not preclude its use in malaria eradication programmes, and in most instances, a satisfactory control of the vector can still be obtained. India and Ceylon are very good examples of this.

4. FIELD OCCURRENCE OF OP AND CARBAMATE RESISTANCE

The results of susceptibility tests with anopheline mosquitos to OP and carbamate insecticides up to the end of 1972 are given in Table 5. While in most of the instances where susceptibility tests have been carried out, the species tested have been susceptible to these compounds, there are cases where tolerance or resistance has been reported. The best studied species is, of course, An. albimanus from Central America and since Georghiou is reviewing his work elsewhere, only a brief mention is made of the present status of resistance of this species.

The WHO Malaria Eradication Division reported in an unpublished review of susceptibility tests the following results in 1970-72.

A few tests with A. pharoensis in Egypt with propoxur and malathion have given almost complete mortality with the lowest concentration.[1] There was a total kill of A. pulcherrimus in Iran with 1.6% malathion and in Iraq with 5.0% malathion.[2] In A. stephensi in the area of Chelow (Minab), which has been sprayed with 17 rounds of malathion, there was a complete kill with exposure to 5.0% malathion for one hour.[3] In Iraq, A. stephensi in Nassiriya locality, which has been under malathion spraying since 1969, a complete kill was obtained with 5.0% malathion for one-hour exposure.[2] Six tests were carried out during September and October 1972 with A. sacharovi in Syria with malathion in Ragga area with 0.5% malathion. Five and seven per cent. mortality was obtained at Factry and Sleuq qeubli respectively after one-hour exposure, whereas 100% mortality was obtained at 3.2 and 5.0%.[4] Tests with A. culicifacies in two localities from the Mahrashtra State resulted in complete kill to 3.2% malathion after one-hour exposure.[5] The results indicate general susceptibility to OP and carbamates. However, a report has been recently received from Jordan (locality Shafa Badran - Ais el Tafieh, Balqa) that larvae of Anopheles sergenti have developed tolerance to difenphos in

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[1] Kamel, O. (1971) Susceptibility tests reported to WHO 1970-1972

[2] Rishikesh, N. (1971) " " " " " "

[3] Eshgy, N. & Manucheri, A. (1971) " " " " " "

[4] Keilany, M. (1972) " " " " " "

[5] Deshpande, L. (1971) " " " " " "

that country. At 0.005 ppm, 54.6% and at 0.025 ppm, 79.5% mortality was observed in a single susceptibility test so far carried out after two years' use of this insecticide. The base line susceptibility level for difenphos is about 0.0008 (LC50) for anopheline mosquitos. The larval mortality was 37% at 0.005 ppm and 80% at 0.025 ppm in a single test.[1]

5. THE IMPLICATIONS OF RESISTANCE

Busvine and Pal (1969) reviewed the implications of resistance in principal malaria vectors. The effect ranges from an inconvenience to an apparently insuperable obstacle. Thus, in temperate regions, such as Europe, where malaria does not reach hyperendemic levels, resistance has not prevented the achievement of eradication. Dieldrin resistance was generally more intense and it was usually DDT that completed the campaigns, dieldrin being abandoned. In warmer climates, where malaria is more fully established, there are even now areas where resistance challenges the outcome of the campaigns (e.g. the area around the Persian Gulf, Mexico and several countries in Central America). Again, dieldrin resistance usually leads to this being abandoned, while a simultaneous DDT resistance (which is less intense) renders the final stages excessively difficult. In many areas, both types of resistance are present in the same anopheline populations, making control particularly difficult in Java, the Persian Gulf area and the Pacific Coast of Central America. Finally, on the African continent, the difficulties of control and eradication are very considerable and could only be attacked with an insecticide as effective as propoxur. The widespread dieldrin resistance in West Africa renders HCH useless there. In Africa, Anopheles gambiae species A and B are apt to be stimulated to leave DDT deposits before they pick up a lethal dose. The situation is aggravated by the development of DDT resistance in certain localities in both these species. The first indications of resistance of An. albimanus to malathion and propoxur are further complicating the picture. The substitute insecticides for DDT, such as malathion, propoxur or fenitrothion, are much more expensive. Malathion is five times the price of DDT and propoxur 20 times, making spraying operations with them three and eight times more expensive, respectively. It was, in fact, the cheapness of DDT that made malaria eradication economically feasible for developing countries. Larvicidal treatment has a place in the malaria eradication programme in places where anopheline larvae breed in circumscribed areas. Thus, A. sergenti and A. stephensi are being attacked in Jordan and Saudi Arabia with temephos applied at 0.05 lb/acre (50 g/ha). However, there are some indications of tolerance developing to this insecticide. Difenphos is also being used in El Salvador. Aerial ULV applications have given good results in Panama (fenthion) and in Haiti (malathion).

Some of the following conclusions may be drawn, which have also been stated by Hamon & Garrett-Jones (1963), Busvine & Pal (1969), and Busvine (1969).

(i) Where resistance has arisen in a given vector, it seldom extends throughout the entire geographical range of the species.

(ii) Dieldrin resistance, when it occurs, appears rapidly and is intense.

(iii) DDT resistance appears more slowly and may or may not prevent malaria control.

(iv) In the case of double resistance, where DDT is not effective, substitute insecticides must be sought among the OP and carbamate compounds.

(v) OP and carbamates are considerably more expensive.

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[1] Abdul Aziz Iswed (1972) Susceptibility tests reported to WHO 1970-1972.

(vi) Resistance to these compounds has already occurred in an anopheline species in some areas and generally conforms to the mosaic distribution. This is due to the use of these insecticides for the control of insect pests of agriculture.

(vii) Although the levels of resistance observed with these compounds are not of a very high order as compared with organochlorine compounds, they are often sufficient to preclude their effective use in the field.

(viii) Very little is understood about the liability of individual new compounds to develop resistance and increasing emphasis is being placed on studies on cross-resistance and speed of development of resistance to these insecticides.

(ix) An integrated control whereby all available methods of control can be deployed, such as residual spraying, larviciding, ULV, biological and genetic control if available should be encouraged.

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TABLE 1. PRINCIPAL SPECIES OF ANOPHELES KNOWN TO TRANSMIT MALARIA, AND REPORTED RESISTANCE TO INSECTICIDES[a]

Species	Resistance[b]	Species	Resistance[b]	Species	Resistance[b]
aconitus	D, Dl	hancocki	-	nili	Dl
albimanus	D, Dl, M	hispaniola	-	nuneztovari	D
albitarsis	D, Dl	jeyporiensis		pattoni	-
annularis	D, Dl	(including candidiensis)	-	pharoensis	D, Dl
aquasalis	D, Dl	karwari	-	philippinensis	Dl
argyritarsis	-	kochi	-	pseudopunctipennis	Dl
aztecus	-	koliensis	-	punctimacula	-
baezai	-	labranchiae		punctulatus	-
balabacensis	-	(including atroparvus)	Dl	quadrimaculatus	D, Dl
bancroftii	-	letifer	-	sacharovi	D, Dl
barbirostris	Dl	leucosphyrus	-	sergentii	Dl
bellator	Dl	maculatus	-	sinensis	D
claviger	-	maculipennis		stephensi	
cruzii	-	(including messeae)	Dl	(including mysorensis)	D, Dl
culicifacies	D, Dl	mangyanus	-	strodei	Dl
darlingi	-	melas	-	subpictus	D, Dl
farauti no. 1	Dl	merus	-	sundaicus	D, Dl
fluviatilis	D, Dl	minimus		superpictus	-
freeborni	-	(including flavirostris)	Dl	tesselatus	-
funestus	Dl	moucheti	-	umbrosus	-
gambiae complex		multicolor	-	varuna	-
(species A, B,)	D, Dl	nigerrimus	-		

[a] See also WHO Expert Committee on Insecticides (1970) Wld Hlth Org. techn. Rep. Ser., No. 443, and Brown, A. W. A. & Pal, R. (1971) Insect resistance in arthropods, Geneva, World Health Organization, 2nd ed.

[b] Resistance: D = DDT resistance; Dl = dieldrin/gamma HCH resistance; M = malathion resistance; - = no resistance reported.

From WHO publication, Vector Control in International Health, 1972.

TABLE 2. FIRST RESULTS OF LT_{50} AND LT_{95} DETERMINATIONS WITH ANOPHELINE MOSQUITOS USING OP AND CARBAMATE IMPREGNATED PAPERS

Species	Country	Area & location	Insecticide & concentration	LT_{50}	C.1	LT_{95}	B	HET	HD	Reference
<u>An. gambiae (A)</u>	Upper Volta	B. Dioulasso, Pala	Propoxur 0.025%	73.3	62.8 82.9	141.9	5.73	4.3	98% at 190M	Hamon & Sales
<u>An. gambiae (A)</u>	" "	" " "	Fenthion 0.25%	106.3	101.3 111.4	192.6	6.38	1.0	100% at 300M	"
<u>An. gambiae (A)</u>	" "	" " "	Malathion 0.8%	91.7	88.2 95.1	153.8	7.32	1.0	99% at 180M	"
<u>An. gambiae (A)</u>	" "	" " "	Fenitrothion 0.4%	44.6	41.8 47.3	101.6	4.60	1.0	99% at 120M	Sales
<u>An. sinensis (A)</u>	Korea	Seoul, Bompo Dong	Fenitrothion 1.0%	14.8	10.9 18.5	80.3	2.24	1.0	100% at 160M	WHO, JEVRU
<u>An. sinensis (A)</u>	"	" " "	Malathion 5.0%	5.9	4.7 6.9	15.7	3.86	1.0	100% at 20M	" "
<u>An. sinensis (A)</u>	"	Cholla Pukdo Sintaein	Malathion 5.0%	8.1	6.8 9.5	21.4	3.92	1.0	100% at 30M	" "
<u>An. sinensis (A)</u>	"	Pusan Sasang	Malathion 5.0%	15.8	-	41.7	3.90	3.2	100% at 120M	" "
<u>An. sinensis (A)</u>	"	" "	Fenitrothion 1.0%	51.9	43.4 60.3	130.6	4.11	1.0	100% at 240M	" "

Explanation of C.1, B, HET, HD.

C.1 = 95% fiducial limits - for LT50, if this space is blank and LT50 is shown, the limits cannot be computed due to large heterogeneity.
B = Slope of the profit regression line.
HET = Heterogeneity-factor.
HD = % response at the highest exposure used.

TABLE 3. CONCENTRATION-TIME VALUES FOR VARIOUS MOSQUITOS EXPOSED TO DIFFERENT INSECTICIDES. REFERENCES: (1) THIS PAPER; (2) SALES & MOUCHET; (3) ARU; (4) JEVRU; (5) SCHOOF; (6) HAMON & SALES

Insecticide	Species	Locality	Ref.	mean CxT; with constant	
				conc.	time
Fenitrothion	Culex p. fatigans	London	1	16.8	17.2
	" "	U. Volta	2	26.0	39.0
	" "	Thailand	3	19.4	16.2
	" "	Taiwan	4	19.0	36.0
	Aedes aegypti	U. Volta	2	12.0	12.0
	" "	U.S.A.	5	12.0	11.8
Fenthion	Culex p. fatigans	London	1	18.8	19.0
	C. tritaeniorhynchus	Korea	4	29.0	24.0
	Aedes aegypti	U.S.A.	5	16.2	15.8
Malathion	Culex p. fatigans	London	1	48.0	52.0
	C. tritaeniorhynchus	Taiwan	4	47.0	66.0
	" "	Korea	4	29.0	24.0
	C. annulus	Taiwan	4	93.0	28.2
	Aedes aegypti	U. Volta	2,6	61.0	69.0
	" "	U.S.A.	5	36.0	35.0
Propoxur	Culex p. fatigans	London	1	3.6	3.2
	" "	U. Volta	2	3.2	4.1
	C.t. summorosus	Taiwan	4	10.8	10.0
	Aedes aegypti	U. Volta	2	7.2	5.5
	" "	U.S.A.	5	6.3	5.5

After Rongsriyam & Busvine (1973)

TABLE 4. REVERSAL OF SUSCEPTIBILITY STATUS IN A. CULICIFACIES TO DDT AFTER WITHDRAWAL OF SPRAY OR CHANGE OF INSECTICIDE

State	Unit	Sub-unit	Village	Period of earlier test	Per cent. mortality with 4 per cent. DDT	Period of recent test	Per cent. mortality with 4 per cent. DDT	Phase of N.M.E.P. operation
1	2	3	4	5	6	7	8	9
Maha-rashtra	Achalpur	Achalpur	Saoli	Feb. 1963	0.0	Oct. 1964	62.2	Last DDT spray on 26.9. 62. Under consolidation phase since 1963.
	"	"	Dhulghat	Feb. 1963	15.0	Nov. 1963	55.0	Last DDT spray in 1962. Under consolidation since 1963.
	"	Chandur	Tewsa	Feb. 1963	42.5	Nov. 1963	66.6	Last DDT spray in 1962. Under consolidation since 1963.
	"	Daryapur	Manlapur	Feb. 1963	48.0	Oct. 1964	72.5	Last DDT spray in 1962. Under consolidation since 1963.
	Akola	Akola	Ugwa	Sept. 1963	47.0	Jan. 1965	85.0	In maintenance phase since 1964.
	Akola	Washim	Rithad	Sept. 1963	38.0	Jan. 1965	88.0	In maintenance phase since 1964.
	Auran-gabad	Kannad	Hatnoor	Jan. 1963	41.1	Aug. 1963	52.7	DDT sprayed since 1957, under consolidation phase since 1963.
	"	"	Faradpur	Jan. 1962	10.6	July 1964	52.2	DDT sprayed since 1957, under consolidation phase since 1963.
	Bhandara	Tumsar	Madgi	Sept. 1963	37.5	Sept. 1964	50.0*	DDT sprayed since 1956, under consolidation since 1963.

*Jan. '66 - 67.2

TABLE 4. (continued)

State	Unit	Sub-unit	Village	Period of earlier test	Per cent. mortality with 4 per cent. DDT	Period of recent test	Per cent. mortality with 4 per cent. DDT	Phase of N.M.E.P. operation
1	2	3	4	5	6	7	8	9
	Buldana	Chikhali	Kolwad	Jan. 1963	0.0	Nov. 1964	70.8	Last DDT spray on 28.9.62. Under consolidation phase since 1963.
	"	"	Amkhed	Oct. 1963	6.0	Nov. 1964	72.5	Focal spray on 1.9.63.
	Buldana	Malkapur	Rajura	Jan. 1963	3.3**	Nov. 1964	80.0	Last DDT spray on 15.9.62. Under consolidation phase since 1963.
	"	Mekhar	Sarangpur	Oct. 1963	21.6	Nov. 1964	83.0	Last DDT spray in 1962. Under consolidation phase since 1963.
	Dhulia	Shahada	Lonkhede	Dec. 1960	53.3	Dec. 1963	69.5	DDT sprayed from 1950; two rounds of BHC in 1963.
	Kolaba	Mahad	Ladvali	Jan. 1963	44.4	Nov. 1964	68.4	Focal spray in 1963. Under consolidation phase since 1963.

**Oct. '63 - 27.5

TABLE 4. (continued)

State	Unit	Sub-unit	Village	Period of earlier test	Per cent. mortality with 4 per cent. DDT	Period of recent test	Per cent. mortality with 4 per cent. DDT	Phase of N.M.E.P. operation
1	2	3	4	5	6	7	8	9
	Jalgaon	Pachora	Wakod	Jan. 1962	11.2	July 1963	71.9	DDT spray from 1951; BHC sprayed from 1961.
	"	Jalgaon	Sakegaon	Jan. 1962	2.2	July 1963	62.7	DDT sprayed from 1951 to 1961; BHC sprayed from 1961.
	Nagpur	Arvi	Gunjikheda	Nov. 1962	40.0	Sept. 1964	75.5	Under consolidation phase since 1962.
	"	Wardha	Kawadghat	Oct. 1962	50.0	Sept. 1964	81.6	Under consolidation phase since 1962.
	Nasik	Malegaon	Kasari	Jan. 1963	15.0	Mar. 1964	45.0	DDT sprayed from 1953 to 1962; BHC sprayed from 1963.
	"	"	Dabhadi	Jan. 1963	0.0	Mar. 1964	87.9	DDT sprayed from 1953 to 1962; BHC sprayed from 1963.
	"	Nasik	Gangapur	Jan. 1963	14.2	Nov. 1964	48.0	Last DDT spray in 1963. Under consolidation phase since 1964.

TABLE 4. (continued)

State	Unit	Sub-unit	Village	Period of earlier test	Per cent. mortality with 4 per cent. DDT	Period of recent test	Per cent. mortality with 4 per cent. DDT	Phase of N.M E.P. operation
1	2	3	4	5	6	7	8	9
	Prabhani	Hingoli	Hingoli	Feb. 1962	40.0	Oct. 1964	86.5	DDT sprayed since 1958; spray withdrawal in 1962; under Maintenance phase since Nov. 1964.
	"	"	Aundha	Sept. 1962	35.5	Oct. 1964	88.0	DDT sprayed since 1958; spray withdrawal in 1962; under Maintenance phase since Nov. 1964.
	"	Jintur	Sos	Sept. 1962	22.0	Oct. 1964	84.2	DDT sprayed since 1958, spray withdrawal in 1962.
	"	Parbhani	Karadgaon	Feb. 1962	34.8	Oct. 1964	93.3	DDT sprayed since 1958, spray withdrawal in 1962.
	"	Sailu	Khupsa	Sept. 1962	29.4	Oct. 1964	80.0	DDT sprayed since 1958, spray withdrawal in 1962.
	Yeotmal	Darwa	Chincholi	Mar. 1962	40.0	Aug. 1964	57.0	Under consolidation phase since 1962.

All tests carried out by Maharashtra State Malaria Organisation

After Raghvan et al. (1967)

TABLE 5. RESULTS OF SUSCEPTIBILITY TESTS WITH ANOPHELINE MOSQUITOS USING OP AND CARBAMATE SOLUTIONS AND IMPREGNATED PAPERS*

RC No.	Insect species	Country	Area & locality	Insecticide	IRS	Investigator
M0025	A. albimanus Adults	El Salvador	La Union	Propoxur	S	Lima
M0028	A. albimanus Adults	El Salvador	San Miguel	Propoxur	S	Lima
A0918	A. albimanus Adults	Guatemala	San Marcos	Malathion	INT	Valladares
A0562	A. albimanus Adults	Nicaragua	Chinandega	Malathion	INT	AMRO
A0926	A. albimanus Adults	Nicaragua	Chinendega	Malathion	INT	Roblets
M0045	A. atroparvus Adults	Romania	Bucharest Bogata	Malathion	S	Duport
M0292	A. culicifacies Adults	Ceylon	Amparai Passardech.	Malathion	S	Badawi
M0286	A. culicifacies Adults	Ceylon	Matale Dambulla	Malathion	S	Badawi
04636	A. funestus Adults	Kenya	Nyanza Tiengre	Fenitrothion	S	WHO ACRU 2
04634	A. gambiae Adults	Kenya	Nyanza Chiga	Fenitrothion	S	WHO ACRU 2
04635	A. gambiae Adults	Kenya	Nyanza Chiga	Fenitrothion	S	WHO ACRU 2
A0944	A. maculipennis Adults	Romania	Moldavia	Fenthion	S	Teodorescu
A0943	A. maculipennis Adults	Romania	Moldavia	Malathion	S	Teodorescu
M0110	A. m. maculipennis Adults	Romania	Arges Piatra	Fenthion	S	Duport
M0108	A. m. maculipennis Adults	Romania	Arges Segarea	Fenthion	S	Duport
M0171	A. m. messeae Adults	Romania	Arges Piatra	Fenthion	S	Duport
M0173	A. m. messeae Adults	Romania	Arges Segarcea	Fenthion	S	Duport

* (Stored in WHO computer program up to the end of 1972).

TABLE 5. (continued)

RC No.	Insect species	Country	Area & locality	Insecticide	IRS	Investigator
M0154	A. m. messeae Adults	Romania	Bucharest Bogata	Malathion	S	Duport
M0144	A. m. messeae Adults	Romania	Bucharest Roseti	Malathion	S	Duport
M0166	A. m. messeae Adults	Romania	Bucharest Stefanesti	Fenthion	INT	Duport
M0167	A. m. messeae Adults	Romania	Bucharest Stefanesti	Malathion	S	Duport
M0117	A. m. messeae Adults	Romania	Dobrogea Colina	Malathion	INT	Sandulescu
M0122	A. m. messeae Adults	Romania	Dobrogea Episala	Fenthion	S	Sandulescu
M0320	A. pharoensis Adults	Egypt	Kafrlshiekh	Fenthion	S	Kamel
M0317	A. pharoensis Adults	Egypt	Qalubia Marg	Malathion	S	Kamel
04847	A. sergenti Larvae	Jordan	Balqa Shafa Badran	Abate	S	Mikdadi
04846	A. sergenti Larvae	Jordan	Balqa Shafa Badran	Abate	S	Mikdadi
05393	A. sinensis Larvae	Korea	Cholla Pukdo Sintaein	Fenitrothion	S	WHO JEVRU
05054	A. sinensis Larvae	Korea	Cholla Pukdo Sintaein	Malathion	S	WHO JEVRU
05288	A. sinensis Larvae	Korea	Cholla Pukdo Wei Do	Fenitrothion	INT	WHO JEVRU
05287	A. sinensis Larvae	Korea	Cholla Pukdo Wei Do	Malathion	S	WHO JEVRU
M0327	A. sinensis Larvae	Ryukyu Islands	Okinawa Ishikawa	Abate	S	Intermill
M0328	A. sinensis Larvae	Ryukyu Islands	Okinawa Ishikawa	Diazinon	S	Intermill
M0325	A. sinensis Larvae	Ryukyu Islands	Okinawa Ishikawa	Fenthion	INT	Intermill
M0223	A. sinensis Larvae	Ryukyu Islands	Okinawa Ishikada	Malathion	R	Pennington

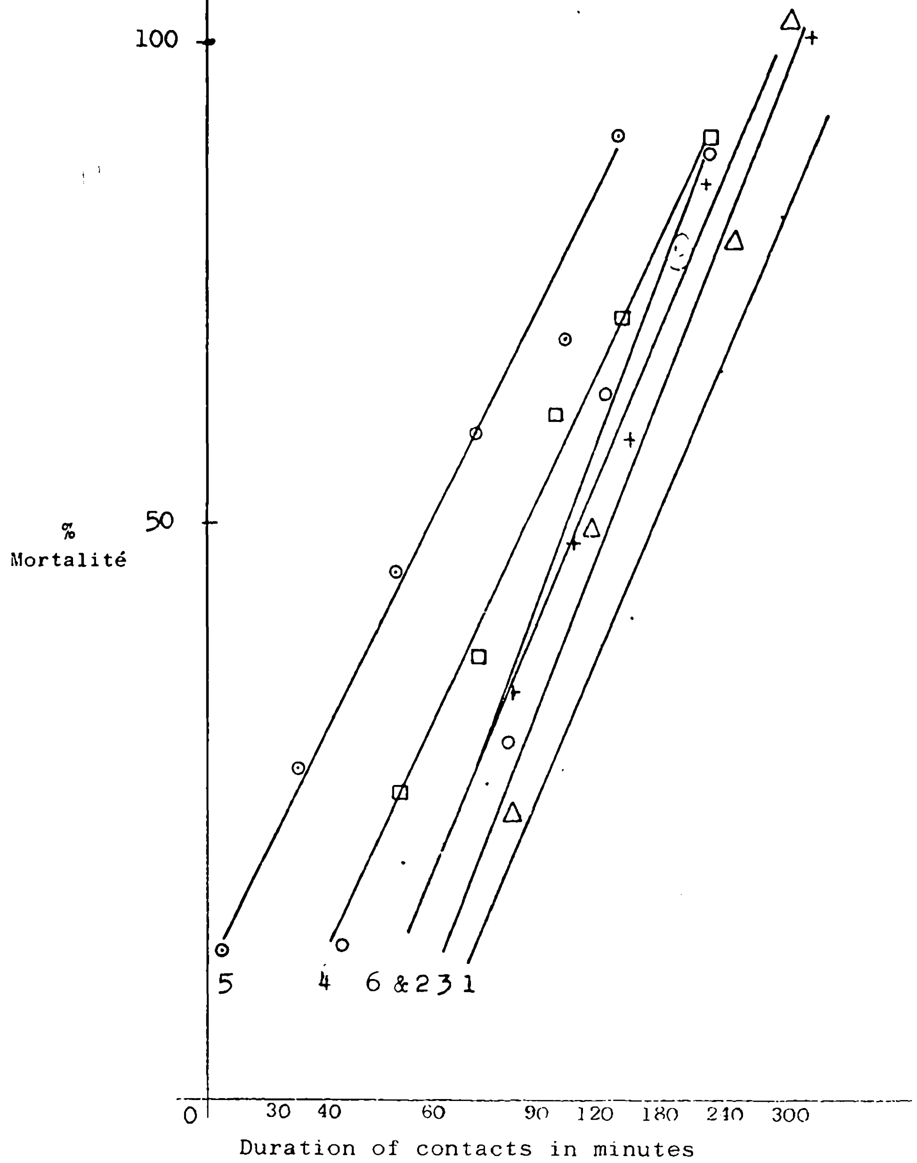
TABLE 5. (continued)

RC No.	Insect species	Country	Area & locality	Insecticide	IRS	Investigator
M0221	A. sinensis Larvae	Ryukyu Islands	Okinawa Ishikawa	Malathion	INT	Pennington
M0222	A. sinensis Larvae	Ryukyu Islands	Okinawa Ishikawa	Malathion	R	Pennington
M0326	A. sinensis Larvae	Ryukyu Islands	Okinawa Ishikawa	Malathion	S	Intermill
04890	A. sinensis Larvae	Ryukyu Islands	Okinawa Ishikawa	Malathion	S	Intermill
M0225	A. sinensis Larvae	Ryukyu Islands	Okinawa White Beach	Malathion	INT	Pennington
05392	A. sinensis Adults	Korea	Cholla Pukdo Kwang Hwal	Malathion		WHO JEVRU
05030	A. sinensis Adults	Korea	Cholla Pukdo Sintaein	Propoxur	S	WHO JEVRU
04868	A. sinensis Adults	Korea	Cholla Pukdo Sintaein	Fenitrothion	S	WHO JEVRU
05035	A. sinensis Adults	Korea	Cholla Pukdo Sintaein	Fenitrothion	S	WHO JEVRU
04867	A. sinensis Adults	Korea	Cholla Pukdo Sintaein	Fenthion	INT	WHO JEVRU
05036	A. sinensis Adults	Korea	Cholla Pukdo Sintaein	Fenthion	INT	WHO JEVRU
04869	A. sinensis Adults	Korea	Cholla Pukdo Sintaein	Malathion	S	WHO JEVRU
04870	A. sinensis Adults	Korea	Paju Chori Myon	Fenitrothion	S	WHO JEVRU
05038	A. sinensis Adults	Korea	Paju Chori Myon	Fenthion	INT	WHO JEVRU
04871	A. sinensis Adults	Korea	Paju Chori Myon	Malathion	S	WHO JEVRU
A0487	A. sinensis Adults	Ryukyu Islands	Okinawa Ishikawa	Malathion	S	US ARMY PREV MED DIV
A0486	A. sinensis Adults	Ryukyu Islands	Okinawa Koza	Fenthion	S	US ARMY PREV MED DIV

TABLE 5. (continued)

RC No.	Insect species	Country	Area & locality	Insecticide	IRS	Investigator
MO231	A. stephensi Adults	Iran	Abadan Haffar	Malathion	S	MALARIA INV-EST. CENTRE
MO234	A. stephensi Adults	Iran	Khoramshaht Arayz	Malathion	S	MALARIA INV-EST. CENTRE
MO228	A. stephensi Adults	Iran	Khuzistan Khoramshahr	Fenthion	S	MALARIA INV-EST. CENTRE

FIG. 1 REGRESSION LINES



Line

1 *Aedes aegypti* (0.4% malathion)

2 *An. gambiae* (0.8% malathion)

3 " (0.25% fenthion)

4 " (0.025% propoxur)

5 " (0.4% fenitrothion)

6 *Culex pipiens fatigans* (0.4% fenitrothion)

After Hamon & Sales (1970)