Bull. Org. mond. Santé
Bull. Wld Hlth Org. } 1973, 49, 475-483

The practical implications of resistance of malaria vectors to insecticides*

G. DAVIDSON[1] & A. R. ZAHAR[2]

Insecticide resistance is an inherent characteristic dependent on relatively simple genetic mechanisms. This seems to be especially true of dieldrin resistance in anopheline mosquitos, though less obvious in DDT resistance among these species; little is known as yet about the inheritance of organophosphate and carbamate resistance as it occurs in Anopheles albimanus. *The speed of selection of resistance depends on the original frequency of the gene or genes involved, the nature of the resistance imparted, and the selection pressure of the insecticide. This in turn depends on the inherent toxicity of the chemical, the efficiency with which it is applied, the proportion of the mosquito population coming under its influence, and the behaviour of the mosquito. In the past, too much reliance has been placed on the determination of the* LD_{50} *in assessing the presence or absence of insecticide resistance. Quite high incidences of resistant individuals can result in such small changes in the* LD_{50} *that resistance may be overlooked. The use of single discriminating dosages is advocated, based on concentrations of insecticides that normally kill all susceptible individuals. The authors discuss such dosages in respect of dieldrin and DDT, and put forward newly-established tentative discriminating dosages for organophosphorus and carbamate insecticides, which await field confirmation.*

From a practical standpoint, an insecticide should not be abandoned or replaced by another as soon as resistance is confirmed. This may not be necessary where the degree of resistance is not high and the vector is not highly efficient. Certain procedures are proposed in order to assess the epidemiological and entomological implications of resistance before the insecticide concerned is abandoned.

Testing with the WHO standard susceptibility test kits[a] has been useful in detecting insecticide resistance and in defining its geographic extent, as Brown & Pal (1) have shown. Although the results of numerous susceptibility tests on adult mosquitos are available, few parallel field observations have been made to determine the practical implications of resistance to insecticides and to provide the information needed for deciding whether a particular insecticide should continue in use or be replaced by an alternative. In some cases, such decisions have been based on the results of susceptibility tests together with the general epidemiological situation. This is justified in the case of dieldrin resistance, which is usually well pronounced, the gene expression being mainly incompletely dominant; once it appears, it grows rapidly from a very low gene frequency (2). Consequently, high vector densities associated with intense malaria transmission can soon be found in sprayed houses. In contrast, when DDT resistance initially emerges, its level may not be easily distinguished from that of the commonly known tolerance. Furthermore, it develops slowly and selection may take a long time before it is completed,

* Presented in abridged form at the International Congress on Tropical Medicine and Malaria, Athens, Greece, 14–21 October 1973.

[1] Reader in Entomology as applied to Malaria, WHO International Reference Centre for the Maintenance and Distribution of Standardized Strains of *Anopheles*, Ross Institute of Tropical Hygiene, London, United Kingdom.

[2] Entomologist, Division of Malaria and other Parasitic Diseases, World Health Organization, Geneva, Switzerland.

[a] Detailed instructions for performing the tests for adult mosquitos, and lists of the different concentrations of insecticides that are available, will be found in Annexes 1A and 1B of: WHO Expert Committee on Insecticides. Seventeenth report: Insecticide resistance and vector control, Geneva, 1970 (WHO Technical Report Series, No. 443). Reprints of the annexes may be obtained on request to: Vector Biology and Control, World Health Organization, 1211 Geneva 27, Switzerland.

though the process may be accelerated by the use of DDT in agriculture.

In many countries, house-spraying with DDT is the main attack measure against malaria vectors, even though some degree of DDT resistance has appeared. Furthermore, the recent appearance of resistance to organophosphorus [a] and carbamate insecticides in *A. albimanus* in Central America (3–5) calls for strengthened entomological and parasitological field observations together with periodical susceptibility testing in order to translate the different levels of mortality obtained by these tests into field reality. Such entomological data, supported by the parasitological findings, will permit a timely decision as to the continued use of an insecticide, its replacement by another, or the additional use of supplementary measures.

This paper has been prepared with a view to providing a better understanding of the role of susceptibility tests and the interpretation of the results and outlining the procedures for determining the practical implications of insecticide resistance.

FACTORS INFLUENCING THE SPEED OF SELECTION FAVOURING INSECTICIDE RESISTANCE

In order to follow changes in the susceptibility level of adult vector populations to insecticides, the different factors influencing the degree and speed of selection favouring resistance should be borne in mind. These factors have been reviewed by Davidson [b] and may be summarized under three headings.

The original frequency of the resistance gene

No records are available to show the frequency with which the gene of DDT resistance occurs 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, whether in public health or agriculture, it is concluded that the gene is quite rare. On the other hand, the frequency of dieldrin resistance in unsprayed areas has been determined in a number of species, including *A. gambiae s.l.* and *A. pharoensis*, and has been shown to be fairly common in many populations.

The nature of the resistance gene

The survival of heterozygous and homozygous resistant individuals in the presence of the selecting agent—the insecticide—depends on the degree of resistance conferred by the resistance gene and its degree of dominance. In the case of dieldrin this gene gives a high degree of resistance and is always either dominant or incompletely dominant. Thus survival with dieldrin resistance is greater in the presence of this insecticide than with DDT resistance, in which the degree of resistance may be quite low and the gene expression incompletely dominant or recessive. Moreover, ancillary genes forming part of the genetic background of DDT resistance may modify the expression of the oligogene and influence the speed of selection (6, 15).

The exerted pressure of the selecting agent

The activity of the selecting agent will depend on a number of factors, among them its inherent toxicity, the efficiency with which it is applied, the proportion of the mosquito population coming under its influence, and the behaviour of the mosquito.

INTERPRETATION OF RESULTS OF SUSCEPTIBILITY TESTS

Interpretation based on the value of LC_{50}

Since some workers still use the LC_{50} for assessing changes in the susceptibility levels of mosquitos, it is relevant to review the validity of an interpretation based on the regression line from which the value of LC_{50} is usually estimated. In principle, the straight log-dosage-probit (ld-p) mortality line relationship can only apply when the population tested is homogeneous. Davidson [c] pointed out that homogeneity means not only a uniform reaction to the poison (within a normal distribution range) but also uniformity in age and general physiological state and in environmental conditions at the time of testing. Apart from homogeneity in the reaction to poison, such conditions can seldom be met in field tests, or even in the laboratory, where variations due to breeding conditions exist. Thus, an insect population that is homogeneously susceptible or resistant to an insecticide may not show a straight-line ld-p mortality relationship, and the straight line that best fits the recorded data is drawn, weight being given to data

---

[a] *A. albimanus* was reported to be resistant to malathion in Guatemala and Nicaragua (WHO, unpublished data, 1966).

[b] DAVIDSON, G. Genetic consideration in the choice of insecticide. Geneva, 1964 (WHO mimeographed document WHO/MAL/435).

[c] DAVIDSON, G. The interpretation of mosquito susceptibility tests. Brazzaville, 1962 (WHO mimeographed document AFRO/MAL/9/4).

based on the largest number of observations and nearest to a 50% mortality. Populations heterogeneous in their reaction to the poison, i.e., containing different genotypes, will also depart from the basic straight-line relationship, posing the problem of how to distinguish between them.

Where resistant and susceptible individuals occur in the population, the ld-p mortality line may show a flattening of the normal slope of the line at higher dosages, but whether this is obvious or not will depend on the proportion of resistant phenotypes in the population.

Table 1 shows the calculated mortalities in various mixed populations of *A. gambiae* (showing resistance to dieldrin) and *A. sundaicus* (showing resistance to DDT) when exposed to the normal range of concentrations of insecticides (except 4% dieldrin) issued with the WHO adult-susceptibility test kit. The mortalities in susceptible, resistant, and hybrid strains of these two species were first recorded from observations made on laboratory colonies. Using these known mortalities, expected mortalities were calculated for various frequencies of the resistance factor, which in the case of *A. gambiae* was established as a single, incompletely dominant one (7) and in the case of *A. sundaicus* a single, recessive one (8). These calculations assume panmyxia and identical survival values of the genotypes, and are derived from the Hardy–Weinberg expression:

$$a^2 + 2ab + b^2 = 1$$

where a is the resistance factor proportion and b the susceptibility factor proportion. For example, where the resistance factor is present to the extent of 0.5, the proportions of the 3 genotypes are: homozygous resistant, 25%; heterozygotes, 50%, homozygous susceptible, 25%. Mortalities of a population of *A. gambiae* mixed in these proportions at different concentrations of dieldrin are then:

Dieldrin concentration (%)	*Mortality* (%)
0.05	25% of 25= 6.25
0.1	69% of 25=17.25
0.2	94% of 25=23.50
0.4	100% of 25=25.00
0.8	100% of 25 +0.1% of 50=25.05
1.6	100% of 25 +13% of 50=31.50

If the figures for dieldrin mortalities given in Table 1 are plotted on log-probit graph paper, it can be seen that the presence of up to 6% of heterozygotes in an *A. gambiae* population will not alter the regression line appreciably if only concentrations between 0.05% and 0.2% dieldrin are used. In fact, the variation in LC_{50} is small, from 0.075% to 0.079% dieldrin. If higher concentrations are used, mortalities will be so near 100% that they are difficult to establish accurately and their importance is minimized, since the lower concentration mortalities lie almost on a straight line. In any case, the few resistant individuals may well be included among those tested at the lower concentrations.

With *A. sundaicus* mixed populations exposed to varying concentrations of DDT, the presence of 1% of homozygous resistant and 18% of heterozygotes only changes the LC_{50} from 0.42 to 0.5% DDT. In fact, no marked departure from a straight-line relationship between concentration and mortality is evident even when the population consists of 25% susceptible, 50% heterozygotes and 25% homozygous resistant; if the nearest straight line is drawn to fit the mortalities of such a population, an LC_{50} of 1.3% DDT would be extrapolated—only some 3 × the normal LC_{50} (Fig. 1).

Thus, sole reliance on the log-probit regression line for the interpretation of susceptibility tests may lead to a failure to recognize resistance, particularly in its early stages of appearance, although this is surely the aim of susceptibility testing. A more certain way is to determine the concentration that normally kills all individuals of a susceptible strain of the species involved.

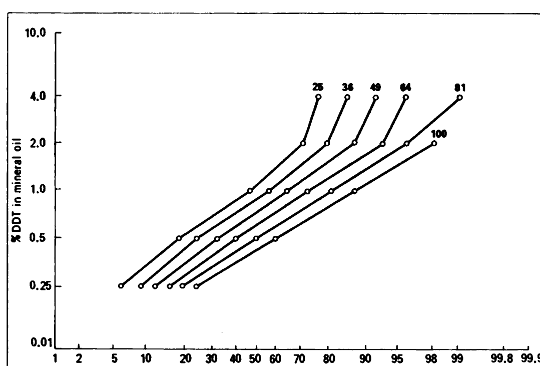

Fig. 1. Mixed *Anopheles sundaicus* populations: log-probit regression lines for a susceptible strain and varying proportions of susceptible, hybrid, and resistant individuals. The numbers on the graph show the percentage of susceptibles.

Table 1. Calculated mortalities for various mixed populations of *Anopheles gambiae* and *A. sundaicus* when exposed to the usual dosages of dieldrin and DDT issued with the WHO adult-susceptibility kit

Gene frequency (F) [a]		% of genotypes [b]			% mortalities of *A. gambiae*, Lagos and Ambursa strains [c]						% mortalities of *A. sundaicus*, Malaya and Java strains [d]				
					Concentration of dieldrin (%)						Concentration of DDT (%)				
F/R	F/S	RR	RS + SR	SS	0.05	0.1	0.2	0.4	0.8	1.6	0.25	0.5	1.0	2.0	4.0
0	1.0	0	0	100	25	69	94	100	100	100	24	59	88	98	100
		0	100	0	0	0	0	0	0.1	13	0.2	8	53	94	100
1.0	0	100	0	0	0	0	0	0	0	0	0	0	0	0	8
.003	.997	1/100 000	1	99	25	68	93	99	99	99.1	24	58.5	88	98	100
.01	.99	1/10 000	2	98	24	68	92	98	98	98.3	23.5	58	88	98	100
.03	.97	1/1 000	6	94	23	65	88	94	94	94.8	22.5	56	88	98	100
.1	.9	1	18	81	20	56	76	81	81	83	19.5	49	81	96	99
.2	.8	4	32	64	16	44	60	64	64	68	15	40	73	93	96
.3	.7	9	42	49	12	34	46	49	49	54	12	32	65	87.5	92
.4	.6	16	48	36	9	25	34	36	36	42	9	25	57	80	85
.5	.5	25	50	25	6	17	23	25	25	31.5	6	19	48.5	71.5	77

[a] R = resistance factor; S = susceptibility factor.
[b] RR = resistant homozygote; RS = hybrid, resistant male × susceptible female; SR = hybrid, susceptible male × resistant female; SS = susceptible homozygote.
[c] Fed females aged 1–6 days.
[d] Unfed females + males aged 1–4 days.

Similar views on the ld-p mortality curve were put forward by Tsukamoto (9) in genetic studies of insecticide resistance in houseflies. His conclusion was that the resistance level of heterogenous populations should be expressed by a whole ld-p curve, but not by the straight regression line or by the LC_{50} value alone, which are based on and only effective for the homogenous normal distribution. Accordingly, the use of serial dosages and the drawing of ld-p mortality lines should be confined to areas where insecticides have never been used, to assist in establishing the discriminating dosage, i.e., the dosage that will kill all susceptible individuals. With the exception of organophosphorus and carbamate insecticides, sufficient data are available on the discriminating dosages for almost all malaria vectors.

Interpretation based on the value of LC_{100}

The use of discriminating dosages requires the establishment of criteria to guide the interpretation of results of susceptibility tests. In its sixth, seventh, and eighth periodical summaries of insecticide resistance in anopheline mosquitos, and in a later memorandum, WHO (unpublished data, 1960-1966) developed the following criteria for classifying test results: susceptible, <10% survival at the normal LC_{100}, i.e., >90% mortality; intermediate, 10-50% survival at the normal LC_{100}, i.e., 50-90% mortality; resistant, >50% survival at the normal LC_{100}, i.e., <50% mortality.

Among these criteria, the intermediate category clearly comprises a wide range of mortalities that indicate the presence of resistant individuals. This can be very misleading. For example, populations from two areas, one showing 90% and the other 50% mortality on 4% DDT for an hour, would be grouped together in the intermediate category, and the classification of a particular population would remain the same even though the mortality in periodic checks fell from 90% to 50%. Similarly, a population in an area showing, for example, 45–49% mortality would be considered as resistant and would remain in that category even if the mortality level fell to 10% or less, indicating a marked increase in resistance. On the other hand the susceptible category, for populations showing a low survival of less than 10% at the discriminating dosage, would not permit prompt action for detection of incipient resistance.

Examples may be cited where emergence of resistance was revealed by the appearance of a low but consistent rate of survival at the discriminating dosage for susceptibles. In Panch Mahals, Gujarat State, India, *Anopheles culicifacies* was reported by Rahman et al. (10) to have shown tolerance to DDT. According to Hamon & Garrett-Jones (11), who reviewed data of Luen & Shalaby (12) and Shalaby (unpublished report to WHO, 1961), a 3% survival rate was recorded on exposure to 4% DDT for one hour in September 1959 in one village. By June 1960 this proportion had increased to 35%, signifying the presence of DDT resistance that culminated in 82% survival in March 1961.

Peffly (13) reported tests by Davidson in 1955 and his own tests from 1956 to 1958 on *A. stephensi* in the Eastern Province of Saudi Arabia. In small samples from an unselected population in an unsprayed locality, mortality was 97–100% following one-hour exposure to 4% DDT, whereas in samples from localities subjected to DDT spraying since 1948, mortality was 23–89%. DDT resistance was correlated with an increase in malaria transmission, so that DDT had to be replaced by dieldrin. Citing Davidson's 1955 results, Peffly (13) confirmed that *A. stephensi* was at that time susceptible to dieldrin, although some of his tests showed a 3–4% survival rate on 0.4% dieldrin for one hour. In 1961, however, *A. stephensi* suddenly appeared in large numbers in areas sprayed with dieldrin and tests made by Peffly and Affifi—cited by Brown & Pal (1)—gave only 10% mortality on 4% dieldrin for one hour.

As reported by Zahar et al.,[a] tests on *A. pharoensis* in Egypt in August 1959 showed an average mortality of 81–91% after one hour's exposure to 4% DDT in unsprayed areas. By 1961, the mortality had dropped to 7–66% in sprayed and unsprayed areas. This fall was correlated with high selection pressure from pesticides used in agriculture.

It is evident that there is no advantage in allotting populations showing an abnormal response to an insecticide to either the intermediate or the resistant category, since both denote the presence of physiological resistance. It is much simpler and more practical to use a system, based on adequate testing, that would indicate that the population is susceptible, that it is resistant, or that verification is required.

To attempt to divide the resistant category into low, moderate, and high classes would be difficult; the distinction would be arbitrary and might not

[a] ZAHAR, A. R. ET AL. Studies on the susceptibility of *Anopheles pharoensis* to DDT in the Nile Delta, Egypt, UAR, 1960–1962. Geneva, 1965 (WHO mimeographed document WHO/MAL/482.65).

adequately illustrate changes in the resistance level over a period of time. It is preferable to examine the actual mortality figures obtained with the discriminating dosage to determine whether selection has progressed or reversion towards susceptibility has occurred.

PROPOSED CRITERIA FOR INTERPRETATION OF TEST RESULTS

Based on the recognized discriminating dosages, the following criteria are proposed for the interpretation of results of susceptibility tests.

Dieldrin

Dieldrin resistance in anopheline mosquitos can be readily assessed by the use of precise discriminating dosages. Exposure to 0.4% dieldrin for one hour kills all susceptible individuals of all species tested (with the exception of *A. sacharovi*, which requires an exposure of one hour to an 0.8% concentration to kill all susceptibles—C. D. Ramsdale, personal communication, 1968). Exposure to 4% dieldrin for 2 hours kills both the heterozygous and the susceptible individuals, but not the homozygous resistant individuals. Thus, tests using the two discriminating dosages of dieldrin permit an assessment of the proportion of each of the three phenotypes.

DDT

DDT resistance is more difficult to assess since the discriminating dosage that kills heterozygous individuals cannot be accurately determined, particularly when the gene of resistance is incompletely dominant. Generally speaking, exposure to 4% DDT for one hour will kill all susceptible individuals and can be taken as the discriminating dosage.

On this basis, the following criteria are arbitrarily proposed for the different levels of mortality following exposure to 4% DDT for one hour (they may possibly also apply to organophosphorus and carbamate resistance using the respective discriminating concentrations).

99–100% mortality	=	susceptible
80– 98% mortality	=	verification required
<80% mortality	=	resistant individuals present (confirmatory tests required; field observations should be intensified with parallel, periodical checking of resistance level)

Due consideration should be given to the size of the mosquito sample tested in assessing the accuracy of observed mortalities. The above criteria should be applied to results obtained from a series of tests in which at least 100 mosquitos per locality are exposed. When smaller batches of mosquitos are tested, reservations should be stated. Occasional survivors on 4% DDT for one hour may be attributable to the failure of a few individuals to make proper contact with the treated paper, for example if they stay longer than others on the plastic mesh. Attention should also be paid to the temperature during testing. Unlike most insecticides, DDT is almost always more toxic at a lower and less toxic at a higher temperature (14).

Some anopheline species may show a small survival after exposure to 4% DDT for one hour (and sometimes even 2 hours), including *A. sacharovi* and other members of the *A. maculipennis* complex, and *A. stephensi*. This may be due to the presence of a few individuals exhibiting the extreme range of susceptibility. Accordingly, for most species of which survivors remain consistently after one hour's exposure to 4% DDT, it will then be necessary to distinguish between susceptible survivors and truly resistant individuals. This should be done by exposure of samples to 4% DDT for 2 hours. If survivors are still found, one of the following procedures should be adopted.

(1) Ideally, when rearing facilities are available, the offspring of survivors of 2 hours of exposure to 4% DDT should be obtained with as little larval mortality as possible and tested within 24 hours of their emergence, using the same concentration and exposure period as in the parent test. A significantly lower mortality than in the parent population would then confirm the suspicion of the presence of resistance and further selection in the laboratory should produce a fully resistant population. If the test shows mortality rates among the offspring similar to those of the parents, tolerance would be interpreted.

(2) The field population should be exposed to serial concentrations with the same 2-hour exposure period throughout. If a straight log-probit regression line is still produced, tolerance would be indicated. If the line has a plateau where increase in dosage gives no increase in kill, then true resistant individuals appear to be present.

(3) Alternatively, tests should be made repeatedly with exposure to 4% DDT for 2 hours; if there is continued survival, exposure should be for 4 hours. Consistent survival on 4% DDT for 2 and 4 hours would normally indicate resistance.

The last procedure has been adopted by many field workers and could help to verify whether DDT resistance exists in a number of vectors.

Organophosphorus and carbamate insecticides

Tentative discriminating dosages of malathion, fenthion, fenitrothion, and propoxur have recently been established for male and female adults aged less than one day from colonies of a number of anopheline species, including populations already resistant to DDT and dieldrin. The species shown in the following tabulation were exposed for one hour at 26° C and 70–80% relative humidity.

Species	*Source population*
A. albimanus	Haiti and Panama
A. atroparvus	England
A. balabacensis	West Perlis, Malaysia
A. farauti No. 1	Rabaul, Papua New Guinea
A. farauti No. 2	Queensland, Australia
A. gambiae species A	DDT and dieldrin resistant, Togo
A. gambiae species B	DDT and dieldrin resistant, Sudan
A. gambiae species C	Southern Rhodesia and Transvaal, South Africa
A. labranchiae	Algeria
A. melas	Gambia
A. merus	Tanzania
A. quadrimaculatus	DDT and dieldrin resistant, USA
A. sacharovi	Turkey
A. stephensi	1947 Delhi strain
A. stephensi, 2RA [a]	DDT and dieldrin resistant, with the basic chromosome 2 arrangement, from Mamlaha, Iraq
A. stephensi, 2RB [a]	DDT and dieldrin resistant, with inverted chromosome 2, from Mamlaha, Iraq

With few exceptions complete kills or only single survivors were obtained with one hour's exposure to 5.0% malathion; 2.5% fenthion; 1.0% fenitrothion; and 0.1% propoxur.

The exceptions were as follows. When *A. sacharovi* was exposed to 0.1% propoxur, only 61% of 61 females and 72% of 53 females were dead after recovery periods of 24 and 48 hours respectively, though the surviving mosquitos were obviously affected and had their wings permanently splayed.

In *A. balabacensis* on 1.0% fenitrothion only 73% mortality was obtained among 516 males and females, while 5.0% malathion killed only 87% of 205 male and female *A. quadrimaculatus*. Lastly, 3.2% malathion failed to kill all *A. stephensi* 2RA (only 39% of 119 males and females), *A. quadrimaculatus* (79% of 182 males and females), *A. balabacensis* (89% of 106 males and females), *A. sacharovi* (83% of 59 females), and *A. merus* (96% of 204 males and females).

These tentative discriminating dosages now need to be tried on field populations using freshly-fed females as advocated for the existing susceptibility test with organochlorine insecticides.

[a] Kindly provided by Dr M. Coluzzi, Department of Parasitology, University of Rome, Italy.

PROCEDURES FOR DETERMINING THE PRACTICAL IMPLICATIONS OF RESISTANCE

As explained earlier, the results of susceptibility tests cannot represent the actual reaction of vector populations to an insecticide as applied in the field, and should not be taken as the sole basis for replacing the insecticide. In fact, when the presence of physiological resistance has been confirmed and its geographical extent has been delineated, the aim of susceptibility testing should be the determination of changes in the resistance level by periodical checking. It is then the task of the entomologist and malariologist to project the results of susceptibility tests in terms of field mortality in the vector population under field dosage and spraying rounds. In addition, they should determine the role played by the proportion of the population surviving to an epidemiologically significant age and the resulting parasitological consequences in the human population. This may vary from one vector to another depending on their vectorial efficiency.

Antimalarial programmes generally include certain evaluation activities in areas under attack measures. The following procedures should be introduced or intensified as soon as the presence of physiological resistance to the insecticide in use, particularly DDT or organophosphorus and carbamate compounds, is confirmed in a vector population.

(1) Selection of indicator villages in a circumscribed area representing the ecological conditions in the sprayed area on the basis of continuing transmission and possibly varying levels of resistance of the vector to the insecticide. Although, in principle, coverage should be complete in the whole area under attack, it is of particular importance that total coverage spraying in the selected study area be well maintained.

(2) Conduct of an operational survey to ascertain that coverage has been adequate and sustained, so that findings on vector resistance can be considered valid.

(3) Estimation of the house resting density and proportions of different abdominal stages according to Sella [a] in samples collected from sprayed premises when the vector is mainly endophilic.

(4) Determination of the vector mortality through trap observations in not less than 10 traps per locality. The specimens should be classified according to the abdominal stages. The observations should be conducted at least twice a week. It would be useful to collect dead mosquitos in trap huts by using floor sheets; [a] this may be difficult to do in local houses, and in this case the indices of mortality should be expressed as trap kill. Trap observation is the most appropriate technique for exophilic species that enter houses to feed and leave during the night to rest out of doors.

(5) Determination of man/vector contact through captures of mosquitos both inside and outside houses using man as bait.

(6) Determination of the parous rate from samples obtained from bait collections.

(7) Susceptibility tests, on a large sample of vectors when possible, once before the first annual spraying round is applied and again before each subsequent round.

(8) In areas under late attack where surveillance activities are undertaken, careful epidemiological investigations of malaria cases with particular attention to determining the date of onset of the primary attack and its relation to the date of spraying and the density and longevity of the vector; in areas under early attack or in control programmes, parasitological assessment through periodic blood surveys (including infants).

In order to reach a decision on continuing the use of an insecticide or replacing it with an alternative, the data collected from all the above-mentioned entomological, parasitological, and operational observations (with due consideration to the prevailing meteorological conditions) should be interpreted as a whole.

[a] See MUIRHEAD-THOMSON, R. C., ED. Practical entomology in malaria eradication. Geneva, 1963 (World Health Organization mimeographed document MHO/PA/62.63).

RÉSUMÉ

CONSÉQUENCES PRATIQUES DE LA RÉSISTANCE DES VECTEURS DU PALUDISME AUX INSECTICIDES

La résistance des vecteurs aux insecticides constitue une caractéristique intrinsèque reposant sur des mécanismes génétiques relativement simples. Tel semble être le cas en particulier pour les moustiques anophélinés en ce qui concerne la résistance à la dieldrine, alors que c'est moins évident pour la résistance des mêmes moustiques au DDT. On ne sait encore guère de choses sur la transmission héréditaire de la résistance aux organophosphates et aux carbamates, récemment apparue chez *Anopheles albimanus*.

Connaissant la nature génétique de la résistance, il devient évident que la rapidité de la sélection menant à la résistance dépendra de la fréquence naturelle du ou des gènes impliqués, du degré de résistance conféré par ce gène, de son expression génétique (gène dominant, partiellement dominant ou récessif) et de la pression de sélection de l'insecticide, qui dépendra à son tour de la toxicité intrinsèque du composé, de l'efficacité de l'application, de la proportion de moustiques soumis à son influence et du comportement propre du moustique.

On accordait autrefois une importance exagérée à la détermination de la DL_{50} comme critère d'identification de la présence ou de l'absence de résistance aux insecticides. Il arrive qu'une forte incidence d'individus résistants se traduise par un changement si faible au niveau de la DL_{50} que la résistance passe inaperçue. Or le but d'une épreuve de sensibilité est de détecter la résistance le plus tôt possible. L'emploi d'une dose discriminatoire unique, calculée d'après les concentrations d'insecticides devant normalement tuer tous les individus sensibles, est préconisé. Ces concentrations ont été calculées pour la dieldrine et peuvent être appliquées à presque toutes les espèces anophélines. Pour le DDT, il n'existe pas de dose discriminatoire parfaite et l'interprétation des épreuves de sensibilité à cet insecticide présente quelques difficultés. Les doses discriminatoires provisoires pour les organophosphates et les carbamates ont été déterminées et devront être confirmées sur le terrain.

On avait également tendance autrefois à abandonner un insecticide pour un autre dès que la résistance était confirmée. Ce n'est pas obligatoire lorsque le degré de résistance est faible et que le vecteur n'est pas parmi les plus efficaces. Les auteurs préconisent une marche à suivre permettant d'évaluer les conséquences épidémiologiques et entomologiques de la résistance avant d'abandonner l'insecticide considéré.

REFERENCES

1. Brown, A. W. A. & Pal, R. Insecticide resistance in arthropods. *Wld Hlth Org. Mon. Ser.*, No. 38 (1971).
2. Macdonald, G. The dynamics of resistance to insecticides by anophelines. *Riv. Parassit.*, **20**: 306-315 (1959).
3. Breeland, S. G. et al. Observations on malathion-resistant adults of *Anopheles albimanus* Wiedemann in coastal El Salvador. *Bull. Wld Hlth Org.*, **43**: 627-631 (1970).
4. Ariaratnam, V. & Georghiou, G. P. Selection for resistance to carbamate and organophosphorus insecticides in *Anopheles albimanus. Nature (Lond.)*, **232**: 642-644 (1971).
5. Georghiou, G. P. et al. Development of resistance to carbamates and organophosphorus compounds in *Anopheles albimanus* in nature. *Bull. Wld Hlth Org.*, **46**: 551-554 (1972).
6. Haridi, A. Inheritance of DDT resistance in species A and species B of the *Anopheles gambiae* complex. *Bull. Wld Hlth Org.*, **47**: 619-626 (1972).
7. Davidson, G. Insecticide resistance in *Anopheles gambiae* Giles: a case of simple Mendelian inheritance. *Nature (Lond.)*, **178**: 863 (1956).
8. Davidson, G. Insecticide resistance in *Anopheles sundaicus. Nature (Lond.)*, **180**: 1333 (1957).
9. Tsukamoto, M. The log-dosage-probit mortality curve in genetic researches of insect resistance to insecticides. *Botyu-Kagaku*, **28**: 91-98 (1963).
10. Rahman, J. et al. Development of increased tolerance to DDT in *Anopheles culicifacies* Giles in the Panchmahal District of Bombay State (India). *Ind. J. Malar.*, **12**: 367 (1959).
11. Hamon, J. & Garrett-Jones, C. La résistance aux insecticides chez des vecteurs majeurs du paludisme et son importance opérationnelle. *Bull. Wld Hlth Org.*, **28**: 1-24 (1963).
12. Luen, S. C. & Shalaby, A. M. Preliminary note on the development of DDT-resistance in *Anopheles culicifacies* Giles in Panchmahals District, Gujerat State, India. *Bull. Wld Hlth Org.*, **26**: 128-134 (1962).
13. Peffly, R. L. Insecticide resistance in anophelines in eastern Saudi Arabia. *Bull. Wld Hlth Org.*, **20**: 757-776 (1959).
14. Busvine, J. R. A critical review of the techniques for testing insecticides, 2nd ed. Farnham Royal, Commonwealth Agricultural Bureaux, 1971.
15. Zulueta, J. de et al. Recent observations on insecticide resistance in *Anopheles stephensi* in Iraq. *Mosquito News*, **28**: 499-503 (1968).