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Large scale field trials - Stages VI and VII *

by

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Résumé

Le stade VI de l'évaluation opérationnelle de l'arprocarb (OMS-33) a montré au Salvador, au Nigeria et en Iran un contrôle efficace des anophélinés sur une période de deux à quatre mois. Cet insecticide a une phase transportée par l'air qui tue les moustiques sur une longue période même s'ils ne se posent pas sur une surface traitée, qualité qui peut être particulièrement utile dans des régions où la transmission péridomiciliaire est responsable de l'apparition continue de nouveaux cas. L'arprocarb est actuellement testé dans des opérations d'éradication du paludisme dans la zone confiée à la F.A.O. en Irak et dans la zone confiée à l'Union au Salvador.

Une évaluation épidémiologique du Malathion en Ouganda a montré que cet insecticide doit être considéré comme un insecticide de rechange pour les régions où une résistance des insectes a diminué l'utilité du DDT. Cependant, la durée relativement brève de son efficacité sur certaines boues, il doit être essayé à petite échelle dans une nouvelle région avant d'entreprendre des opérations de pulvérisation à grande échelle.

Le dichlorvos ne s'est pas montré efficace pour interrompre la transmission du paludisme dans les essais à large échelle réalisés jusqu'ici sur le terrain, probablement par suite d'une ventilation excessive des habitations ou d'une transmission extra-domiciliaire. Cet insecticide a toutefois trouvé une place très utile dans le contrôle des insectes domestiques et pour la désinfection des gros avions pressurisés utilisés dans les transports internationaux.

Le fénitrothion est un insecticide rémanent très efficace pour le contrôle des moustiques anophélinés rencontrés à proximité et à l'intérieur des habitations, mais des problèmes de formulation ont empêché son évaluation complète. De nouvelles formulations existent à présent et la poursuite de l'évaluation sur le terrain de cet insecticide est envisagée si elles devaient se montrer satisfaisantes.

SUMMARY.

Operational evaluation Stage VI of arprocarb (OMS-33) has demonstrated effective control of anophelines in El Salvador, Nigeria and Iran for 2 to 4 months. This insecticide has an airborne phase which kills mosquitos for a considerable period even though they do not rest on a sprayed surface ; a quality which may be of particular value in areas where peridomiciliary transmission is responsible for the continued occurrence of

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new cases. Arprocarb is presently being tried out in malaria eradication operations in the FAO area of Iraq and the Union area of El Salvador.

An epidemiological evaluation of Malathion in Uganda indicated that this insecticide should be considered as an alternative insecticide for areas where insect resistance has minimized the usefulness of DDT. However, because of its relatively short effective life on certain muds, it should be tried out on a small scale in a new area before undertaking large scale spraying operations.

Dichlorvos was not effective in interrupting malaria transmission in the large scale field trials so far carried out, probably because of excessive ventilation of houses or extra domiciliary transmission. However, this insecticide has found a very valuable place in the control of household pests and for disinsection of large pressurized aircraft used in international transportation.

Fenitrothion is a very effective residual insecticide for control of house frequenting anopheline mosquitos but problems of formulation have hampered its full evaluation. New formulations are now available and it is planned to continue field evaluation of this insecticide should these prove to be satisfactory.

Of the more than 1,300 chemical compounds which have been entered into the WHO Collaborative Programme for the Evaluation and Testing of New Insecticides many have been eliminated at stage I for various reasons. However, approximately 100 of these have been recommended annually for further evaluation. Each year some 4 to 7 of the compounds which have successfully passed the criteria for stages II and III are selected for field trials in experimental huts (stage IV). Each year one or two compounds are investigated in village scale trials (stage V). To date four of these new insecticides have been given stage VI Operational Evaluation or stage VII Epidemiological Evaluation in large scale field trials against anopheline mosquitos.

STAGE VI OPERATIONAL EVALUATION

As indicated in a previous paper the purpose of the stage VI trial is to recognize and eliminate any operational difficulties which may arise in the spraying of the new insecticide under field conditions. This stage was incorporated into the WHO evaluation programme in 1966 as a result of field experiences in which it was found that commercially produced formulations of new insecticides may vary from those produced in a research laboratory and furnished for testing at the earlier stages.

Specifically the objectives of the stage VI trial are to assess the stability (active ingredient content and suspensibility) of commercially produced formulations and to identify problems that may arise from their use under general field conditions. This trial also affords an opportunity to observe further the effectiveness of the safety precautions recommended and to secure more entomological data for evaluation of the insecticide's usefulness in controlling anophelines. Entomological evaluation is carried out by means of pyrethrum-spray, window-trap, floor-sheet, night-biting and outdoor-resting collections and the bioassay of sprayed surfaces. The abdominal condition of captured mosquitos is observed and recorded and they are dissected to determine the nulliparous/parous ratio. Mosquitos are periodically collected and tested serologically to determine the hosts. Certain special studies are designed and carried out to measure any unusual characteristic of an insecticide such as irritant, deterrant or airborne effects. A medical toxicologist is present during the stage VI trial to evaluate the extent to which the recommended safety precautions are being carried out by spraymen and to carefully examine spraymen and villagers for any signs of absorption of the insecticide. All spraymen are given physical examinations and biochemical tests of their blood are carried out during the spraying.

Results of Stage VI trials with arprocarb (OMS-33).

Stage VI trials of arprocarb have been carried out in El Salvador, Nigeria and Iran.

El Salvador.

An operational evaluation was carried out in Southeastern El Salvador in 1966 and 1967 by a WHO/PAHO Insecticide Testing Team. Seven rounds of spraying of arprocarb (OMS-33) at 2 g/m^2 were completed with an interval of 4 months between the first and second rounds and approximately 3 months interval thereafter. The area included about 3,000 houses and 13,500 people. The houses are mostly of fairly open construction with walls of poles or mud and roofs generally of thatch. The principal vector is *A. albimanus*, a facultative feeder which spends only a comparatively short time in houses, even when feeding on man and can occur in very large and rapidly fluctuating numbers.

Because of the habits of this vector, DDT was only partially effective in this area, even before resistance occurred. Since the development of resistance it has become ineffective in interrupting malaria transmission.

Results with arprocarb (OMS-33) varied between well ventilated and poorly ventilated houses, between villages with houses close together and those with scattered houses and between dry and rainy seasons. In some compact villages the entire vector population apparently disappeared for up to 14 weeks after spraying, while in scattered rural houses well ventilated and exposed to winds, satisfactory kills were obtained over a shorter period. For most of the area the duration of effective control of *A. albimanus* was considered to extend from 8 to 12 weeks.

To a considerable extent the effectiveness of OMS-33 against more or less exophilic vectors such as *A. albimanus* is due to its ability to kill mosquitos at a distance from a sprayed surface. This effect (referred to as the airborne effect) has been investigated in some detail in El Salvador. When *A. albimanus* adults were exposed for 12 hours in cages near (but outside of) sprayed houses, more than 70 % were killed for 21 days or longer after spraying. Mortalities of 100 % resulted for 14 weeks (98 days) or longer when the *A. albimanus* were exposed inside sprayed houses. Mortalities among caged *A. albimanus* used as checks were negligible.

Nigeria.

An area containing about 1,800 houses and 4,000 people near Kaduna was sprayed at 2 g/m^2 with arprocarb during 1967 by the WHO *Anopheles* Control Research Unit I. The main vectors are *A. funestus* and *A. gambiae* (sibling species A and B). Practically all of the houses are of mud walls with grass roofs, some being large and square and others small and round. Entomological assessment based on morning pyrethrum-spray catches, door exit trap collections and bioassay tests indicated effective control of *A. gambiae* and *A. funestus* for 3 to 4 months in this area. (See figure 1).

Studies of the airborne effect of arprocarb in this trial using *Aedes aegypti* exposed for 12 hours indicated that in the immediate outdoor vicinity (within 4 feet) of sprayed huts, satisfactory mortalities (70 % or more) occurred among caged mosquitos for more than 30 days and within the sprayed houses such mortalities occurred for more than 51 days (See table 1).

Iran.

One of the most successful trials with arprocarb was carried out in south western Iran by a joint team of WHO and the Institute of Public Health Research, Iran (Carmi-

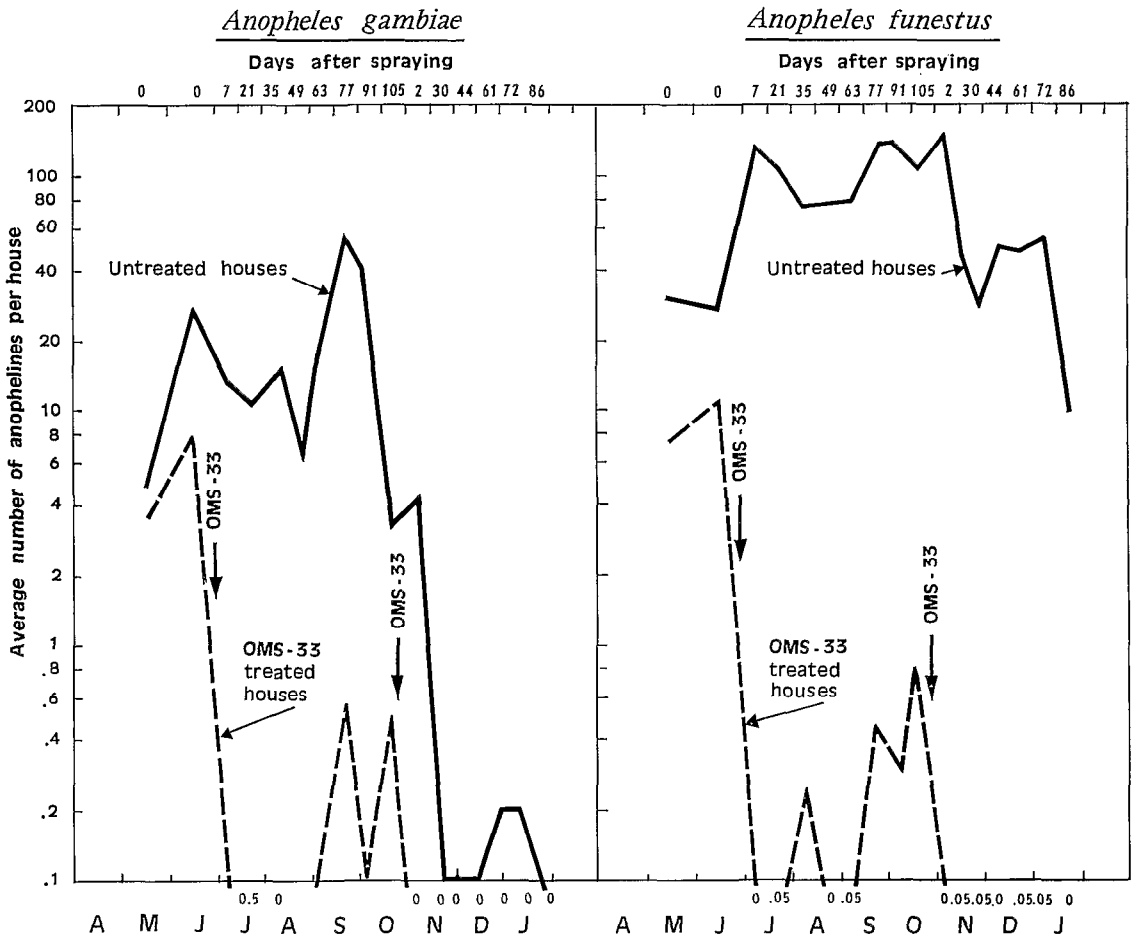

FIGURE 1

CHAEL *et al.*, 1968). In this area *Anopheles stephensi* has been found to be resistant to both DDT and dieldrin. The results of this trial have been given in detail in the previous paper by Drs MOFIDI and FAGHIH. It is sufficient here to indicate that arprocarb was effective against *A. stephensi* for 3 to 4 months and against *A. dthali* for 2 to 3 months and that its airborne effect was pronounced on both species.

STAGE VII EPIDEMIOLOGICAL EVALUATION OF NEW INSECTICIDES

The purpose of the stage VII trials is to assess the effectiveness of the new insecticide in interrupting transmission of malaria. This epidemiological evaluation is carried out under the aegis of the Malaria Eradication Division of the World Health Organization. In order to minimize the effect of movement of people on malaria incidence an area up to 7,800 km² (3,000 sq. miles) containing about 200,000 population may be desirable, but sometimes smaller areas must be utilized. Evaluation consists of careful epidemiological (including entomological) studies in certain key index villages in the sprayed area and

TABLE 1

Bioassay of airborne effect of arprocarb (O.M.S.-33) at Kaduna, Nigeria, 1967

Distance from nearest sprayed hut - feet		Days after spraying at 2 g/m²											
		2	9	16	23	30	37	44	51	59	65	72	79
		Percentage mortality after 24 hours											
Controls	550 ..	6 (16)	0 (20)	0 (14)	0 (16)	0 (20)	0 (20)	0 (17)	0 (20)	0 (21)			
	320 ..	0 (13)	6 (16)	6 (18)	0 (15)	0 (17)	0 (19)	0 (18)	0 (18)	0 (16)			
	160 ..	—	8 (13)	5 (20)	0 (17)	0 (19)	0 (20)	—	—	—	—	—	—
	101 ..	57 (14)	33 (12)	7 (14)	0 (18)	5 (19)	0 (22)	—	—	—	—	—	—
	27 ..	100 (26)	97 (29)	41 (39)	0 (33)	17 (42)	0 (40)	—	—	—	—	—	—
	10-13 .	100 (28)	97 (29)	61 (36)	8 (64)	4 (75)	1 (82)	—	—	—	—	—	—
	5-7 .	—	—	—	71 (63)	54 (79)	5 (79)	—	—	—	—	—	—
	1-4 .	100 (180)	100 (145)	99 (168)	84 (183)	70 (237)	43 (246)	33 (258)	4 (358)	2 (42)	—	—	—
	Inside Huts .	100 (64)	100 (35)	100 (29)	99 (75)	100 (78)	100 (76)	100 (61)	96 (198)	62 (27)	80 (343)	66 (367)	56 (394)

Note : Figures in parenthesis show number of *Aedes aegypti* exposed in cages from 18:00 to 6:00 hours.

in an adjacent unsprayed comparison area. If it is demonstrated in this trial that the insecticide is capable of interrupting malaria transmission then it can be considered for use in the Malaria Eradication Programme wherever a new insecticide is required.

Results of a Stage VII trial of malathion (OMS-1).

SOUTHERN UGANDA.

A field trial was carried out during 1963-1964 covering an area of approximately 500 km² with a population of 26,000 in Masaka District, Southern Uganda by the WHO Malaria Eradication Insecticide Field Trials Team. (NAJERA *et al.*, 1967). Housing consisted of mud walled houses with thatch of corrugated iron roofs and « beehive » type huts constructed completely of poles and thatch located in scattered compounds. All houses and animal shelters were sprayed with malathion at 2 g/m² at approximately 4 months intervals. The densities of *A. gambiae* and *A. funestus* as measured by pyrethrum spray and exit trap collections were drastically reduced after application of the insecticide, and for the duration of the trial. Normal seasonal populations of *A. gambiae* and *A. funestus* were recorded for the unsprayed comparison villages. *A. funestus* was found to be the most abundant anopheline prior to spraying and in unsprayed villages. Wall bioassay tests in which *A. gambiae* were exposed to treated thatch surfaces for one hour gave mortalities above 80 % for 220 days. On wood 100 % mortalities were obtained for 243 days. Bioassays on corrugated iron roofs indicated satisfactory lethal deposits (causing mortalities of 70 % or more) up to 120 days after spraying. On mud the effectiveness of malathion lasted only about one month.

Bioassays using caged mosquitos indicated an airborne lethal effect in the vortex of the thatch roofs which lasted for 236 days after spraying. This airborne effect adjacent to the mud walls lasted for only a short period. The epidemiologic significance of this phenomenon is not known.

A very active case detection programme provided information from which it was concluded that the transmission of malaria was interrupted, in spite of a number of imported cases and a few introduced cases which occurred in sprayed villages.

As a result of this trial and those of village scale trials, malathion is recommended for use in Malaria Eradication operations where DDT has failed to interrupt transmission due to the occurrence of resistance in the vector. However, before undertaking large scale operations with malathion in new areas, especially where mud house construction predominates, a small trial should be undertaken to ascertain its effectiveness under the local conditions.

Results of a Stage VII trial of dichlorvos (OMS-14).

KANKIYA, NIGERIA.

An extended field trial of dichlorvos was carried out in the Kankiya district of Nigeria during 1963 by the WHO Malaria Eradication Field Trials Team (FOLL *et al.*, 1965). Two types of dispensers were used ; the National Communicable Disease Center montan wax solid and the Ciba liquid. Approximately 1,500 houses were treated with each type of dispenser. During the first round one dispenser was applied for each 750 ft³ (21 m²) of living space and in the second and third rounds the dosage was increased to one dispenser per 400 to 500 ft³ (11 to 15 m²).

Entomological observations indicated that a considerable reduction in numbers of house resting anophelines occurred in both treated areas, but the densities never fell to zero. Bioassays using caged *A. gambiae* gave irregular results after initial high kills. It was concluded that the solid dispensers gave good immediate kills of mosquitos but densities increased gradually to indicate little effectiveness after 6 to 8 weeks. Maximum

efficacy lasted for one to two weeks only. The liquid dispensers did not give such high initial kills of mosquitos but were more uniform in performance. In view of these results, the ventilation of houses in the area was investigated. It was found that in June there were about 30 air changes per hour during the night and 69 air changes per hour in the morning. Parasitological data indicated that interruption of malaria transmission was not achieved during the period of the trial. It was concluded that excessive ventilation of houses prevented the maintenance of a concentration of dichlorvos adequate to interrupt transmission indoors.

In follow-up studies during 1964 (FOLL and PANT, 1966) it was found that children aged 2-4 years living in the previously treated area had a considerably reduced spleen and average-enlarged spleen rates. It was postulated that, since dichlorvos reduced the house densities of anophelines, these children received less infective bites.

In spite of the results of this trial to control house entering anophelines, dichlorvos has proved very effective in killing insects where its vapour is not rapidly dispersed by excessive ventilation. Dichlorvos has been recommended as the method of choice for disinsection of large international aircraft and has also found any other uses in controlling insects, particularly the household pests.

Results of a Stage VII trial of fenitrothion (OMS-43).

KANKIYA, NIGERIA.

Fenitrothion 40 % wdp was applied at the target dosage of 2 g/m^2 of active ingredient to more than 15,000 houses and shelters in the Kankiya area during 1964 and 1965 by the WHO Malaria Eradication Insecticide Field Trials Team. Six and a partial seventh round of spraying were carried out. The first spraying drastically reduced the numbers of *A. gambiae* and *A. funestus* from about 50 per hut to 0.15 per hut and the average pyrethrum spray collection rose above 3 per sprayed hut on only two occasions during the course of the trial. Peaks of about 18 *A. gambiae* and 16 *A. funestus* per hut occurred in unsprayed huts during the 1965 mosquito season. Following the early spray rounds there were indications that fenitrothion was effective for slightly more than two months. Evidence of transmission of malaria to new born babies was found. For these reasons it was decided to spray the fifth, sixth and seventh rounds at two month intervals. Entomological evaluation showed almost complete control of anophelines in the treated houses. A few cases of malaria among infants still occurred however.

During the trial a number of operational problems were encountered. Early batches of the formulation lost their suspensibility quickly. A subsequent batch retained good suspensibility but was found to erode spray nozzles excessively. Two of the batches were apparently more readily absorbed by spraymen as indicated by lowered blood cholinesterase values. These formulation difficulties caused operational delays and threatened the validity of the epidemiological evaluation of the insecticide. For these reasons, it was decided to terminate the trial and to defer further testing until a satisfactory stable formulation could be provided.

Several manufacturers have now indicated that they are in a position to provide satisfactory formulations of fenitrothion, these are being examined. If the manufacturers claims are confirmed, the evaluation of this insecticide in the field will soon be resumed.

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REFERENCES

CARMICHAEL (A. G.), MOTABAR (M.), SUNDARARAMAN (S.), ROWHANI (F.), GOLESTANI (J.), 1968. — Entomological studies evaluating 0-isopropozyphenal Methylcarbamate in an operation field trial in Iran. In manuscript for WHO/VBC series.

NAJERA (J. A.), SHIDRAWI (G. R.), GIBSON (F. D.), STAFFORD (J. S.), 1967. — A large-scale field trial of Malathion as an insecticide for anti-malarial work in Southern Uganda. *Bull. Wld. Hlth. Org.* **36** : 913-935.

FOLL (C. V.), PANT (C. P.), LIETAERT (P. E.), 1965. — A large-scale field trial with Dichlorvos as a residual fumigant insecticide in Northern Nigeria. *Bull. Wld. Hlth. Org.* **32** : 531-550.

FOLL (C. V.), PANT (C. P.), 1966. — The conditions of malaria transmission in Katsina Provinces, Northern Nigeria and the effects of Dichlorvos application. *Bull. Wld. Hlth. Org.* **34** : 395-404.

WORLD HEALTH ORGANIZATION. — Evaluation of insecticides for vector control. Part I. WHO/UBC/68.66, 201 p.