C. Anderson
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INSECTICIDES OF CHOICE IN MALARIA CONTROL PROGRAMS

Recent developments have made it apparent that there is a need to clarify Agency policy on the insecticide of choice for spraying of houses in A.I.D. supported malaria control programs. In order to provide appropriate guidelines for a choice of insecticides A.I.D. has requested current views from World Health Organization (W.H.O.) Headquarters in Geneva and also from the Centers for Disease Control (C.D.C.) in Atlanta, Georgia on their recommendations as to insecticides. A.I.D. has traditionally relied upon these two organizations for technical judgments in the field of malaria.

As far as the continued use of DDT is concerned, the World Health Organization has emphasized in the 16th Report of the W.H.O. Expert Committee, 1974 (TRS 549) that since the newer insecticides are much more costly than DDT it should continue to be used where levels of resistance in local Anopheline populations were not so high as to prevent interruption of transmission. W.H.O. in its "Official Records of the World Health Organization," No. 190, 1970 concludes:

> Indoor spraying of DDT in routine anti-malaria operations does not involve a significant risk to man or wildlife. The withdrawal of DDT from malaria programmes would be fraught with great danger and is unjustifiable in the light of present knowledge. The Organization should do everything in its power to ensure that DDT remains available for this purpose."

While DDT remains effective in some malarial areas of the world, by the mid-1970's it became apparent that in a number of countries DDT was no longer effective against certain Anopheline vectors and that levels of malaria were increasing dramatically in these countries.

Over the past twenty years a total of more than 2000 compounds have been tested to determine if they could be used as insecticides to replace DDT in anti-malaria vector control programs. The World Health Organization took the lead in the field testing of the more likely prospects in field spraying trials in Kaduna, Nigeria in Kisumu, Kenya and, most recently, in Central Java, Indonesia. These stage trials begin with the exposure of test mosquitos to insecticide impregnated filter paper, continued with the spraying of huts and culminated in large scale village trials. These tests have resulted in only three or four compounds which could have some value in a country-wide malaria program. The most effective alternative pesticides are the organophosphorous compounds, malathion and fenitrothion, and the carbamate propoxur. At the presesnt time, therefore, these are the three primary insecticides which could be used where the mosquito vector has developed resistance to DDT.

Propoxur, a carbamate insecticide, is considered to be at the upper limit of acceptable toxicity for extensive indoor application. Until now it has been used primarily in Latin America where widespread resistance to organophosphate

compounds and DDT had developed. At present, however, the high cost of the insecticide and its toxicity have limited its use markedly in malaria programs.

Since only a limited use of propoxur appears feasible, the choice of an insecticide to replace DDT where it is no longer effective must lie between malathion and fenitrothion. The W.H.O. has stated "It is clear that malathion has a decided cost advantage; while its period of persistence is generally not as great as that of fenitrothion, in some areas--especially those with limited transmission periods--the length of persistent activity may be quite adequate for interruption of transmission.

Regarding the cost factor in comparing malathion and fenitrothion one must take into consideration not only the basic cost of the pesticide but also the cost of application and surveillance of the workers. In its recommendations on the safe use of insecticides for residual indoor application, W.H.O. requires that weekly cholinesterase determinations be conducted on all personnel exposed to fenitrothion where as this is not necessary in the case of malathion (see W.H.O./V.B.C./78/704, Annex I).

In its seventeenth report, the W.H.O. Expert Committee on Malaria (W.H.O./T.R.S. 640, 1979) stated: "The development of resistance to malathion may occur without cross-resistance to other organophosphate insecticides, leaving it feasible to use fenitrothion or similar OP compounds."

The Pesticide Branch of the Center for Disease Control of the U.S. Public Health Service makes a similar recommendation. Dr. James Miles, Chief, Pesticide Branch, writes "It is our opinion that malathion is the pesticide of choice to be used for house spraying in areas where DDT resistance has developed. Our position in this matter is based on two considerations. Firstly, malathion is less toxic to mammals and is less expensive than fenitrothion. Secondly, the biochemical mechanisms of organophosphate resistance are such that resistance to malathion will not necessarily impair the effectiveness of fenitrothion. Conversely, it is reasonable to expect that the fenitrothion resistance mechanism will confer resistance to malathion. We now have mosquito strains which are malathion resistant but fenitrothion susceptible. We know of no case where fenitrothion resistance has failed to involve, concurrently, resistance to malathion."

"Unless we find evidence to the contrary we must assume that the most rational approach to the long-term control of Anopheline mosquitoes would be to use malathion until resistance develops and hold fenitrothion in reserve for this eventuality."

Dr. G. P. Georghiou, Professor of Entomology and Head, Division of Toxicology and Physiology of the University of California is a leading authority on the subject of insecticide resistance and has served as an expert consultant for both A.I.D. and W.H.O.

Dr. Georghiou in a recent consultant report for U.S.A.I.D./Haiti entitled, "Report on Potentiality for Resistance to Insecticides in Anopheles albimanus and Observations on Current Control Projects in Haiti" has this to say on the choice of insecticides: "In most cases in which malathion was the first organophosphate employed against a mosquito population in the field (or in laboratory selection experiments), the resistance that eventually developed was due to the enhancement of the enzyme carboxylesterase. This enzyme degrades malathion but does not affect fenitrothion since the latter does not possess a carboxylester bond. Carboxylesterase confers resistance that is specific for malathion and phenthoate, two compounds having carboxylester bonds. Several such cases have been recorded involving Culicine as well as Anopheline mosquitoes (W.H.O. 1980, Matsumura and Brown 1963, Bigley and Plapp 1962, Busvine 1968, Rathor et al. 198). Thus, the use of malathion as the first organophosphate of choice preserves the usefulness of fenitrothion and other organophosphates when malathion has lost effectiveness due to the selection of carboxylesterase."

"Although not enough cases of fenitrothion resistance have yet been studied due to the more recent introduction of this chemical, the resistance that is selected by it in insects presents a wider spectrum of cross resistance, one that includes malathion. This is because the enzyme phosphatase, which is responsible for fenitrothion resistance, has a wider spectrum of action among organophosphates. More research is needed on fenitrothion metabolism by

mosquitoes. For the time being it would be prudent to employ malathion as long as this chemical is effective, thus retarding or avoiding the onset of wider spectrum organophosphate resistance."

In selecting an insecticide for residual spraying, all of the above factors should be taken onto consideration. However, before any large amount of money is spent for an alternative insecticide for residual spraying, a field trial comparable to the W.H.O. Stage V Village Scale Testing should be carried out in the country against the vector to be controlled. In two cases residual spraying of village huts with malathion was ineffective even through susceptibility tests showed the vector in both cases to be completely susceptible. This was the case with Anopheles aconitus in Central Java and with Anopheles albimanus in Haiti. In both cases fenitrothion tested against the same vector under the same conditions was effective.

In Summary

1. The insecticide of choice for residual spraying against malaria mosquitoes is DDT.

2. When and if the vector is demonstrated to be resistant to DDT, in alternative insecticides should be chosen.

3. At the present time available alternative insecticides include malathion and fenitrothion (both organophosphates) and propoxur (a carbamate, (Actellic and Bendiocarb) may be available in the future, but at present are only available for testing.

4. The alternative insecticide should be chosen on the basis of a comparative field test in country of all available insecticides with the decision made taking into consideration effectiveness, safety, resistance potential and cost.

5. Since it is virtually inevitable that insecticide resistance will eventually develop in the Anopheline vectors, comparative testing of all available alternatives should be initiated as soon as possible in each country.

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