MOSQUITO CONTROL

by

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The practical implications of insecticide resistance in the control of culicine mosquitoes has been reviewed by PAL (1964) and in Anophelines by COZ et al. (1964). The consequence of such resistance to the operational programmes in Malaria Eradication campaigns were pointed out in a paper submitted to the 11th Expert Committee on Malaria (1964) by HAMON and COZ. These authors have emphasized the necessity of developing new insecticidal compounds capable of supporting the operational mosquito control programmes threatened by the widespread insecticide resistance which has developed among many culicine and anophelines mosquitoes, adults and larvae.

Since the late 1940's a large number of field trials have been carried out on alternative compounds to the chlorinated hydrocarbons for mosquito control; most interest has centered around the organo-phosphorus group. The literature on these trials is now voluminous and was reviewed by GRATZ (1962) for the Third African Malaria Conference in an unpublished working paper. O-P resistance, however, has been detected both in *Culex* and *Aedes* spp. (PAL, Ibid) and the search for compounds which will give effective control should therefore be intensified.

In the case of those mosquito species where it is feasible, there is obviously no substitute for preventing the development of the immature stages by altering the environment so as to deny them the availability of suitable larval habitats. As an example, the "source-reduction" programme in California to reduce or prevent the accumulation of standing irrigation water is the most effective control step against chlorinated hydrocarbon and O-P resistant ***Aedes nigromaculis*** and ***Aedes dorsalis***. Similar programmes are undertaken against ***Aedes sollicitans*** and other marsh or irrigation water breeders in North America and other areas of the world. Drainage, stream clearance, fluctuation of water levels and like measures have long been part of the classical control of certain *Anopheles* species.

Perhaps the species whose larval habitats is most related to man's effect on his environment is *Culex fatigans*. MATTINGLY (1963) has documented how this species has successfully utilized highly polluted urban breeding places caused by man specially in cities where urbanization has been so rapid that satisfactory sewage facilities have lagged for behind. Equally the installation of well-engineered sewage disposal will greatly reduce the breeding of this species, perhaps sufficiently to prevent its reaching the population density required to act as a disease vector.

Such permanent corrective measures of effective drainage and sewage systems represent an ideal that will, unfortunately, take long to implement towards the control of marsh or swamp

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breeding species or of *C. fatigans* in urban and semi-urban environments. In the interim insecticides, and primarily larvicides must be relied upon. For the control of other species such as *Anopheles gambiae* and similar anthropophilic, endophilic mosquitoes whose breeding places include rainwater collections and temporary pools, contact residual insecticides must be applied to control them when they enter man's dwellings to feed upon him. Global commitments to mosquito control in efforts and funds are so vast that it is essential that suitable insecticides be available for all types of operations and especially against mosquitoes that have developed insecticide resistance to compounds already in use.

In order to ensure the uninterrupted continuity of its mosquito-borne disease control programmes in many parts of the world, the World Health Organization has initiated a collaborative scheme for the evaluation and testing of new insecticide compounds. While the candidate compounds are tested against many insects of public health importance, prime interest is in those who may prove to be effective mosquito adulticides or larvicides. Candidate compounds received from the insecticide industry, universities and research institutes, are initially tested against insecticide-susceptible and resistant mosquito adults and larvae (as well as houseflies); compounds which appear to have promise are then subject to advanced laboratory and small-scale field tests, eventually leading to larger scale tests under operational conditions. It is hoped that eventually a sufficient number of insecticides will become available for use in each given situation to ensure a longer period of effective control even though resistance may develop to each after some years or field use.

1 - ANOPHELES

1 - 1. Adulticides

Since the advent of the synthetic, organic long-acting insecticides in the mid-1940's the usual method of controlling adult anophelines is by the application of residual sprays to the interior of dwellings, mostly as water dispersible powders.

In those areas of the world where no resistance to them has developed, or in several instances of DDT, where the resistance is of a very low order, the chlorinated hydrocarbons remain the insecticides of choice. DDT is the most widely used, is cheap, has a low mammalian toxicity and is effective on many different types of building surfaces. Dieldrin, while considerably longer lasting than DDT, has given rise to a high degree of resistance in many *Anopheles* species. In addition, its mammalian toxicity is considerably higher than that of DDT. Dieldrin resistance will also cause resistance to lindane (or gamma-BHC).

In situations where double resistance excludes the use of either DDT or dieldrin and lindane the 13th Expert Committee on Insecticides has recommended that the organo-phosphorus malathion be applied at 2 gm/m^2. While this compound is rapidly absorbed (within 2-3 weeks) on mud surfaces, it is effective for 3 to 5 months on such impervious surfaces as wood, grass or thatch. Recent field trials by the WHO in East Africa have indicated that this insecticide may be reasonably effective even in mud huts providing that there is a sufficient percentage of organic surfaces such as thatch roof, wooden doors, etc. Another O-P fenthion (BAYTEX) has shown promise in field trials (SCHOOF *et al*, 1961 - GRATZ and CARMICHAEL, 1963); however, its mammalian toxicity is probably too high to allow its routine use (TAYLOR, 1963 - ARNAN, 1964).

Recent village-scale trials with OMS-43 (or 0,0-dimethyl 0-(4-nitro-m-tolyl)phosphorothioate) have shown that this compound has considerable promise on both mud and organic surfaces as well as a comparatively low mammalian toxicity. The WHO is now undertaking a large-scale field evaluation in Northern Nigeria with OMS 43 to determine if this compound will interrupt the transmission of malaria.

Considerable interest has been shown in a new concept of adult mosquito control - the use of dichlorvos as a residual fumigant and a number of field trials have been carried out in Africa (QUATERMAN *et al.*, 1963 - GRATZ *et al.*, 1963 -FOLL, 1964) using solid or liquid state dichlorvos dispensers. These showed that in types of dwellings where there is comparatively little ventilation, the material is likely to be an effective adulticide; however, when the number of air exchanges per hour is such that the dispensers presently in use are unable to replace the insecticide vapours as fast as they are swept out of the structure, the method will not be effective. Further trials are planned in areas where a low degree of ventilation is likely to permit the use of this technique. The minimum insecticidally effective concentration of dichlorvos in air has been shown to be well below the threshold which is likely to have any toxic effect on man. Trials are currently under way studying the use of dichlorvos in the disinsection of aircraft.

Some of the carbamate insecticides appear to have considerable promise against adult anophelines. Preliminary tests have been carried out with several of these in Africa and as soon as more information is available on their degree of mammalian toxicity, these trials will be extended.

OMS-33 or 2-isopropoxyphenyl N-methyl carbamate when applied at a rate of 1,5 g/m^2 in huts in the area of Lagos, Nigeria, gave an indication of controlling the natural mosquito population for up to 13 weeks (ITU, 1963). A consideration of prime importance in the evaluation of any new residual spray for the control of *Anopheles* mosquitoes in dwellings is the degree of toxic hazard which its use may cause both to man and his domestic animals. In judging the safety of the material to man to acute toxicity to spraymen is the first factor. While protective clothing, if properly worn (and including hat, overalls, respirator and gloves) will give almost complete protection, experience has shown that in tropic climates such uncomfortable clothing is not readily accepted and unless the spraying is closely supervised, will often be taken off. Men bagging or mixing the insecticide from the technical strength (usually containing 40% to 50% of the active ingredient) to the ready-to-use formulation may be under a particular degree of risk and their work with a material of even only moderate toxicity must also be closely supervised. Spraymen applying an insecticide for long periods of time as part of a malaria eradication campaign may develop chronic sequellae though no danger was envisaged from short periods of exposure. Inhabitants of sprayed houses are also exposed to the insecticides and their decomposition products, for long periods of time and the possible chronic effects of such exposure must also be studied.

Because of the possible toxic hazards involved in the application of almost any new insecticidal compound in such close contact with man, part of the Organization's collaborative scheme, which has been described above, is to subject each new compound to a careful toxicological scrutiny first in the laboratory and later in preliminary field trials. Any compound whose initial oral or dermal toxicity is considered too high for safe normal use is dropped from further consideration as a residual spray no matter how promising an insecticide it may be. Before field trials an effort is made to understand the mode of action of any new compound on warm blooded animals as well as the possibility of any novel route of absorption such as by vapours, etc. In the course of the first small scale field trials most careful laboratory and clinical studies are carried out on all individuals exposed under the guidance of experienced toxicologists. Finally the results of all such studies are considered by the Organization's toxicological advisers and a decision reached by them as to whether or not the compound is sufficiently safe to allow its large scale field use.

1 - 2. Larvicides

Although little use has been made of larvicides in malaria eradication campaigns in recent years, in certain circumstances such treatment may be of value and an increasing number are becoming available. In cases where access to the larval habitats is difficult, aircraft may be used for spreading granular or pellet formations to penetrate vegetation. Where no resistance to them has occurred, the chlorinated hydrocarbons -DDT, dieldrin, heptachlor, lindane or chlordane may be sprayed as solutions or emulsions. These persistent insecticides may leave residues in fish inhabiting treated streams and this possibility should be considered where food fish may be affected. Some of the O-P compounds are highly effective as larvicides, e.g. parathion, fenthion, OMS 43, dichlorvos, Dipterex, etc. Although the carbamates as a group have not been as effective mosquito larvicides as the O-Ps, (GEORGHIOU & METCALF, 1961), some may be effectively used should larval resistance develop to the O-P compounds.

There has recently been a renewed interest in the use of Paris green both against anopheline and culicine larvae and a series of papers have been published on this (RODGERS & RATHBURN, 1958 - RODGERS & RATHBURN, 1960). In these a description is given of the development of a new granular form either made light weight for ground application or heavy for application from the air, at an application rate of about 0.375 lbs of toxicant per acre. This material is safe to apply, has comparatively little toxicity to fish or wildlife and has no record of resistance ever having developed to it in over twenty years of intensive larvicide use prior to the advent of the chlorinated hydrocarbons.

2 - CULICINES

Since most culicine mosquitoes will take blood meals equally readily in and out of doors, the emphasis in their control has been upon the immature stages. Where feasible, as previously stated, it is of course desirable to prevent their breeding altogether. As an example, the destruction of aquatic vegetation will prevent the breeding of *Mansonia* spp. Efficient irrigation practices will both save water and eliminate some of the worst culicine breeding. Drainage of coastal salt marshes will eliminate the *Aedes* larvae adapted to this brackish environment (and extend recreational areas). The implementation of urban sewage disposal will reduce the breeding of *Culex fatigans* and *Armigeres* and a municipal piped water supply may reduce the household storage of water and the resultant breeding of *Aedes aegypti, Culex* and *Culiseta* spp. as will disposal of tin cans, tyres and other containers which may store rain water.

Where it is necessary to use larvicidal compounds the choice will depend on several factors such as the type of water to be treated, its degree of pollution and its likelihood and manner of being utilized by man or animals and as to whether or not fish are present. Consideration must also be given to the mosquito species' degree of insecticide susceptibility or cross-resistance to each compound considered.

The control of *Culex fatigans* breeding in polluted water is one of the most important problems in mosquito control today. The rapid expanse in urbanization over the last decade has outpaced sewage disposal schemes - especially in the already crowded cities of South-East Asia and Africa. In many urban areas this has resulted in vastly increased breeding of *C. fatigans* and a concomitant increase in the transmission of filariasis.

Control of *C. fatigans* by DDT has not, in general, been satisfactory both due to the species' general lower degree of susceptibility to this insecticide and the rapid development of resistance where it has been used. The latter has also been the case with other chlorinated hydrocarbon insecticides. In certain areas it is felt that nothing superior to the use of oil in privies and sewage ditches is available (BURTON, 1964). However, the labour cost involved in weekly re-applications of oil and the poor spreading quality over the surface of the larval habitat make this material less than optimum.

C. p. fatigans is the main vector of filariasis in India and much attention has been given by Indian workers to various possibilities for its control. RAMAKRISHNAN *et al* (1960) carried out a series of laboratory and field studies on several O-P compounds to determine their effect on the larvae and adults of *C. p. fatigans;* fenthion (BAYTEX), trithion, methyltrithion, diazinon, malathion and phosdrin were all examined. In the laboratory trithion and fenthion were the most effective against the immature stages; in the field fenthion gave 100% control at 0.05 lb per acre of water surface and when applied at a dosage of 0.6 lb per acre appeared to give persistent control for over 15 days. No persistent effects resulted with the use of trithion, malathion, and phosdrin even at doses of 0.6 lb per acre although initial mortality in the check plots was completely satisfactory. When tested in the field as a residual spray in houses with mud walls and roofs of thatch or wooden planks, fenthion at 100 mg per sq. ft showed an effective residual action to adult *C. p. fatigans* for eight weeks while trithion the only other compound tested was ineffective.

Recent work (LEWALLEN & WILDER, 1963 and BARKAI, 1964) indicate that fenthion may perform well under such circumstances. The WHO has set up a research unit in Rangoon, Burma, to carry out laboratory and field research on the most effective means of controlling *C. fatigans.*

For the last year and a half, surveys and basic studies have been carried out on the ecology of the larva and adult, and baseline data established on the degree of susceptibility to various insecticides. Small and large-scale field trials, mainly in highly polluted water habitats favoured by *C. fatigans* are now being commenced with fenthion and other O-P and carbamate insecticides. At the same time, selection studies are being carried out in Canada and Rangoon on strains of *C. fatigans* from that city in order to determine how long a period of time might pass before resistance is likely to develop to the candidate compounds and to determine what is the degree of cross-resistance to newer compounds prior to their introduction.

Laboratory tests in Japan (SUZUKI & MIZUTANI, 1962) have shown that OMS 43 appears to be very effective against both the larvae and adults of *C. pipiens.* The LD 50 for the adult female mosquito was established as 0.00195 micrograms and the LC 50 for the larvae and pupae was established as 0.0291 ppm and 0.650 ppm respectively. In California, however, OMS 43 has not proved to be a very effective larvicide when tested in the field against the larvae of *A. nigromaculis* and *A. freeborni* even at dosages of 0.25 to 0.3 lbs per acre (LEWALLEN, 1963).

Mansonia larvae, the main vector of *Brugia* filariasis in the Far East, can be controlled by the use of herbicides to destroy *Pistia* and other water plant hosts to which the larvae and pupae attach themselves. Oils would not be particularly effective but some O-P compounds in emulsions or solutions might prove useful against this group.

In the control of irrigation water and marsh breeding culicines, much success has been obtained through the use of organophosphorus larvicides such as malathion at 224-560 g per ha, fenthion at 28-56 g per ha, parathion or methyl parathion at 56-112 g per ha. Sprays may be applied with ground equipment if the area is accessible from the ground or be sprayed or dusted by light aircraft. The latter mode of treatment is particularly advantageous and economical when large areas must be covered. If the area to be treated is covered by much vegetation, it may be desirable to use granular or pellet formulations to ensure better penetration of the larvicide through the cover. In the case of flood-breeding *Aedes,* it may often be possible to apply the insecticide on the dry ground where breeding is expected to occur prior to flooding and the insecticide will take effect when tide, rain or irrigation water causes flooding. Most of the extremely extensive mosquito abatement operations in the US are carried out against such flood, irrigation or tidal water breeding mosquitoes such as *Culex tarsalis, Aedes nigromaculis, A. dorsalis, A. sollicitans,* etc.

A particular problem of control is posed with *Aedes aegypti;* throughout the Americas where the species is entirely domestic, an eradication programme under way for several years is now threatened by the development of resistance to DDT and dieldrin and, as recently reported a tolerance to malathion and fenthion. Control measures had, in the main, been based on the perifocal concept where the larval habitat and all adjacent surfaces where adults were likely to rest were treated by the same insecticide - an approach which appears to have hastened the development of resistance. With the spread of Thai haemorrhagic fever in the Far East, the vector of which is also *A. aegypti,* the necessity of effective insecticides has become even more pressing. Since *A. aegypti* breeds primarily in clear water habitats much of which are used by man for drinking purposes, a most desirable criteria of any insecticide in such circumstances would either be a very low degree of mammalian toxicity or, secondly, such a high degree of toxicity to mosquito larvae that it could be applied in minute quantities. A very long degree of persistence would also be desirable as the labour costs involved in frequent retreatment of the multitude of breeding places such as water jars, drinking throughs, cisterns, water tanks, etc. would be very high. The last requirement might be met through the use of slow release briquettes, granules or pellets. Indeed, much success has been obtained with the use of dieldrin pellets or briquettes against *Aedes polynesiensis.* The pellets or briquettes weigh 10g and contain 16% dieldrin Treatment of freshwater containers and tree holes gave excellent control of *A. pseudocutellaris* in Fiji (BURNETT, 1960). Initial field trials with dimethrin granules also show promise.

3 - FUTURE CONSIDERATIONS

While for the time being no practical alternative methods for mosquito control are available other than the use of insecticides or environmental manipulation, nevertheless the Organization is giving considerable attention to long-term studies on a number of possible alternatives.

Among the possibilities being considered is the use of the sterile male technique, similar in principle to the successful campaign carried out against the screw worm fly *Cochliomyia hominivorax* and a great deal of basic research has been undertaken on the physiological effect of chemosterilants and irradiation on mosquitoes as well as on the various chemosterilants now available. It has, however, already been realized that far more will have to be known about the population dynamics of mosquitoes before such a campaign can be successfully undertaken, even assuming the availability of a chemosterilant of low mammalian toxicity or a satisfactorily facile method of irradiation. Great hope is put in the potentiality of genetic manipulation of mosquito populations and a possible control through the introduction of lethal or incompatible genes.

Close study is also being given to the feasibility of the use of biological agents in the control of mosquito populations such as the introduction of specific mosquito pathogens, nematode-parasites, parasitic fungi, etc. Here too, however, very considerable research must be carried out before any practical use is likely to be made of even already known biological agents.

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