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MALARIA VECTOR CONTROL: A CRITICAL REVIEW ON CHEMICAL METHODS AND INSECTICIDES

by

M. COOSEMANS[1] & P. CARNEVALE[2]

[1] *Prince Leopold Institute of Tropical Medicine, Nationalestraat 155, B-2000 Antwerpen 1, Belgium.*

[2] *Control of Tropical Diseases Division, W.H.O., Geneva, Switzerland.*

Prevention of malarial disease based on selective and sustainable measures is one of the four basic technical elements of the Global Malaria Strategy (66). Preventive measures include chemoprophylaxis, which is largely compromised by the increase of drug resistance and limited to pregnant women or travellers, immunization, which is still at the experimental stage, and vector control. It is expected that vaccines will not replace other prevention methods but will be used "as a component of strategies that include other measures" (67). The Global Malaria Strategy underlined the importance of vector control, with emphasis on site-specific approaches that are taking into account the local malaria epidemiology and the vector behaviour. More selective, well targeted vector control is a key factor for a cost-effective result (52). Sustainability of a vector control activity mainly depends on the perception that people have of its usefulness.

The direct output (Fig. 3) of a vector control activity must be an important reduction of the vectorial capacity. The vectorial capacity is a concept which attempts to combine the various entomological variables relevant for the transmission of malaria, i.e. the vector density, the human biting rate and the daily probability of survival of the vectors (*in* 13). A decrease of vectorial capacity keeps place with the reduction of transmission, although immunity and drugs may interfere with this process. But this will not necessarily lead to a decrease of malaria infection, disease incidence, malaria related morbidity and mortality. Before starting a vector control activity, a good knowledge of the local epidemiological characteristics, mainly the level of transmission and its seasonality, is therefore required in order to define what could be expected from the vector control activities (13).

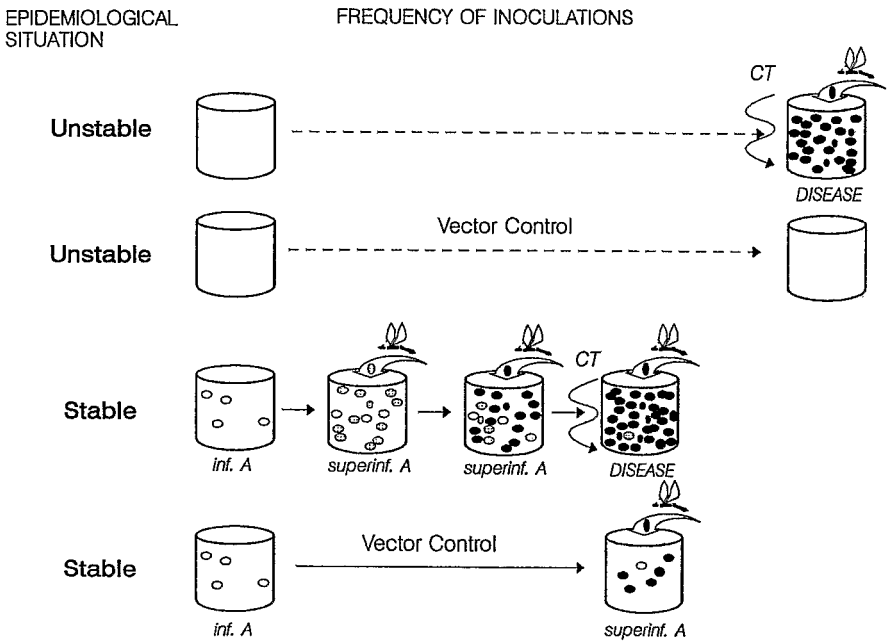
In **unstable** malaria areas, where transmission is occasional or where transmission periodically occurs at low level, development of protective immunity will not occur. Consequently every malaria infection leads to disease, and all age groups are at risk. In such a situation, a well planned vector control activity will prevent or contain epidemic outbreaks.

In **stable** malaria areas transmission is high enough to maintain a high parasite rate in the population and immunity develops in the early years of life so that most infected persons are asymptomatic carriers. However malaria morbidity and mortality are observed in young age groups, which are not yet immune. In areas with moderately intense and seasonal transmission, vector control can considerably reduce the highly seasonal malaria morbidity and mortality, while malaria infection in the population will be little affected (3). In stable areas

where very intense seasonal or perennial transmission occurs, a reduction of transmission by over 90% will not affect the parasite prevalence since the remaining infective bites are still responsible for superinfection in humans. However, some small scale trials suggest that the disease episodes are reduced (7).

The results of vector control programmes in stable areas suggest that superinfecting sporozoite inocula act as a trigger of disease (Fig. 1). This could be explained by the novelty of inocula, i.e. variants of parasites not yet encountered by the host so that no strain specific immunity has been developed (31). Besides the type of strain, the size of the inocula plays an important role as only large inocula of new variants for the host can develop and reach clinical threshold of parasite density before being neutralised by the host response. Moreover large inocula contain a wider range of genetic variants including some that the host has not yet experienced (31). The consequences of this hypothesis are important in relation to long-term benefits of vector control in stable malaria areas. Trials have so far been done in areas where children have grown up in the absence of vector control and have acquired some immunity. But the benefit for children growing up in the presence of sustained vector control is so far uncertain (31). The number of different strains they will encounter will probably

Figure 1: In unstable malaria areas, transmission occurs occasionnaly and acquired protective immunity is almost absent. Every infective bite will lead to disease. A decrease of transmission by vector control will decrease malaria morbidy and mortality.

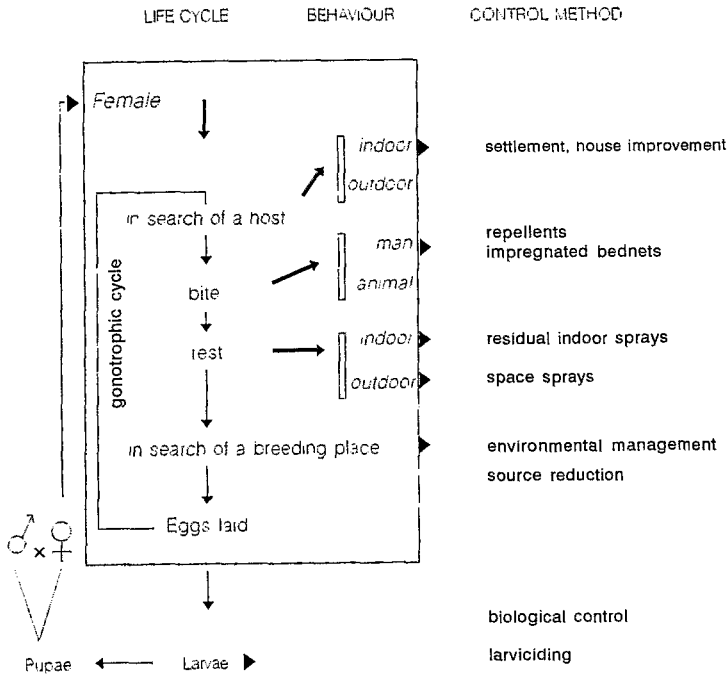


In stable malaria areas, transmission is high and responsible for superinfection. Acquired protective immunity will limit parasite densities, but new strains of inocula may act as a trigger of disease. The hypothesis is that vector control will reduce the speed of successive waves of inocula, which will allow the immune system of the host to respond more adequately. A decrease of the incidence of malaria disease will be observed, but parasite prevalence remains unchanged.
CT: clinical threshold; inf. A.: infected asymptomatic carrier; superinf. A.: superinfection of asymptomatic carrier.

not be reduced by vector control. However the convalescent time between the attacks will be greater. During high transmission periods, the defense mechanism of the host is overwhelmed by successive waves of new variants. We believe that the most important impact of vector control in stable areas could be the reduction of the speed of these successive waves. This will allow the immune system of the host to respond more adequately (13). This means that vector control will influence the incidence of malaria disease.

Chemical control has proven to be very effective to reduce vectorial capacity. Other methods like environmental management (45, 59) or biological control (47) could only be applied in a limited number of situations (39). Insecticides can be used both against the adults and the larval stages (Fig. 2).

Figure 2: Life cycle of anophelines and control measures related to vector behaviour.



Larviciding

The objective of source reduction and larviciding is to reduce vector density to a point where vectorial capacity and thus transmission could be significantly reduced.

This objective can be achieved only where:

– the man-vector contact and vector longevity are low and

– the breeding places are relatively scarce, few in numbers, well known and easily accessible by sprayers.

This last condition is fulfilled in rather exceptional circumstances (25, 39).

Larviciding combined with impregnated bednets could be helpful to control urban malaria. The urban african ecosystem is generally unfavourable for anophelines: reduced longevity and low density of the vectors explain the low level of transmission (9, 39). Destruction of larvae with habitats restricted to cisterns or underground tanks, such as *Anopheles stephensi* in Indian towns, have been showed effective.

An important limitation is the low persistence of usual larvicides so that larviciding has to be repeated frequently (generally every week), which requires considerable funds to cover labour and insecticide costs. The persistence of a compound is negatively correlated to the amount of suspended organic matter in the breeding place.

Insecticides

Today, there is no reason any more to recommend the very toxic Paris Green (arsenical), that has been widely used in the past. The slightly to moderately hazardous larvicides are mainly organophosphates: temephos, malathion, pirimiphos-methyl, chlorphoxim, chlorpyriphos, fenthion (25). Synthetic pyrethroids like permethrin show high larvicidal activity but they must be used with care according to their toxic effect on non target fauna. Little information is available on the use of growth regulators in malaria control programmes (24). Compounds like diflubenzuron or methoprene, which have a very low mammalian toxicity are still expensive. Results with monolayers have been disappointing since it is difficult to maintain the integrity of the film under operational conditions (25).

Some strains of the bacterial species *Bacillus thuringiensis* (0.5 to 6 kg/ha of the concentrate formulation or 4 to 10 kg/ha of granular concentration) and in lesser amount *B. sphaericus* show high level of larvicidal activity (35). They are very safe for non-target organisms. However, the residual effect of available bacterial insecticide formulations does not exceed 48 hours which limits their use, despite their stability under tropical storage conditions. Development of resistance to bacterial insecticides is rare, because they contain a mixture of toxins. This advantage would be lost if other organisms are used after transfer of a single toxic gene from *Bacillus* species (15). But in all cases correct use (choice of the insecticide, dosage) of these pesticides are important to avoid contamination of drinking water and water inhabited by non-target organisms.

Formulations

Anopheline larvae live and feed below the surface of the water. It is, therefore, important to develop floating formulations that will maintain the active ingredient on the water surface. Quick degradation of the active ingredient should also be limited. To compensate degradation of these molecules, slow release formulations, like microcapsules, will increase the intervals of treatment. New formulations are needed but they are often very expensive.

Imagociding

Several methods can be used to control adult mosquitoes:

1° Residual indoor sprays

2° Impregnated bednets, curtains

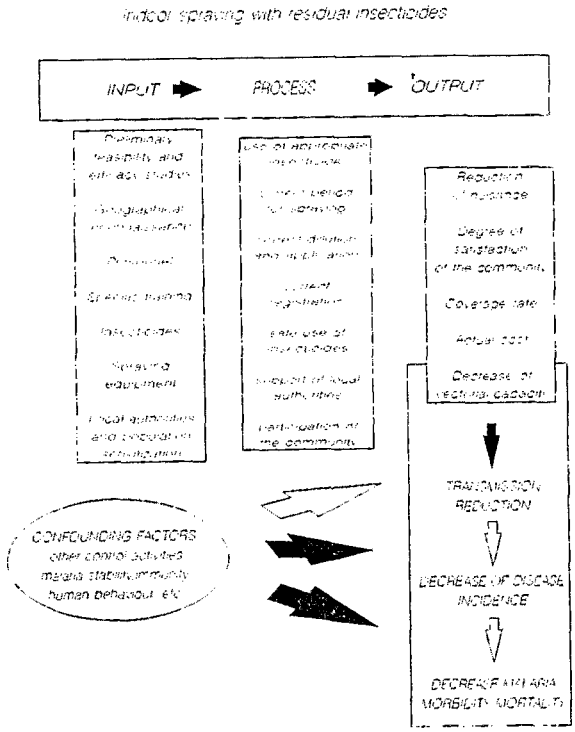
3° Space sprays

Residual indoor sprays (R.I.S.)

During the gonotrophic cycle, the female spends most of her time digesting bloodmeals on resting places. If these resting places are inside the houses and a large proportion of houses are treated, the probability for the vectors to come into contact with the treated surfaces is high. This means that vectors are generally killed after feeding on a host, however contact with treated surfaces prior to biting may also be important.

The admitted objective of R.I.S. is to reduce the longevity of the vector and thus the probability of a vector to become infective. However indoor spraying will only kill the endophilic fraction of the vector population, while the exophilic fraction will not be affected. This means that the average longevity of the remaining vector population remains unchanged. The efficacy of residual insecticides in terms of vectorial capacity reduction will thus be largely dependent on both the coverage and the resting behaviour of the vector populations. So is house-spraying not effective to control malaria transmission in areas of Mexico where *An. pseudopunctipennis* occurs: this vector has a very exophagic and exophilic behaviour (33). An indicator of pre-treatment resting behaviour appears to be a good predictor of the reduction of the man-biting rate that could be achieved by a residual insecticide, irrespective the choice of the insecticide (37). However some insecticides, like DDT and the pyrethroids, may enhance the exophilic behaviour. The different steps of this activity are described in Figure 3.

Figure 3: Different steps of a malaria vector control activity, here illustrated for indoor spraying. The process is followed by a direct output. Indirect output is influenced by the direct output and confounding factors which are independent of the process itself.



Operational constraints

Residual spraying programmes require a highly efficient organization for planning, implementation and evaluation. Human, technical and financial resources are often lacking to maintain a sustainable coverage. Many of these programmes have become routine programmes without appropriate evaluation and operational research. The spraying activity must be permanent with specialised teams going from one village to an other. However, the timing of residual spray applications is a crucial factor in obtaining maximum benefit. The round should be completed in a short period of time before the onset of a transmission peak (69). For this a high mobilization capacity is needed. Temporary and local personnel, after a short training may be used successfully for this. Hand-operated compression sprayers using a standard nozzle (No. 8002) are recommended for this type of insecticide application. Only few sprayers are conform to WHO specifications (61): Hudson X-Pert and Gloria 165. Practical information on house spraying has been provided by Fontaine (23).

Community acceptance is of course important. The first spray round is generally well accepted by the householders, but if no efforts are undertaken to take into account the comments of the population, doors will be closed during the following spray rounds and spray coverage will be insufficient. In several countries, householders deny access to spraymen, because they do not like unsightly deposits of powders, the smell of an insecticide or the visit of a stranger. Often these problems can be overcome by providing appropriate information to the householders in collaboration with the local representatives. Involvement of the community has often been overlooked. However without active implication of the householders this activity will be doomed to failure. Householders are invited to remove foodstuffs, to pull out furniture and to provide water for the dilution of the insecticide.

The insecticides

Important characteristics of formulated residual insecticide are:

1° The high biological toxicity for the vector species. The lethal effect should last for at least two months after the application. The choice of an insecticide is dependent on the required persistence of the compound on the treated surfaces (2 months to 8 months) which is determined in relation to the local anopheline ecology and the epidemiology of the disease. Insecticides that will induce a quick development of resistance by selective pressure will be avoided. Vector resistance to one particular insecticide may confer resistance to some others belonging to the same class of insecticides, but this phenomenon is not systematical (63). Monitoring of insecticide resistance must be done on a regular basis.

2° Repellent or irritating effect should be as low as possible. However with some insecticides the excito-repellent effect occurs after the insect has picked up a lethal dose of the compound.

3° Low acute and/or chronic toxicity to man and domestic animals. When properly applied, the risk to contaminate the outdoor environment is minimal.

4° Stability during storage in tropical conditions, good mixing properties and non corrosive for spraying material.

5° All the previous conditions at an affordable cost.

These criteria are important to select a suitable active ingredient and formulation. More than 2000 potential insecticides (adulticides, but also larvicides)

have been tested in the framework of the WHO Pesticides Evaluation Scheme (WHOPES). Compounds accepted into the WHOPES scheme are given a number with an OMS prefix. Village-scale trials and large scale trials using new compounds have been published in the WHO/VBC documents and were summarized in several publications (43, 54, 60).

Several compounds fulfil the above mentioned criteria:

Chlorinated hydrocarbons

– DDT (2 g active ingredient – a.i. – per m^2) was considered as the insecticide of choice for residual spray to control endophilic and non-resistant vectors until 1993 (60). The compound is stable, of low cost and relatively safe for operators and inhabitants of sprayed houses. However its excito-repellent effect on the mosquitoes may considerably alter the efficacy of the compound. During the seventies, DDT represented more then 90% of the total insecticides used in mosquito control programmes in Africa, the Americas and Western Pacific and more than 70% in South East Asia (43). Nowadays the use of DDT has been banned in many countries for environmental reasons. DDT is manufactured only in a limited number of countries, i.e. Bangladesh, China, Pakistan, and South Africa (58). Moreover it is now difficult to find DDT wettable powder produced according to the standards of the WHO at an affordable price and donors are more reticent to purchase a compound which has been banned in their own country. Apart from politico-ecological considerations and possible adverse effects on humans, which are still based on non conclusive data (40), the position of DDT as the insecticide of choice is becoming questionnable (1). Indeed new compounds may offer operational advantages and could be more cost-effective than DDT (16). This does not mean that DDT should be banned from the arsenal of the insecticides used in malaria control programmes. In the absence of resistance, and when properly used, DDT can still be very efficacious in controling the malaria disease as was recently demonstrated in the control of the malaria epidemics in Madagascar and Burundi. However many anopheline populations are nowaday resistant to DDT (63).

– Dieldrine is no longer recommended, because its high toxicity and the rapid development of resistance in many vector species. Lindane shows cross-resistance to dieldrine, and its use is now limited.

The organophosphorus insecticides (OP)

Effective control of a susceptible mosquito population with one round (2 g a.i./m^2) can be obtained for two to three months with the compounds mentioned below. Spraying activities should not exceed 5 hours per day and cholinesterase activity must be checked.

– Malathion (OMS-1) is a safe insecticide, if formulations used are of good quality (isomalathion < 1.8% of the nominal malathion content). The slight smell of this compound may reduce the acceptability by the community.

– Fenitrothion (OMS-43) is classified as a slightly hazardous compound. Beside contact it has also an important airborne toxic effect. This compound is currently used in malaria control programmes.

– Pirimiphos-methyl (OMS-1424) has a long-lasting vapour effect similar to that of fenitrothion (44, 48). In Pakistan, where emergence of resistance to malathion has been observed, *Anopheles culicifacies* and *A. stephensi* were drastically reduced in areas sprayed with this compound and no new cases of

malaria were detected (42).

– Chlorphoxim (OMS-1197), a slightly hazardous compound, is not commonly used. Impact on indoor and outdoor man-biting rate is limited (56).

– Dichlorvos (OMS-14) is used as a residual fumigant (solid or liquid dispenser) and was widely used by householders under the form of impregnated strips of resin for the control of domestic insects (Vapona®). Dichlorvos was considered as a very promising compound, but due to excessive ventilation in treated huts, it is difficult to maintain an adequate concentration of dichlorvos in order to have a significant impact on transmission (22)

– A new formulation of chlorpyriphos methyl (methyl dursban, Reldan, OMS-1155) is actually under evaluation in Pakistan.

The carbamate insecticides

Residual effect is generally of two to three months.

– Propoxur (OMS-33) – 2 g a.i./m^2 – has been used in countries (Americas, Eastern Mediterranean Area) where vectors were resistant to chlorinated hydrocarbons and to organophosphates. An extensive field trial was performed in Nigeria on *A. gambiae* and *A. funestus* (28). This compound is about ten times more expensive than malathion, the cheapest organophosphate.

– Bendiocarb (OMS-1394) – 0.2-0.4 g a.i./m^2 –. Because of the higher toxicity for mammalians it is important to restrict exposure of the operators. Therefore the 60% wettable powder should be supplied in preweighed sachets made of laminated paper foil and plastic film. Field trials were performed in Iran against *A. stephensi*, resistant to DDT and dieldrin, and in Indonesia on *A. aconitus* (43).

– Carbosulfan (OMS-3022) is still under evaluation.

Synthetic pyrethroids:

Photostable pyrethroids show remarkably high toxicity against anophelines but relatively low mammalian toxicity. Three compounds have been evaluated with success by the WHOPES programme (8, 11, 12, 38, 49, 50, 56) and are now currently used in public health control projects: permethrin (OMS-1821) – 0.5 g a.i./m^2 –, deltamethrin (OMS-1998) – 0.025 g a.i./m^2, lambda-cyhalothrin (OMS-3021) – 0.030 g a.i./m^2 –. These compounds are biodegradable, and showed long persistence on treated walls (between 3 and 8 months). However exophilic behaviour is accentuated in the presence of these insecticides, and survival of escaping mosquitos may increase two months after treatment. Both in the Tanga region (Tanzania), and in the Rusizi Valley (Burundi), where the main vector is *A. arabiensis*, high *P. falciparum* parasitaemia were significantly reduced by house spraying with respectively lambda-cyhalothrin and deltamethrin (4, 36). Other promising compounds are still under evaluation although some of them are already used: Cyfluthrin (OMS-2012), Alfamethrin (OMS-3004), Cypermethrin (OMS-2002) (5), Etofenprox (OMS-3002 – Trebon®).

Formulations

The effectiveness of the treatment is largely dependent on the formulation. For indoor sprays it is important that the insecticide remains available on the treated surface. Insecticides presented as emulsions or solutions penetrate in larger amounts in sorbent material than those presented as suspensions. This

does not mean that emulsions are not efficient. Malathion emulsion was proven to be as effective as a malathion suspension, despite its low residual activity on dried mud walls (27). Good suspensions can be obtained with water-dispersible powders (wettable powders, WP) which are relatively cheap. When applied on porous surfaces, the water is absorbed and the solid particles (carriers and the active ingredient) are retained on the surface (26). An optimal particle size of the active ingredient is required to ensure the diffusion from the deposit to the integument of the insect and/or the pick up of particles of the insecticide that will diffuse in the mosquito after it has left the deposit. Abrasive carriers present in some formulations may cause rapid erosion of nozzle tips of the compression sprayers. Solution and emulsion concentrates must be used with care due to the inflammability of solvents. Flowable concentrate is a more expensive formulation for suspension. The advantage of this formulation is its easy application without risk. Calculation of dilutions and speed of application are given in annex 1.

Indoor low volume (I.L.V.) insecticide spray

This method is an alternative for conventional indoor spraying. Faster insecticide applications using knapsack mistblowers, run by a two-stroke engine, can be performed. Two trials, one in Nigeria against *A. gambiae* (6), and, more recently, one in a coastal plain of Mexico against *A. albimanus* (2) compared both I.L.V. and R.I.S. methods. Residual activity was slightly reduced with I.L.V. applications but similar indoor and outdoor mortality of both species was observed.

Compared to the conventional WP spray methodology the advantages are the following:

– the operational cost may be reduced, particularly where personnel cost are high (by 43% in Mexico using bendiocarb),

– the I. L.V. spray is about 70% faster than conventional WP spray, which could be crucial to prevent or to control epidemic outbreaks.

Disadvantages are the following:

– equipment and maintenance costs (motorized mistblowers) are indeed more costly than usual sprays.

– more qualified personnel is required.

Impregnated bednets (I.B.N.)

The objective is to reduce man vector contact and the lifespan of the vectors, the two main factors of vectorial capacity. With untreated bednets, mosquitoes are diverted to unprotected people. Pyrethroids impregnated bednets act as baiting traps: unfed females looking for their bloodmeal are attracted by the sleepers and come into contact with the treated material. This means that with IBN, vectors are killed before biting their hosts, where RIS will mainly kill the vectors after their bloodmeal. The regular use of impregnated bednets will provide personal protection against malaria. However a good coverage is required to obtain an impact on vectorial capacity, transmission and indirectly on the disease burden in the population. Community protection can thus be achieved only if a high proportion of the people can afford those nets and use them continuously (7, 14). Under these circumstances, non-users of impregnated bednets will also benefit of the protection (51, 65).

In several trials throughout the world it was possible to decrease the transmission by more than 80%, when dealing with endophagous species. However poor results may be obtained with vectors such as *A. albimanus* in Haiti (19) or *A. culicifacies* in Sri Lanka (20) which exhibit exophagic behaviour early in the evening when the majority of people are still active outdoors. The degree of reduction of malaria prevalence, parasite load, incidence of clinical attacks, malaria-specific and overall mortality depend upon the initial level of transmission. However, all trials suggested some significant impact on the disease. Impregnated curtains are less efficacious but may be appropriate if the acceptability of bednets is low (46).

Operational aspects

Planning and implementation of this activity request less input than indoor spraying, and could be organized at peripheral level. However, it is unfair to present this control method as an activity easy to organize by local communities, without an external technical and financial support. Five points must be stressed:

– Mosquito nets must always be available at an affordable price:

Some communities already manufacture their own bednets with different materials, but most of them have to buy nets on the market. Local availability of cheap, mass produced, mosquito nets enhances their large-scale use in many countries of South East Asia. However in most African countries locally made mosquito nets are often of poor quality and expensive (57). The production of small workshops is too limited to face needs for wide scale applications. Import of bednets from South East Asia is still the most economical solution in Africa. Donors may play an important role in stimulating local production of bednets but competitivity must be be improved. Distribution networks and outlets have to be developed in order to make the bednets also available in the remote areas (65). Multisectorial collaboration is here an absolute necessity.

– Initial and subsequent impregnation should be done on a regular basis under the supervision of trained local health staff. The community should be fully involved in the impregnation process by using collective or individual dipping methods. Spraying of the netting material may be an alternative method when working at a large scale, like in China, or with farmers who are used to spray insecticides.

The local health staff is responsible for obtaining insecticides, but orders should be regrouped by one unit responsible for the purchase and permanent availability of the insecticide conform to the WHO specifications and at the lowest price.

– A good health education programme and mass media campaigns are key points for the success of the activity (65). The message should include more than only health aspects, but should also emphasize social improvement, improvement of life and money saving (18, 32).

– The perceived need to use nets depends on local attitudes. Where nets are already used traditionally it will be easier to implement this activity. The most important benefit expected from the families is the reduction of the nuisance. The willingness to pay for a bednet could increase with the experience in the community. Model, size, colours can be adapted to the local demand. Therefore an in depth knowledge of usual behaviour of the population must be obtained (Knowledge, Attitude, Practice surveys), before lounching any programme (18, 32, 68).

– Contrary to indoor spray activities, it would be difficult to have an idea of the actual "coverage"of a I.B.N. programme. From routine data, it is possible to have an idea of the number of bednets sold and the frequency of their reimpregnation. Surveys should be performed to know the compliance with net usage in the households. Sleeping habits must here be considered. But this lack of information is compensated by two elements: – a large scale use of I.B.N. induces prevention of malaria in the community even if their is not full coverage – field trials have clearly showed that people who initially are not willing to use I.B.N., claimed them when neighbours expressed their satisfaction "to sleep peaceful". This "social coverage" is important for malaria prevention even if it can't be strictly quantified.

Insecticides

Photo-stable pyrethroids are particularly appropriate for impregnation of bednets, because their long persistence on usual materials and their relative safety to humans. Permethrin (200-500 mg a.i./m^2), deltamethrin (15-25 mg a.i./m^2), lambda-cyhalothrin (10-30 mg a.i./m^2), cypermethrin (100 mg a.i./m^2), cyflutrin (100 mg a.i./m^2), each one at different dosage, can be used for impregnation of mosquito nets. Results of bio-assays may vary depending of the insecticide used and its dosage, mosquito species and the nature of the fibres. Permethrin is more effective on polyester and nylon than on cotton, while little difference appears between fabrics when deltamethrin is applied. However polyester or a mixture polyester cotton are preferred to cotton, or nylon nets because there are more durable. Most of the dose of pyrethroids will be removed after washing the impregnated nets in cold, soapy water (14, 34). Permethrin-impregnated bednets were shown to reduce considerably the number of mosquitoes entering the huts. This deterrent effect, which enhanced personal protection, is produced by the components of the formulation and not by the insecticide itself (30). Insecticides, which kill higher proportions of endophagic mosquitos, such as deltamethrin or lambda-cyhalothrin, may be preferred to obtain a better community protection against malaria transmission (34). The procedure for impregnation is given in annex 2. The persistence of DDT on nets is very low and this insecticide cannot be recommended for impregnation of nets. However there is a need to evaluate compounds of other groups of insecticides on bednets to face the problem of resistance to pyrethroids. Reduced susceptibility of *A. gambiae* to permethrin has already been reported in Kenya (55)and in Ivory Coast (21). A mixture of insecticides from different classes will probably delay the appearance of resistance, but this implies the development of new long lasting insecticides belonging to other classes of insecticides than the pyrethroids. Emulsifiable concentrates are generally used for impregnation of bednets, but WP were also successfully used (29). Flowable formulations are recommended because they do not induce irritation, skin problems, coughing to workers involved in large scale dipping of bednets.

Space sprays

The objectives are a fast reduction of the adult population and by renewed applications, a reduction of the lifespan of the vector population. Space sprays are performed by thermal fogging or cold aerosol sprays (ultra low volume) (41, 43, 60, 61). Flying mosquitoes come into contact with the small droplets of

insecticides, which are suspended in the air. The killing effect of such an application is very fast but repeated applications are necessary due to the non-persistence of the insecticide. No optimal meteorological conditions, such as wind, vertical turbulence associated to ground-based temperature inversion or rain, will compromise this control activity. Several towns are regularly or occasionally treated by vehicle-mounted aerosol generators or aerial ULV application. But often search of a political impact excels the search of an impact on the disease. This technique can be used on exophilic vectors during epidemic outbreaks.

Resistance management strategies

Two strategies are generally opposed: sequential application of insecticides in time and/or in space and the use of mixtures of unrelated insecticides (15, 63). Some theoretical models and experimental laboratory work suggest that pre-planned rotation of residual insecticides will have little, if any, advantage. Mixture of insecticides, particularly where only females are exposed to the insecticides – this is the case with impregnated bednets- would be much more efficient than rotation if resistance is not fully dominant. A mixture of one photostable pyrethroid and an OP (pirimiphos methyl) has been proposed for bednet impregnation (65). But the persistence of these compounds is very different. Moreover the cost of a mixture should preferably not exceed the cost of the use of a single insecticide, which implies that the dose of each compound should be reduced in the mixture. On the other hand many vector control programmes maintain an insecticide pressure throughout the year. An insecticide pressure maintained only during the transmission peak period could be enough to decrease the disease to an acceptable level. In Burundi one spray round a year, with a low persistent insecticide (malathion) was successful in decreasing the disease without modifying the susceptibility of the vector after more than ten years of spraying (10). Therefore any vector control programme must be based on a sound knowledge of entomological and epidemiological conditions which prevail in the considered area. A regular monitoring of resistance must be done as an integrated component of the programme itself.

Specifications of the insecticides and equipment

Efficacy of any product used in public health depends to a large extent on the physical and chemical properties of the formulated compound. WHO specifications for pesticides meet the requirements of public health programmes and may differ in many respects from the requirements for pesticides used in agriculture. Every purchase order or request for bids should include the WHO specifications (64, and interim specification of WHO). A report of conformity of the batch to the WHO specifications should be send by an independent institution before the insecticide leaves the country of origin. This will be the only guarantee for a health programme to have compounds of good quality and acceptable from the safety point. In the same way, WHO specifications should be consulted for equipment used for the dispersal of insecticides (61).

Cost and cost-effectiveness

In Burundi, the cost of the insecticide used for indoor spraying is of 0.38 $, 0.50 $ and 0.56 $/inhabitant/round for respectively DDT, malathion, deltamethrin. Total cost including insecticides, manpower, transport, depends on the dispersion of the habitat, and thus the number of houses treated by one spraymen per day. For malathion, the cost per protected person rises from 0.6 $ to 0.9 $ according to 10 or 3 households that can be sprayed by one man per day (57).

The cost of bednets may vary from one country to an other, depending also on the quality, and size. In Burundi, a locally produced bednet costs about 9.5 $ and lasts for about 4 years, a bednet imported from Thailand costs about 4.5 $, transport cost included, and lasts for about 6 years. The estimated cost per protected person/per year with impregnated bednets varies from 1.8 $ for a local bednet to 0.6 $ for an imported one (57). In China, the cost has been estimated at 0.065 $/person/year compared to 0.15 $ with DDT house spraying (14).

The initial investment for a family to buy 3 to 4 bednets may be considerable. This may be overcome by introducing credit facilities, subsidized prices, and reduction of the taxe rates. On the other hand some studies, mainly in cities, clearly demonstrated that householders spend a relative high amount for less effective methods to control the nuisance of mosquitos. In 1990, a family in Kinshasa spent a medium sum of 5 $ in one month (68). In 1991, a household living in Douala (Cameroon) spent for vector control about 190 $, which represents more than two times the price of bednets for the entire familly (75 $) (32).

Based on the analysis of economical impact of malaria in Africa (53) the number of malaria cases was expected to rise for about 28% from 1987 to 1995. Direct cost (treatment) for the community will increase from 0.29 $ to 1 $ per capita, per year due to severity, chloroquine resistance, the use of more expensive drugs and the increased number of patients. Indirect cost (value of lost time due to morbidity and premature mortality) will increase in the mean time from 1.05 to 3.02 $ per capita.

If we assume that appropriate vector control measures may reduce 60% of the morbidity (7), as observed in several trials using impregnated bednets in Africa, we can spend 60% of the direct cost to vector control (0.6 $ per capita/per year) and 40% for case management (0.4 $ per capita). The total cost will then be reduced from 4.02 to 2.21 $ per capita per year which means a total cost reduction of 45%.

Conclusions

Vector control is an undisputed and integral component of a malaria control programme. Before the implementation of any vector control activity in countries of Category I (those that were not included in the efforts of the global malaria eradication programme to end the transmission of infection) it will be important to estimate the expected output on disease reduction in relation to the level of malaria stability. Operational feasibility should be evaluated in terms of human and financial resources, and acceptability in the communities. In countries of Category II (those in which large-scale programmes of house-

spraying with insecticdes have been in operation since the 1950s or 1960s), the existing control measures, although imperfect, may still contribute to limit the importance of the disease's burden. Most of these countries need reorientation and restructuring of their programme, but it is essential to implement the changes progressively in order to avoid an increase of the disease as a result of not well prepared activities performed or supervised by poorly trained personnel. These considerations lead to two of the main issues of vector control programmes: technical and human issues.

• From the *technical point* of view the arsenal of available insecticides and tools for the control of anopheline vectors is sufficient and effective. The need of new pesticides belonging to the existing groups of insecticides is certainly not the first priority. But there is a need for guidelines that should compare formulated compounds for persistence, mode of action, hazard, operational ease and cost. Specifications of the available insecticides should be updated. However new groups of insecticides with different modes of action are required to face resistance problems.

The efficacy of one vector control method in reducing the vectorial capacity will depends much more on the local vector ecology and behaviour, than on the choice of one particular insecticide. Frequency of application by scheduling spray or reimpregnation rounds should be synchronized with seasonal peak periods of transmission in considered area. Protection may be required for only a few months of the year. On the other hand vector control activities should be more confined to well-defined risk areas, rather than pursuing a total coverage programme encompassing all situations especially in areas with unstable malaria.

• From the *human point* of view two elements must be considered:

– Priority should be given to control methods where community involvement will be the greatest. However it should be remembered that personal protection is different from community protection which cannot be achieved unless a high proportion of the people can afford impregnated bednets and use them on a sustained basis.

– The main problem today, is the lack of "health engineers", who should also be involved in operational research. They must be able to conceive a strategy and to implement it at an operational scale and not only in pilot projects. They appeal to existing skills and knowledge, and should identify the most appropriate structure to implement the programmes. How could the communities, local health workers be fully involved in control activities if the insecticides have not been ordered or are of bad quality, if mosquito bednets are not available, if the proposed control method will not give the expected output, because it is not adapted to the epidemiological, social, economical situation? Sustainability begins here.

ANNEX 1:

Indoor sprays with residual insecticides
Calculation of dilution and speed of application

- the *dosage* (**D**) is the amount of active ingredient (=insecticide) applied per square metre of surface (g/m^2)
- the *concentration of a formulated insecticide* (**F**): expressed as a fraction. For example: 1 kg wettable powder (WP) of deltamethrin 2.5% contains 25 g deltamethrin.
- one liter of diluted insecticide ready for use allows to treat 22.5 m^2
  The amount of formulated insecticide per liter solution ready for use (**C**) can be calculated as follows:

$$C = (22.5 \times D)/F$$

Examples:

Insecticide	% a.i. (F)	dosage (D*)	Conc. (C**)	Conc. for 8 liters ***
DDT WP	50%	2 g/m^2	90 g/l	720 g
DDT WP	75%	2 g/m^2	60 g/l	480 g
Malathion WP	50%	2 g/m^2	90 g/l	720 g
Deltamethrin WP	2.5%	0.025 g/m^2	22.5 g/l	180 g
Deltamethrin EC	2.5%	0.025 g/m^2	22.5 ml/l	180 ml

a.i.:% active ingredient EC: Emulsifiable Concentrate WP: Wettable Powder

(*): dosage rate: active ingredient in g per m^2

(**): of the formulated insecticide

(***): usual volume of one tank

A standard type of compression sprayer (Gloria Rex 163, Hudson X-pert) equiped with a standard nozzle (TEEJET N° 8002) discharges at the standard pressure 0.760 l of spray per minute as a flat, fan-type spray, with a spray angle of 70°.

A distance of 45 cm is maintained between the nozzle and the surface to be treated. In one minute a sprayer must treat 0.760 l x 22.5 m^2 = 17.1m^2. About 15 cm of one swath should be overlapped to produce a uniform deposit. Training should continue until the spraying technique has been mastered.

A compression sprayer with a capacity of 8 liters allows to treat a surface of 180 m^2, which corresponds to the sprayable surface of a middle size house.

ANNEX 2:

Procedure for treating bednets

1. Calculate the surface (**S**) of a net (in m^2).

for a rectangular net:	example:
breadth (*b*)	1.5 m
height (*h*)	1.2 m
length (*l*)	2.0 m
$S = 2\,b\,h + 2\,h\,l + 1\,l\,b$	11.5 m^2

2. Determine the amount of water necessary to saturate a bednet (A). A cotton net absorbs more water than a nylon one.
   Example: In a container of 20 liters of water, 10 bednets are submerged; The bednets are taken out and excess of liquid are drained back, 11.6 liters remains in the container. The absorption of 10 bednets is of 8.4 liters of water, or 0.84 l per bednet.

3. Calculate the amount of formulated insecticide
   – *per bednet:*

   (S x D) / F

– *per liter solution ready for use (**C**):*

$$C = (S \times D) / (F \times A)$$

where:

C is expressed in g or ml of the formulated insecticide per liter water
S: surface of the bednet in m^2
D: the dosage rate of treatment expressed in g active ingredient per m^2
F: proportion of active ingredient of the formulated insecticide: example 0.025 and not 2.5%
A: amount of water absorbed per bednet expressed in liters.

	Formulation (F)	**Dosage rate (D)**
permethrin	EC 55%, 25%	0.2 – 0.5 g a.i./m^2
deltamethrin	WP 2.5%	0.015 – 0.025 g a.i./m^2
	E C 2.5%	
	CS 2.5%	
lambda-cyhalothrin	CS 2.5%	0.025 g a.i./m^2
	EC 2.5%, 5%	
	WP 10%	

WP: wettable powder
EC: emulsifiable concentrate
CS: capsule suspension (flow)

Example: For one bednet of 11.5 m^2, that will be impregnated with deltamethrin EC 2.5% at a dosage of 15 mg a.i./m^2, 6.9 ml – (11.5 m^2 x 0.015 g/m^2) / 0.025 – formulated insecticide is needed. Per liter of solution ready for use 6.9 ml / 0.84 l = 8.21 ml fomulated insecticide will be used. With one liter deltamethrin EC 2.5%, 143 bednets can be treated.

4. The calculated amount of formulated compound is mixed with water and bednets are submerged. Rubber gloves are used during treatment, contact with eyes and skin are avoided. Bednets are taken out and excess of liquid are allowed to drain back, without wringing. Place on flat non absorbant surface to dry. By hanging the nets some of the insecticide may be lost due to dripping. Excess of product should be limited, and are disposed on level ground away from water supplies or water courses.

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