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CHOICE OF METHODS FOR THE ATTACK PHASE IN MALARIA ERADICATION PROGRAMMES[1]

by

E. J. Pampana, M.D., Florence (Italy)

1. There is evidence that malaria transmission may be interrupted in tropical Africa, at least in some areas, by house spraying with residual insecticides. There is as yet no evidence of the interruption of transmission by the use of drugs alone.

> The successful projects have taken place in regions of various endemicities, from the unstable seasonal malaria of Swaziland to the hyperendemic areas of Uganda and the holoendemic areas of Liberia.

2. There is also sufficient evidence that interruption of transmission by house spraying with residual insecticides in tropical Africa cannot be obtained unless total coverage is ensured.

> This is of course a condition that would also apply to any attempt to eradicate malaria through drugs. It is easier, however, to obtain total coverage in house spraying operations than in direct mass drug distribution. It may well be that the reason drugs have failed to interrupt transmission anywhere is that total coverage of a sufficiently large population has never been achieved.

3. If it is foreseen that total insecticide coverage can be attained in a malaria eradication programme (m.e.p.), the question arises whether house spraying should be chosen a priori as the only, or the principal, method of attack in planning a malaria eradication programme, or whether it should first be tried in a pilot project before the method of attack is finally chosen. The following considerations are perhaps pertinent.

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4. In tropical forest areas, house spraying could, with great chances of success, be chosen as the single method likely to interrupt transmission, and consequently used for the attack phase. A pilot project would seem to be superfluous.

This opinion is based on the success of the pilot projects in South Cameroun (Yaoundé pilot project) and in Liberia (Kpain zone). The interruption of transmission was achieved in the two zones, and was associated with the disappearance of the vector species. A. gambiae and A. funestus disappeared entirely, while in the Yaoundé project the density of A. moucheti and A. nili also decreased enormously, adults being very rare or entirely absent, although larvae of both species persisted. The factors that could explain the success of house spraying in tropical forest areas, such as those of the two projects quoted, are that in both the forest does not lend itself to producing abundant breeding places, that the inhabitants generally remain indoors after dark, that no domestic animals exist near the houses (although wild animals, besides rodents and birds, may exist in the forest), so that the main vectors, A. gambiae, A. funestus and A. moucheti, can more easily feed indoors than outdoors.

5. In savannah areas, the projects which were successful in interrupting transmission - or, more exactly, in bringing the infant parasite rates down to zero - were either accompanied by a change in the habits of the main vector, A. gambiae, or simply by some decrease in density or perhaps disappearance of the vectors (as was the case in Kigezi highlands, Uganda), and probably by a lowering of their average duration of life.

5.1 Infant parasite rates were brought down to zero, as a consequence of a change in the habits of the vector, i.e. the deviation of A. gambiae from man to animals, from indoor resting and feeding to outdoor resting and feeding, in some areas of the southern savannah of Africa (Swaziland, Southern Rhodesia, Transvaal). In all these areas, which are at the limits of tropical Africa, malaria is mainly seasonal, and, particularly in Swaziland and Transvaal, of an unstable rather than a stable character. Before spraying, A. gambiae used to frequent houses; after some rounds of spraying this vector disappeared from houses but could still be found in great numbers outdoors, feeding entirely, or mainly on animals.

There are two hypotheses to explain this deviation from man. The first one supposes that the irritability due to the insecticide has caused the survival of the most irritable females so that, if this hyper-irritability has a genetic character, the progeny would be highly irritable and would therefore avoid sprayed surfaces, the population would have become exophilic and would therefore have more chance of feeding upon animals than upon man. It should be emphasized, however, that the programmes where this deviation from man was achieved were based on applications of BHC, which is much less irritant to mosquitos than DDT. The second hypothesis supposes that, prior to spraying, the A. gambiae population was a mixture of two populations, one primarily zoophilic and exophilic, the other anthropophilic and endophilic. House spraying would destroy the latter, while the former population would survive.

On the basis of the evidence one would think that in other savannah areas of Africa with epidemiological conditions similar to those of Transvaal, Swaziland or Southern Rhodesia, house spraying should be the method of attack, particularly if the insecticide chosen ensures high mortality and little irritation of the vectors. (An irritant insecticide would allow the survival of the hypothetical anthropophilic fraction.)

One wonders, indeed, whether the deviation from man, observed in A. gambiae in these areas, was not largely due to the fact that BHC, and not DDT, had mainly been used. We would go as far as to say that, in conditions comparable to those of the above areas, BHC - or perhaps dieldrin - could be chosen for the phase of attack without the necessity of having a pilot project.

5.2 But infant parasite rates were also brought down to zero in some savannah areas without achieving the deviation of the vector to animals. This happened, for example, in the Kigezi project, Uganda, and in some areas of Sudan (and probably, at least temporarily, in some localities of Somalia) - all areas where malaria was not holoendemic.

> One may consider that the successful savannah projects, besides originally having an intensity of transmission lower than the holoendemic level, were also, perhaps, characterized by some favourable circumstance which may have been absent in other projects which were

unsuccessful. It is true that in the case of the successful Kigezi project people do not sleep outdoors, and huts can be and are closed after 9 p.m. They seem to consist of non-sorptive material; there are no field shelters in the area and the spraying operations covered not only all the inside walls, but also the "ingress surfaces", i.e the eaves, and the outside surfaces of doors and windows, which certainly increased the risk to the mosquito entering or leaving the room.

In the Blue Nile province of the Sudan the area was, however, one where there were many movements of people (nomads or seasonal labour) and an abundance of field shelters, but, as in the case of Kigezi, there was very little chance of outdoor man-biting because the vector was only exceptionally found outdoors. It is this last finding which would easily explain why the infant parasite rate reached zero wherever total coverage was achieved at the appropriate time.

In epidemiological conditions similar to those prevailing in these two projects - and in which we believe a common denominator was the absence of outdoor man-biting at night[1] - one would think that total coverage spraying could be chosen as the method of attack, without a pilot project, provided that migrant tents and field shelters were also efficiently dealt with, if they exist.

6. But we are not aware of infant parasite rates having been brought down to nil in any lowland, tropical, holoendemic, savannah project.

In the summer of 1960 a Secretariat meeting was convened in Geneva to review the African projects. All the failures to interrupt transmission were attributed by the meeting to lack of total coverage. The meeting, indeed, expressed the hope that the project then going on in the North Cameroun, if total coverage were really obtained (DDT twice a year) would succeed in interrupting transmission. It did not - not even in the two sectors where the attack was strengthened by mass drug distribution, carried out once or twice during the year and involving a high proportion of the population (90 per cent.).

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[1] At least in the sprayed area as in the Sudan.

But why did this project fail and why did two other closely studied projects, those of Bobo-Dioulasso and Taveta Pare, also fail? Do they show that house spraying definitely cannot interrupt transmission in lowland tropical savannah areas where transmission is very intense?

In analysing the three projects, one realizes that it cannot be ruled out that some modification of technique might have achieved success.

> In two cases, for example, it is doubtful whether total coverage was indeed attained and certainly the eaves, porches and the external sides of doors and windows were not sprayed; such spraying could be very important where vectors bite man outdoors also. Some field shelters were left unsprayed in one project and in both the problem of movements of groups of people was not dealt with satisfactorily.
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> As regards the North Cameroun project, the records show that after the first total coverage spraying (April/May 1960), vector density was greatly reduced. The vectors came back in August, some new cases of malaria were found in September, and a high rate of transmission was noted in November. One's reaction is to wonder, if, three months after spraying, the anopheline density starts to increase again, a new spraying could not be successful? After all, de Zulueta sprayed DDT every four months in the successful Kigezi project, where malaria transmission was naturally less intense than in the North Cameroun. In the latter, moreover, domestic and wild animals abound, people sleep outdoors during the hot months, and both A. gambiae and A. funestus bite man outdoors. And in Northern Nigeria it was concluded that DDT 2 g/m^2 twice a year was perhaps not sufficient to produce adequate mortality of A. gambiae.

7. Lowland holoendemic savannah areas, where vectors are not entirely endophilic, will often be subject to extradomiciliary transmission, hence the advisability of bringing the indoor vector kill to the highest possible level, and also of spraying the outside surfaces of the houses where vectors are liable to rest before or after feeding outdoors. As a corollary, spraying may have to be done more than twice a year, as it should be repeated whenever indicated by entomological data, and while

no part of the interior surface should remain unsprayed, the eaves, porches and the outdoor surfaces of windows and doors should also be sprayed. It will be remembered that in very severe conditions of transmission Macdonald & Davidson (1953) estimated that a daily mortality rate of 85 per cent. of mosquitos coming indoors is required to interrupt transmission.

If it cannot altogether be excluded that vectors enter houses and that total insecticide coverage can be attained, then it cannot be excluded that the method of attack to be chosen - for holoendemic tropical lowland savannah areas also - should be house spraying, either alone or aided by mass drug distribution. But we feel that the method should be tried in a pilot project area, or in more than one before the method to be used in the attack phase is decided upon. This would be an expensive approach, but less expensive than failure in a malaria eradication programme.

8. If house spraying is chosen, which insecticide should be selected?

In recent years, largely on account of the development of resistance and of its toxicity, dieldrin has lost much of the popularity it enjoyed some years ago. BHC, both due to the danger of developing resistance to the BHC/dieldrin group, and also, even more important, because of its short residual activity, has never been very popular. Phosphorus insecticides are now being tested in the field in malarious areas; the one that may indeed represent the best insecticide in the near future, DDVP, has not yet reached the stage at which it can be tried in the field, consequently, it seems to be taken for granted that DDT mainly should be used in the near future.

We are not so sure that this is always the best course. It is more difficult to obtain a daily mortality of 85 per cent. with DDT than it is with dieldrin or BHC in the case of A. gambiae, which is so much irritated by DDT. Further, a smaller number of mosquitos enter DDT-sprayed huts. DDT may achieve success in spite of irritability - and a consequent lowering of room-kill - if the vectors of the area are highly endophilic or if the inhabitants do not spend the night hours outdoors, for the mosquitos would either be killed indoors, or, if chased away, would be prevented from transmitting the infection. Consequently a lower daily

mortality rate would be sufficient to interrupt transmission, even when this is severe. But in savannah areas in the plains such behaviour would be exceptional; mosquitos chased away by their reaction to the irritant insecticide might survive outdoors and from time to time give rise to extradomiciliary transmission. It follows that non-irritant insecticides are preferable. Where dieldrin resistance is absent we wonder, therefore, whether it would not be advisable to start spraying with dieldrin rather than with DDT. Of course we must be sure that the dosage and timing of the cycles of dieldrin are appropriate. Dieldrin spraying might perhaps be limited to one or two years, should resistance appear, but the shock action of dieldrin should not be wasted.

Neither dieldrin nor BHC resistance has so far been found, as we all know, in the eastern half of Africa (except in the case of A. pharoensis) and south of Pointe Noire. There would therefore be a large field for the initial use of these insecticides. Further, according to recent findings, it would seem that, even where dieldrin resistance is present, BHC might still be used.

9. Drug administration

If it is foreseen that total coverage by insecticide is impossible, or that, even if attained, it could not interrupt transmission, then mass drug administration should be considered.

Mass drug administration can be direct or indirect. For the first, every individual in a population should take regularly, at the prescribed intervals, the appropriate dose of anti-malarial; for the second, all the population, except the youngest age-groups, take the drug in a staple food additive, which so far has always been common salt (Pinotti's method).

9.1 Mass drug administration as the sole method of attack

We feel that direct mass administration of drugs at present available could not be chosen as the sole method of attack for malaria eradication. If drugs were regularly administered (possibly weekly) to the whole population, transmission could certainly be interrupted, but such total coverage is possible only in very small and well-controlled communities, and therefore cannot be considered for a malaria eradication programme.

One of the most recent attempts to interrupt transmission by means of direct mass drug administration alone, in a holoendemic savannah area, is that made by Clyde (1961). Even in the areas where the drug was given every week (amodiaquine plus primaquine) for 39 weeks there was an infant parasite rate of 5.3 per cent. at the end of the treatment, and the sporozoite rate in the vectors (A. funestus and A. gambiae) was still 0.9 per cent. The author succeeded in treating, in this particular zone, perhaps never less than 93.8 per cent. of the total population; he feels that more than 97 per cent. of the population should receive unbroken treatment to attain interruption of transmission. This is practically impossible.

Indirect mass drug administration, i.e. medicated salt distribution, might be chosen as a method of attack, when insecticides are not being applied, provided that:

(a) no unmedicated salt is used for human consumption in the area;

(b) the daily "exogenous" salt intake of the population is known, is more or less regular, and no pre-salted conserves are consumed, so that the prescribed quantity of medicated salt is regularly ingested;

(c) the medicated salt is palatable, does not leach out, and is either distributed free or is at least sold at a price no higher than unmedicated salt;

(d) provision is made in the plan that children below the age at which their diet would contain an adequate amount of medicated salt, are under special surveillance, starting at the beginning of the medicated salt distribution, so that they may be immediately radically cured should they show malaria, or be submitted to direct controlled suppressive treatment wherever indicated.

Although no evidence exists so far - anywhere - that medicated salt alone can interrupt transmission, if the scheme outlined above can be strictly applied, medicated salt could be the method of choice in an area where transmission is carried on by vectors which never rest indoors or where total coverage by insecticides is not possible.

9.2 Mass drug administration as an adjuvant to insecticides

Medicated salt distribution would also appear to be the best adjunct to house spraying with residual insecticides where these alone cannot interrupt transmission. It would seem that even without strict surveillance of the children as would be required above in the absence of insecticides, medicated salt distribution might help to reduce the parasite reservoir so quickly that it would be very difficult for the few surviving mosquitos to become infected. But this possibility has not yet been demonstrated, so that a pilot project would be required.

Direct mass drug administration would be the second best adjuvant. There is no evidence, as far as we are aware, that it has interrupted transmission where insecticides alone have not. But it should certainly help even if the drug is administered only at the time of the spraying rounds by the spraymen or their foreman. From the Kigezi experience it seems likely indeed that this method at least contributed to the rapid deduction of the parasite reservoir. As this type of distribution does not create major administrative problems, one wonders whether it should not be systematically used in those holo- or hyper-endemic savannah areas where it is foreseen that interruption of transmission will be difficult. This would apply also to the pilot projects which we believe are indispensable in many savannah areas.

It seems however that mass drug administration as an adjunct to house spraying may facilitate interruption of transmission only if house spraying per se brings that goal very near.

In the Haute-Volta, Bobo-Dioulasso experiments, mass distribution of choroquine and pyrimethamine once every three weeks, on eight occasions, did not interrupt transmission. This however does not preclude the possibility of success by another method, for instance, if, in addition to two (or more) rounds of DDT spraying a year, a fortnightly distribution of the drugs had taken place during one full year, or weekly distribution during the most dangerous six months. Obviously methods in these difficult cases must be tried in a pilot project.

10. As a summary of this paper the following table is presented:

A TENTATIVE SCHEME FOR THE CHOICE OF THE METHOD OF ATTACK

1. Vectors do come indoors and total coverage by insecticide house spraying can be achieved 2
   Vectors never do come indoors or total coverage by insecticide house spraying cannot be achieved 4

	Method of attack to be chosen
2. (a) Tropical forest area	House spraying alone (DDT or others) -
(b) Savannah areas	
b.1 South of 16°S with seasonal malaria, with epidemiological conditions like Swaziland	House spraying alone, preferably with BHC
b.2 In other parts of tropical Africa	
b.2.1 Where a transmission is lower than a holoendemic level, there is no significant outdoor man-biting by the vector; the problems of field shelters and of migrants either do not exist or can be solved	House spraying alone, perhaps assisted by direct mass drug administration at the time of spraying ..... -
b.2.2 Where conditions differ from b.2.1	House spraying, assisted by direct mass drug administration at the time of spraying; to be tried first in a pilot project 3

3. If the pilot project achieves interruption of transmission, apply the method to the attack phase ..... -
   If the pilot project does not achieve interruption of transmission 4

4. Apply indirect mass drug administration. If all the conditions for the success of the scheme are fulfilled as listed on page 8 this method alone might be sufficient ..... -
   But if such conditions do not apply 5

5. In such circumstances, it seems advisable to have a combination of house spraying plus medicated salt; should be tried first in a pilot project 6

6. (a) The pilot project achieves interruption of transmission; apply the method to the attack phase ..... -

   (b) The pilot project does not achieve interruption of transmission; it would be advisable to wait until new insecticides or drugs promise better results, rather than attempt a phase of attack based on other methods - like antilarval methods which are not likely to be applied with the coverage and periodicity required to interrupt transmission. -

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