# B. TRANSMISSION FACTORS RELEVANT IN MALARIA VECTOR CONTROL PROGRAMMES

## Introduction

During the fifties, most countries adopted a strategy of malaria erad ication rather than malaria control. This was justified by the fact that a once-only capital investment could finally eliminate a serious disease with great economic and social impact. The eradication strategy was based mainly on the use of residual insecticides, like DDT, in order to stop transmission by the Anopheles vectors. It was foreseen that the vector control activities would be maintained until the reservoir of infective cases was exhausted. This strategy required that eradication should be achieved within a limited period of time, before insecticide resistance could appear (Najera 1989). Some success was achieved in temperate areas; but resurgences occurred in many other countries during the consolidation and maintenance phase.

At the Kampala conference (1950), no unanimous decision was reached about the undertaking of control measures in tropical Africa, because of the danger of disrupting the balance between the parasite and the host which gives the human population a high degree of protective immunity. However this balance is not perfect; and protective immunity is acquired at the price of high infant mortality (Swellengrebel, 1951). During that time only pilot projects were organized in tropical Africa. Local interruption of transmission was obtained in some forest areas of Cameroon and Liberia, on the high plateaux in Uganda, and in Zaire (Katanga, area of Elisabethville). However complete failure was observed in the savannah areas of East and West Africa, the coastal zone of East Africa and Madagascar (Hamon et al.,1963, Vincke et al.,1966).

The idea that malaria could be eradicated within the foreseeable future became unrealistic. At the end of the seventies, malaria control, aiming at least to reduce mortality, became a part of primary health care. But an effective peripheral health infrastructure was not implemented in most of the countries; and the malaria situation deteriorated in the eighties through lack of early diagnosis and prompt curative treatment. Moreover, major ecological and social changes alter the epidemiological position, and vector control activities were abandoned in most African countries (Coosemans, 1991a). The Global Malaria Control Strategy adopted at the Ministerial Conference on Malaria in Amsterdam (1992) represents a crucial step in reactivating national malaria programmes. The strategy includes the planning and implementation of selective and sustainable preventive measures, including vector control. To plan appropriate control measures a good knowledge is required of the local factors determining the transmission of malaria.

*Definition of the basic reproduction rate and vectorial capacity*

The malaria infection of one person has a very great multiplication potential through the vectorial system. a) The possible number of secondary infections as a direct result of one single case is, in classic malariology, expressed by the *basic reproduction rate* of Macdonald (1957), assuming that the population is fully receptive and thus non-immune (fig 3).

Fig. 3 – Basic reproduction rate (Zo) and vectorial capacity (VC)

$$Zo = b\,\frac{2\ n}{m\ a\ p}$$

$$VC = r\,\frac{1}{(-Ln\ p)}$$

m : man-biting rate
a : man-biting habit
p : daily survival rate
1/r : days of infectivity per case (gametocytes)
b : proportion of successful inoculations
n : sporogonic period (12 days for *Plasmodium falciparum* at 25° C)

This model is the expression of a never realized potential, except at the onset of an epidemic. In an area with stable malaria (see p. 1455), this rate may reach several thousands.

b) In this same model, the *vectorial capacity* is the reproduction rate of the infection per day.

This model has been conceived with the prospect of eradication; and, due to immunity, it gives no indication of the expected decrease in malaria morbidity, which is a priority objective of malaria control in a major part of the world and particularly in Africa.

The basic reproduction rate has the advantage of breaking down the different entomological and parasitological factors involved in malaria transmission and of showing their relative importance. However, it is only a model allowing to attract the attention on its components, in the study of their influence on the transmission of the malaria infection. The model should therefore not be applied as a mathematical formula. Nevertheless, it shows that a vaccine against gametocytes would be ineffective to protect the members of a community.

On the other hand, we actually know that the assumed habits of the mosquito and the human host were oversimplified (Molineaux, 1988). Estimates of the different parameters are biased because of sampling problems and the use of rudimentary techniques, like dissection of the ovaries in order to estimate the survival rate of the vector population (Najera, 1974).

*Transmission factors*

The review of the different factors contributing to malaria transmission shows a relation with malaria epidemiology (stable and unstable malaria, see p. 1455); those factors explain what may be expected from vector control programmes in different epidemiological situations.

## 1. Human carriers and their infectivity

The gametocyte reservoir, essential link for transmission, has a relatively limited weight compared to the entomological factors, summarized in the formula of the reproduction rate. However, little information is available on the intrinsic physiological variability of the infectivity of *Plasmodium falciparum.*

In regions with seasonal transmission, with a prolonged dry season, strains of *P. falciparum* with a long duration of infectivity present a selective advantage over strains with a short one, which are unlikely to be transmitted from one transmission season to another. In regions with continuous transmission, this selective process will not be required (Carnevale and Mouchet, 1980). On the other hand, the adaptation of the parasitological cycle to different local climatic conditions has been well documented for *P. vivax* (Bray and Garnham, 1982).

Recently it has been argued that chloroquine pressure may have selected genotypes of parasites with high short-term infectiousness. Lines et al. (1991) observed, in Tanzania, a 2.5% increase in human infectiousness in the last 25 years, probably as result of chloroquine pressure, and estimated that about 21% of blood-meals were infectious for the mosquitoes.

## 2. Entomological factors

Entomological factors are influenced by the natural environment, but adaptation of man to his environment is certainly more determinant (Coosemans and Mouchet, 1990).

### 2.1. *Vector density*

The vector density in relation to humans will depend on the type of breeding places and their distance from the human habitat. The nature of breeding-places for species of the *Anopheles gambiae* complex, such as shallow open sunlit pools, insures a wide distribution of these species in tropical Africa. Even every footprint is a potential breeding place. The most productive breeding places for *An. gambiae* are semi-permanent sites, regularly excavated, like bored pits and rice fields. The extent and the erratic character of the breeding sites of *An. gambiae* make in many cases larval control impracticable, so much the more that the chemical or biological insecticides have a short active life.

However ecological changes call for particular attention. In the primary forest, sunbeams do not reach the ground, while vector density and thus malaria are increased if the forest is cleared (Mouchet, 1976).

In northern Somalia, cisterns are permanent breeding places; and, since no other breeding places are available, larval control using fishes combined with drug administration has been successful (Alio et al., 1985).

### 2.2. *Man-vector contact*

The frequency of contact between man and vector is a much more important factor of transmission than vector density. It involves two components: the duration of the gonotrophic cycle (fig 4 on p. 1482) and the man-biting habit. The gonotrophic cycle in optimal conditions is about two to three days (Carnevale et al. 1979)

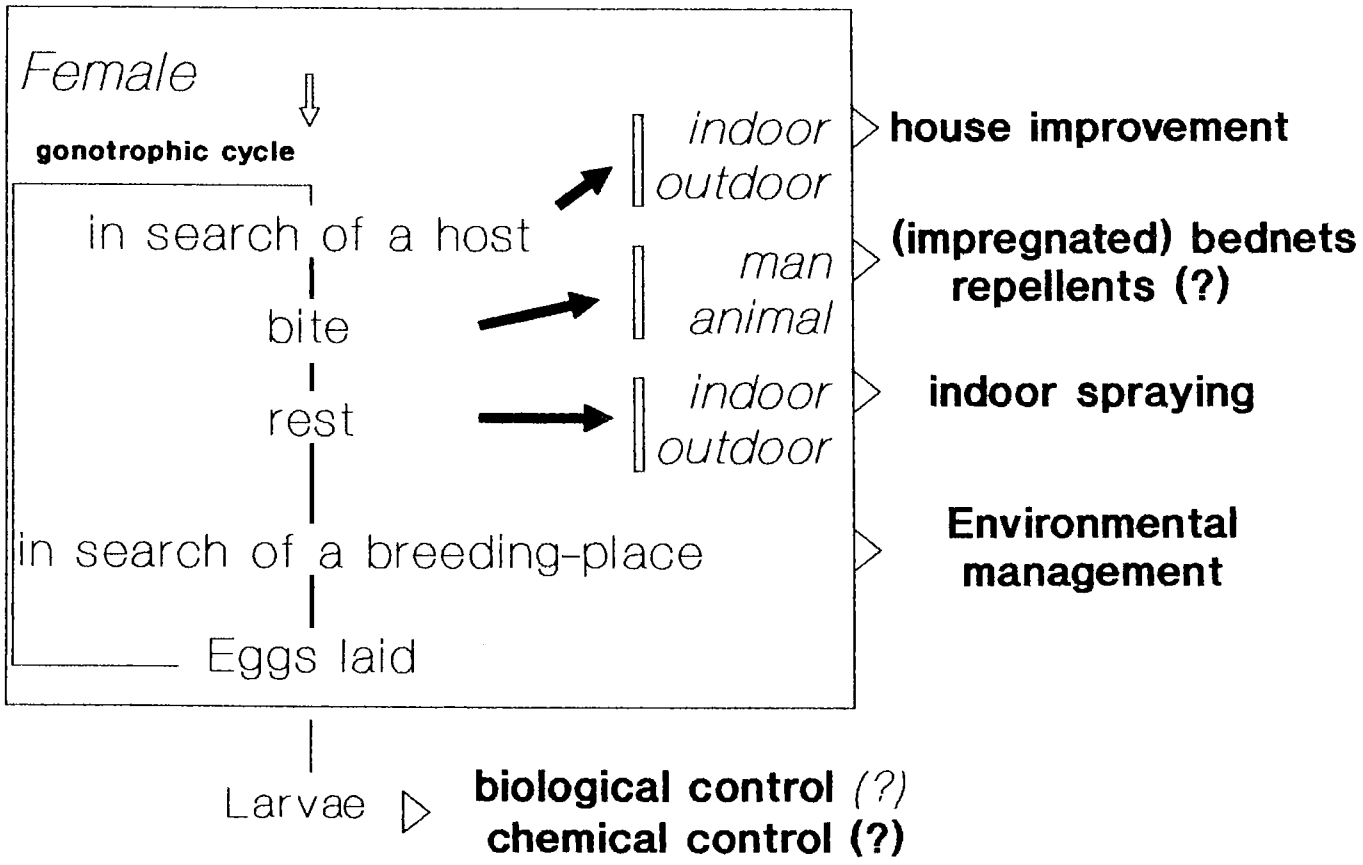



Fig. 4 – Gonotrophic cycle of mosquitoes and vector control measures related to vector behaviour

Gonotrophic dissociation may be observed during the dry season. In the absence of breeding places, mosquitoes survive at the adult stage and take blood-meals but the laying of eggs seems postponed until the first rains (Omer and Clodsley-Thomas, 1970); this has still to be confirmed.

The man-biting habit varies for each species, but also depends on the availability of alternative hosts. *An. funestus* is highly anthropophilic (94 to 100%). This behaviour is also associated with a high degree of endophagy and endophily, which explains the high reduction in this species after indoor spraying. *An. gambiae* and *An. arabiensis* are largely anthropophilic, although *An. arabiensis* is less anthropophilic when cattle-feeding opportunities also exist. Since cattle often stay outdoors, it is not surprising to find a considerable proportion of *An. arabiensis* biting and resting outside where residual insecticides have no impact. In an urban area of Senegal, where domestic animals are absent, *An. arabiensis* takes its blood meals almost exclusively (99%) on man (Vercruysse et al.,1983). In Burundi on the contrary, the presence of herds in the villages deflects about 30% of *An. arabiensis* onto cattle (Coosemans et al., 1989). This zoophilic tendency of *An. arabiensis* partly explains the difference inf sporozoite rates observed between *An. gambiae* and *An. arabiensis* in regions where those species are found together (Gillies and Coetzee, 1987).

In the Kisumu area of Kenya, Highton et al. (1979) observed different sporozoite rates for both species; while Joshi et al. (1975), in the northern part of the same region, observed similar sporozoite rates. Those differences are explained by the man-biting habit of the vectors (table 1).

Table 1: Influence of the host choice on the sporozoite rate in Kisumu (Kenya)

| | Highton et al. 1979 | | Joshi et al. 1975 | |
|---|---|---|---|---|
| | *An. gambiae* | *An. arabiensi* | *An.gambiae* | *An. arabiensis* |
| Proportion of species | 10% | 90% | 75% | 25% |
| Human blood index | 92% | 39% | 6% | 3% |
| Sporozoite rate | 5.3% | 0.3% | 8% | 7.5% |

In the South of Cameroon, it has been possible to eliminate *An. gambiae* temporarily by indoor spraying. Cattle were absent and the Anopheles had no other choice than to bite man inside the house where they came into contact with the insecticide (Livadas et al., 1958).

In West Africa, the low rate of transmission close to the mangroves is explained by the low man-biting habit of *An. melas* (Bryan, 1983).

### 2.3. *Longevity of the vector*

Malaria transmission by a vector will be possible only if the longevity of the vector is sufficient to complete sporogony. The great stability of malaria in the major part of Africa is due to high longevity of *An. gambiae* s.l. and *An. funestus,* combined with a high anthropophily.

Seasonal and climatic variations affect the survival rate of vectors; but density has a regulating effect on longevity which is probably very important and not well understood. For a certain level of density, there is an inverse relationship between density of vector population and survival rate, and thus the sporozoite rate. A high survival rate, and thus a high transmission, can be observed when the vectorial population decreases. This phenomenon has been observed near irrigated schemes. Highly dense vectorial populations being made up of a large proportion of young females, it is normal that high seasonal density should be associated with a low incidence rate of malaria.

In the rice-field area of Burundi, *An. arabiensis* is abundant during the rainy season (9 months) without any effect on parasitic incidence. It is only at the end of the rainy season that the vectorial capacity is raised as a consequence of the increase in longevity of the vector, which caused an important rise in parasite incidence and in frequency of clinical malaria during the dry season. The study of seasonal variation makes it possible to develop anti-vectorial control using a minimum amount of insecticide at the moment of increased longevity (Coosemans, 1985, 1991b). On the contrary, the survival rate is constant and high in a stable vectorial population, such as those observed in degraded forest (Carnevale et al. 1985) or in savannah (Molineaux and Gramiccia, 1980; see also fig. 5 p. 1485).

In Burkina Faso, Robert et al. (1985) observed similar sporozoite rates for *An. gambiae* et *An. funestus*; however these vary considerably in the same region depending on the kind and the availability of semi-permanent breeding places (table 2).

Table 2: Sporozoite rates (yearly average) according to breeding places in Burkina Faso (Robert et al. 1985)

| | Savannah without semi-permanent breeding places | Savannah with semi-permanent breeding places | Rice fields |
|---|---|---|---|
| *An. gambiae s.l.* | 4.8% | 1.7% | 0.5% |
| *An. funestus* | 4.6% | 2.1% | 0.6% |

These results may suggest that the occurrence of permanent breeding places facilitates the oviposition by the females, but acts negatively on their survival rate. If this is true, then the use of the rate of parity to estimate the survival rate is not appropriate. In Papua New Guinea, Charlwood et al (1988) suggest that the search for a permanent breeding place by *An. farauti* involves some form of memory on the part of the mosquito. Similar studies do not exist for *An. gambiae*. In the laboratory, preliminary results show an increase of the survival rate of females in the absence of laying-places compared to females allowed to lay eggs (Coosemans, pers. comm.). In these conditions environmental management to reduce *high* vector density could increase transmission by enhancing vector longevity.

### 2.4. *Polymorphism of the malaria vectors*

The species of the *gambiae* complex present a great ecological plasticity. In West Africa, there are several chromosomic forms of *An. gambiae* and *An. arabiensis*. When relative humidity decreases, *An. arabiensis* is usually dominant, and well established in coastal towns due to a particular chromosomic form (Coluzzi et al., 1979).

In Mali several taxa of *An. gambiae s.s.* can be present in the same locality, but the seasonal abundance of these different taxa presents important variations (Colluzi, 1984). The Mopti form or taxon of *An. gambiae* is particularly well adapted to rice fields (Touré, 1989; Robert et al., 1986). Hybrids between the different taxa are not frequent (particularly between Mopti and Bamako), but it is not clear how these different taxa maintain themselves from one season to the other (Touré, pers. comm.)

In Nigeria, Coluzzi et al. (1979) observed an association between resting behaviour (exophily or endophily) and certain chromosomal inversions suggesting a genetic mechanism involved in the behavioural modulation of the vector and non-uniform exposure to insecticides, but so far no specific behavioural selection by indoor spraying could be observed. This high level of polymorphism in West Africa is less pronounced in East Africa and could explain the greater impact of insecticides in Kisumu, Kenya and more recently in the Rusizi Valley in Burundi (Coosemans, 1991), compared with the disappointing results obtained in the West African savannah (Molineaux and Gramiccia, 1980: Garkin, Nigeria and the pilot zone of Bobo-Dioulasso, Burkina-Faso).

### 2.5. *Refractory strains of vectors*

In the laboratory it has been possible to select strains of *An. gambiae* refractory to infection (Collins et al., 1986). In the field, however, the consistent increase of the sporozoite rate with age of *An. gambiae* females implies the absence or rarity of genetic refractoriness to infection (Lines et al., 1991). Observing a low sporozoite rate (0.58%) after immediate dissection, *Vincke* (1965) determined delayed sporozoite rates: sporozoite rate reached 14% two weeks after capture, suggesting that no intrinsic refractory mechanism was involved.

### 2.6. *The particular situation on the high plateaux*

The greatest changes in malaria transmission in this environment have occurred since the end of the years eighties. In highland regions, the emerging of vectors is often a recent phenomenon. In Burundi and Rwanda, the rural development of papyrus marshy valleys, and the settlement of concentrated populations close to these valleys, are responsible for proliferation of *An. gambiae* or *An. funestus* which leads to dramatic epidemics. In these regions, the temperature often drops below 15°C, stopping the development of the parasite in the mosquito. However *An. gambiae* and mainly *An. funestus*, through their endophilic behaviour, found the appropriate temperature inside houses or in shelters (Jadin and Fain, 1949). Indoor spraying in these regions has been very successful (Munyantore, 1989; Meyus et al., 1962, Jadin et al., 1952, Delacollette et al., 1990). On the other hand, global warming may be responsible for malaria epidemics in these areas. In Rwanda, a peak in temperature observed in 1987 coincided with a high mortality due to malaria. This may partially explain the epidemics on the high plateaux of Madagascar.

## 3. **Relation between transmission and malaria infection or malaria disease**

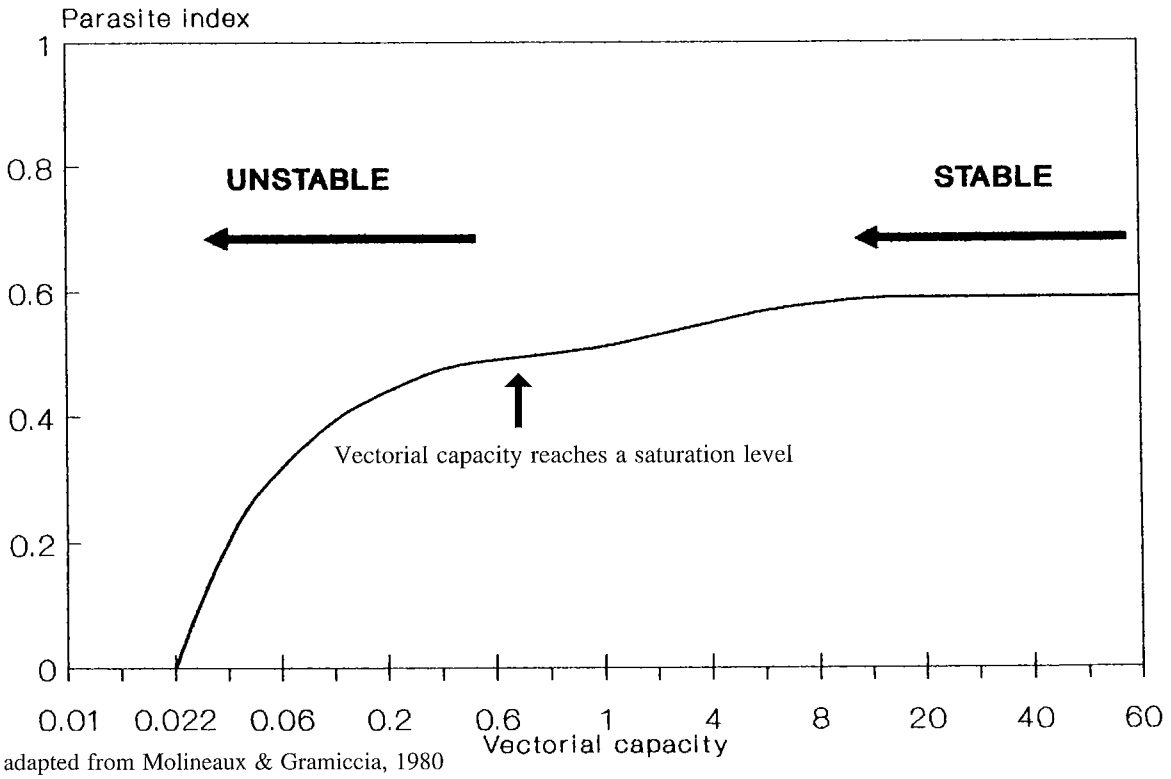
The relationship between vectorial capacity (VC) and malaria prevalence is relatively well known. A non-zero critical value of the VC is required below which malaria cannot maintain itself.

– In a region with *unstable* malaria the VC is close to this critical value, and relatively small changes in VC will produce large changes in prevalence. The lack of contact with the parasite, and thus the absence of immunity, will translate every increase in transmission into epidemics with high morbidity and mortality rates.

– In a region with *stable* malaria, the VC is far above the critical level and even large variations in VC will hardly change the prevalence. Protective immunity is well developed at the age of five years. Adults develop no clinical symptoms. Malaria disease appears in infants (Molineaux, 1988).

In tropical Africa, the high level of transmission and thus the stability of malaria is mainly the result of the mosquitoes of the *Anopheles gambiae* complex and the *An. funestus*. The preference for human hosts and the high longevity of these mosquitoes make them the most efficient vectors in the world (fig. 5, see next page).

The main objective recommended nowadays by WHO is the reduction of malaria morbidity and mortality by treatment of presumptive attacks of malaria. This activity is carried out by peripheric health centres and by self-treatment of the population. Vector control has so far been recommended in areas where sustainable reduction in malaria prevalence is an additional goal, but this limits vector control to regions with unstable malaria. To achieve the first objective solely by chemotherapy is becoming difficult due to increasing drug resistance.




adapted from Molineaux & Gramiccia, 1980

Fig. 5 – Relation between parasite index and vectorial capacity

The remaining basic question is to know the relation between transmission (intensity, distribution) and malaria-related morbidity and mortality. Does vector control reduce malaria morbidity in areas with stable malaria?

The principal difficulty is certainly to measure objectively the duality of specific malaria mortality and morbidity.

*Examples of vector control projects*

Vector control methods have to be adapted to vector behaviour (Fig 3, p. 1480).

Research projects on the control of malaria have been carried out in different geographical areas of Africa. Evaluation of vector control measures takes into account not only their impact on the endemicity, but also their impact on the disease.

In Kisumu, Kenya, eight indoor spraying rounds with Fenitrothion in two years reduced the parasitic incidence by 96% (Payne et al., 1976). A new equilibrium was reached with a malaria prevalence of 6%. After two years the general mortality was reduced by 44%. This high reduction cannot only be explained by specific anti-malarial measures; a better medical and social coverage probably contributed to improve health in general (Carnevale and Vaugelade, 1987).

In the study area of Garki, Sudan Savannah in Nigeria, three to four annual spraying rounds with Propoxur reduced the vectorial capacity by 90%; however the malaria prevalence decreased only by 25%. At the same time, it was observed that the sporozoites introduced by mosquito bites were more successful in establishing patent parasitaemia than before intervention. In the control villages, infant mortality rates and parasitic incidence were strongly correlated throughout the year. In villages treated with Propoxur only, the seasonal correlation of these two parameters disappeared, and mortality decreased much less than the incidence (Molineaux and Gramiccia, 1980).

The poor results on prevalence in Garki were attributed to the high initial transmission level and to non-uniform exposure of *An. gambiae s.l.* to the insecticide, which is explained by the exophilic behaviour of certain chromosomal variants. This was not the case in Kisumu (Kenya), where the *An. gambiae* population is much more endophilic and characterized by a low chromosomal inversion polymorphism. From the results in both areas, an indicator of resting behaviour (the pre-spraying ratio of indoor man-biting rate on the anthropophilic fraction of the residual density of the vector)

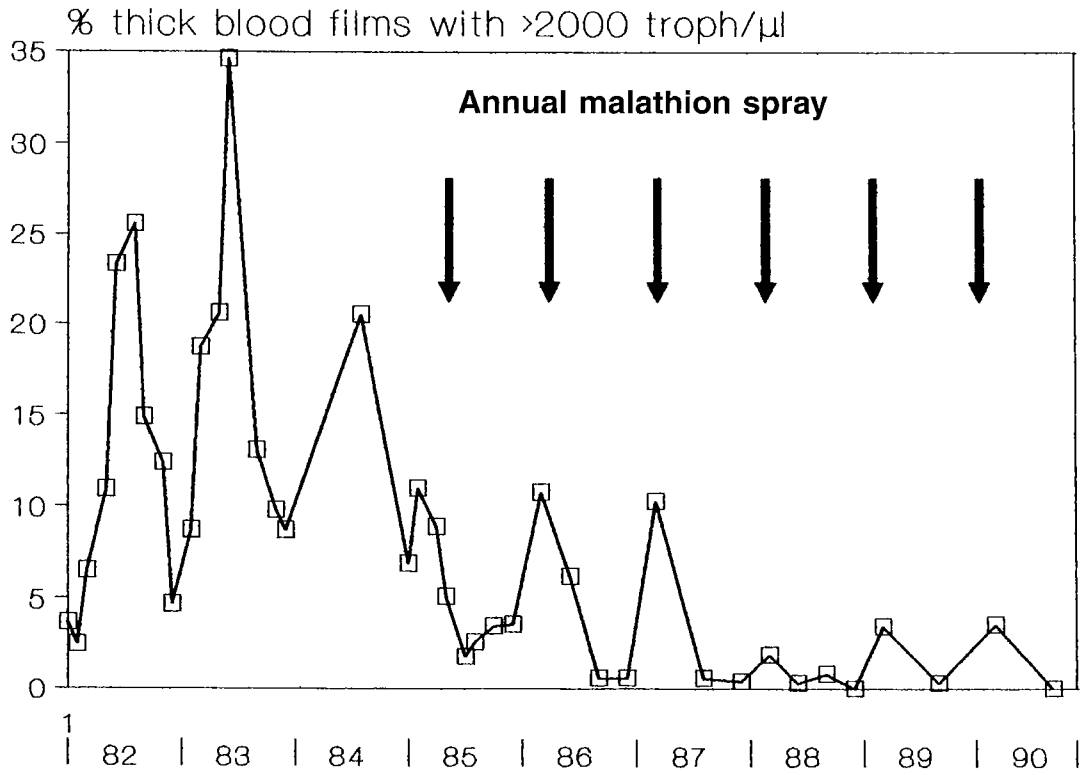



Fig. 6 – Percentage of positive children below 5 years with high parasitaemia of *P. falciparum*, before and during the intervention phase in a rice field area of Burundi, 1982-1984 (from Coosemans et al.)

The intervention was limited to one spray campaign per year with malathion (2 g. active ingredient per $m^2$). Treatment did not reduce the nuisance of *An. gambiae* s.l. Impregnated bednets were introduced in August 1987 and have protected about 40% of the population.

appears to be a good predictor of the reduction of the man-biting rate by a residual insecticide, and this independently of the choice of the compound, Fenitrothion or Propoxur (Molineaux et al., 1976).

In the rice-field area of Burundi, with a transmission of 77 infective bites per man /year, and a vectorial population with a low polymorphism of chromosomal inversion, only one annual spraying all over with malathion (residual effect of two months) considerably reduced the prevalence of malaria after six years. High parasitaemias, responsible for malaria morbidity, were reduced from 70% to 8%, and almost to nil (Fig. 6). However these treatments have not altered the nuisance, since they covered only the end of the rainy season when the anopheline population naturally decreases, together with an increase of transmission.

These selective treatments with insecticide exert a minimal selective pressure on the anopheline population, and sensitivity to Malathion has not changed since the start of the operations (Coosemans and Barutwanayo, 1989; Coosemans 1991b; Barutwanayo et al., 1991).

During recent years, trials at village level were performed with impregnated bed-nets in areas of intense transmission. Different study designs of these trials make comparison of data difficult; however most of the authors reached the same results: a reduction of malaria transmission by about 90% and a reduction in malaria morbidity of about 60% without any change of endemicity (Carnevale et al., 1991). In a rural holoendemic area of Gambia, insecticide-treated bed-nets reduced the overall mortality and mortality attributable to malaria for children by 70% and 63%, respectively, while chemoprophylaxis gave no additional protection in preventing deaths. The decrease of mortality not directly attributable to malaria leads the authors of this study to suggest that malaria may be an important indirect cause of death (Alonso *et al.*,1991).

Wide-scale evaluation is now required, preferably spread over several years, to confirm these results. Pyrethroids are at this stage the only insecticides convenient for impregnation of bed-nets because they are quick-acting, highly insecticidal and stable. These compounds are now widely used in agriculture and the

appearance of resistance is not to be excluded. It is the Achilles heel of the impregnated bed-nets. But the combination of pyrethroids with other insecticides is now being studied (Curtis, personal comm.).

## 4. Conclusions

Molecular genetic techniques are now applied to the study of vectors, and will provide new tools for field research (Miller 1989). The means to make some progress will rest on research activities in the framework of vector control programmes, and one of the research priorities is certainly the density-dependent regulation of the vector population in relation to the survival rate of the mosquitoes.

The expectation of vector control activities differs according to the epidemiological characteristics of malaria, mainly its stability. In areas where the transmission period is very short, (unstable malaria), vector control will have an important impact on the disease and on the endemicity.

In tropical Africa, vector control is justified in regions with unstable malaria such as the highlands and the Sahel, where the suppression of epidemics is feasible. The numbers of populations that could be protected in these areas are already considerable (Mouchet *et al.*, 1991).

In areas with perennial and high transmission (stable malaria), vector control may reduce malaria morbidity and malaria mortality without modifying the endemicity; but this needs further wide-scale investigations. During these trials, community participation and appropriate structures for delivery, management and operations should also receive more attention (Mouchet and Coosemans, 1991).

In regions with stable malaria, priority should be given to areas with a low polymorphism of chromosomal inversion, such as towns or irrigated areas. A more uniform exposure of the vector population to the insecticide may be expected, but a better organization of the community may also offer important advantages in such environments.

Vector control often appeals on the grounds of personal or collective protection, but, as for vaccination, this preventive measure can reduce malaria-related morbidity and mortality only if a certain degree of coverage is assumed.

The national budget for public health is generally limited and considering additional expenses for vector control is not realistic. However, vector control programmes can be supported by more ambitious projects of integrated (rural) development, while personal protection can be afforded by individuals.

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