

TRANSMISSION FACTORS IN MALARIA EPIDEMIOLOGY AND CONTROL IN AFRICA

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Genetic and environmental components of factors contributing in malaria transmission are reviewed. Particular attention is given to density dependent regulation of vector populations in relation to the survival rate of anophelines. The expectation of vector control activities are different according to the epidemiological characteristics of malaria, mainly its stability. In areas with perennial and high transmission (stable malaria) vector control could reduce malaria related morbidity and mortality, without any effect on the endemicity. However this need further investigations. 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. Control projects using indoor spraying with insecticide and impregnated bed nets are discussed.

Key words: malaria – epidemiology – transmission factors – vectors – control

The potential of multiplication of a malaria infection through a vectorial system is enormous. The potential number of secondary infections as direct result of one single case is, in classic malariology, expressed by the basic reproduction rate of Macdonald (1975) (Fig. 1), assuming that the population is fully receptive and thus non-immune. It is the expression of a potential never realized, except at the onset of an epidemic. In an area with stable malaria, this rate may reach several thousand. This model has been conceived with the perspective of eradication and due to immunity gives no indication on the expected decrease of malaria morbidity, priority objective of malaria control in a major part of the world and particularly in Africa.

Nevertheless, the basic reproduction rate has the advantage to decompose the different entomological and parasitological factors involved in malaria transmission and their relative importance.

On the other hand we actually known that the assumptions of random habits of the mosquito and the human host constitute simplifications (in Molineaux, 1988). Estimations of the different parameters are biased due to sampling problems and the use of rudimentary technics, like ovaries dissections for the estimation of

the survival rate of the vector population.

We propose here to review the different factors contribution in malaria transmission, its relation to malaria epidemiology (stable and unstable malaria) and what could be expected from vector control programmes in these different epidemiological situations.

TRANSMISSION FACTORS

Infectiousness of human carriers – The gametocyte reservoir, essential link for transmission, has a relatively limited weight comparing to the entomological factors, resumed in the formula of vectorial capacity. However little information is available on the intrinsic physiological variability of 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 on strains with a short one, which are unlikely to be transmitted from one transmission season to the other. In regions with continuous transmission, this selective process will not be required (Carnevale & Mouchet, 1980). On the other hand, the adaptation of the parasitological cycle to different local climatic conditions has well been documented for *P. vivax* (Bray & Garnham, 1982).

vectorial capacity

$$Z_0 = b \left[\frac{2 n}{m a p} \right] \frac{1}{r} (-L n p)$$

ma : 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 P.f. at 25 °C)

Fig. 1: basic reproduction rate.

Recently it has been argued that chloroquine pressure may have selected genotypes of parasites with 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 bloodmeals are infectious for the mosquitos.

Entomological factors – Entomological factors are influenced by the natural environment, but modification by man to his environment is certainly more determinant (Coosemans & Mouchet, 1990).

Vector density – The vector density in relation to humans will be dependent of the type of breeding place and its distance to the human habitat. Nature of breeding-places of the species of the *Anopheles gambiae* complex, e.a. shallow open sun-lit pools, assumes a large distribution of these species in tropical Africa. Every footprint, is a potential breeding place. In many cases larval control is thus not feasible. In the primary forest sunbeams do not reach the ground. Vector density and thus malaria is increased with clearing of the forest (Mouchet, 1976).

The most productive breeding places for *A. gambiae* are semipermanent breeding places, regularly excavated, like borrow pits and rice fields. In northern Somalia, cisterns are permanent breeding places and since no other breeding places are available, larval control using fish combined with drug administration has been successful (Alio et al., 1985).

The species of the *gambiae* complex present a great ecological plasticity. In West Africa, there

are several chromosomic forms of *A. gambiae* and *A. arabiensis*. *A. arabiensis*, usually dominant when relative humidity decreases, is well implanted in coastal towns due to a particular chromosomic form (Coluzzi, 1984). The MOPTI form or taxon of *A. gambiae* is particularly well adapted to rice fields (Robert et al., 1986; Touré, 1989). 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 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 *A. gambiae* or *A. funestus* which leads to dramatic epidemics. In these regions, temperature drops often under 15 °C, stopping the development of the parasite in the mosquito. However *A. gambiae* and mainly *A. funestus*, through their endophilic behaviour, found the appropriate temperature inside the houses or in the shelters. 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. Probably the same phenomenon happened on the high plateaus of Madagascar. Indoor spraying in these regions has been very successful (Meyus et al. 1962; Munyantore, 1989; Delacollette et al., 1990).

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 and the man biting habit.

Gonotrophic dissociation may be observed during the dry season. In the absence of breeding places, mosquitoes survive at the adult stage, and take bloodmeals, eggs deposition being postponed up to the first rains (Omer & Clodsley-Thomas, 1970). Man biting habit varies for each species, but also depends of alternative host disponibility. So is *A. funestus* highly anthropophilic (94 to 100%). This behaviour is also associated with a high degree of endophagy and endophily, which explains the high reduction of this species after indoor spraying.

Anopheles gambiae and *A. arabiensis* are

largely anthropophilic, although *A. arabiensis* is less anthropophilic when cattle feeding opportunities do exist. Since cattle stays often outdoors, it is not surprising to find a non negligible proportion of *A. arabiensis* biting and resting outside where residual insecticides have no impact. In an urban area of Senegal, where domestic animals are absent, *A. arabiensis* takes its blood meals almost exclusively (99%) on man (Vercruyse et al., 1983). In Burundi on the contrary, the presence of herds in the villages deviates about 30% of *A. arabiensis* on cattle (Coosemans et al., 1989). The zoophilic tendency of *A. arabiensis* partially explains the differences of sporozoite rates observed between *A. gambiae* et *A. arabiensis* in regions where those species are sympatric (in Gillies & 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. Differences in results are explained by man biting habit of the vectors (Table I).

In the South of Cameroun, it has been possible to eliminate *A. gambiae* temporarily by indoor spraying. Cattle was absent and the anopheline had no other choice than biting man inside the house where they came into contact with the insecticide (Livadas et al., 1958). In West Africa, the low transmission close to the mangroves is explained by the low man biting habit of *A. melas* (Bryan, 1983).

Resting behaviours – In Nigeria, Coluzzi (1984) observed an association between resting behaviour (exophily or endophily) and certain chromosomal inversions suggesting a genetic mechanism involved in the behavioural modu-

lation 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 (Molineaux & Gramiccia, 1980) and more recently in the Rusizi Valley in Burundi (Coosemans et al., 1989), compared to the disappointing results obtained in the West African Savannas (Garki, pilot zone of Bobo-Dioulasso).

The longevity – Malaria transmission by a vector will only be possible 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 *A. gambiae* s.l. and *A. funestus* combined with a high anthropophily.

Seasonal and climatic variations affect the survival rate of vectors but density-dependent regulation and its effect on longevity is probably more 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.

Highly dense vectorial populations are composed of a great proportion of young females, it is thus normal that highly seasonal density is associated with low incidence rate of malaria. 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.

In the rice field area of Burundi, *A. arabiensis* is abundant during the rainy season

TABLE I

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

	Highton et al., 1979		Joshi et al., 1975	
	<i>gambiae</i>	<i>ss. arabiensis</i>	<i>gambiae</i>	<i>ss. arabiensis</i>
Proportion of species	10%	90%	75%	25%
Human blood index	92%	39%	96%	93%
Sporozoite rate	5.3%	0.3%	8%	7.5%

(9 months) without any effect on parasitic incidence. It's only at the end of the rainy season that the vectorial capacity raised as the consequence of the increase of longevity of the vector, which caused an important rise in parasite incidence and frequency of clinical malaria during the dry season. The study of seasonal variation permits to develop antivectorial control using a minimum amount of insecticide at the moment of increased longevity (Coosemans, 1985, 1991).

On the contrary, the survival rate is constant and high in a stable vectorial population, such as observed in degraded forest (Carnevale et al., 1985) or in savanna (Molineaux & Gramiccia, 1980).

In Burkina Faso, Robert et al. (1985) observed similar sporozoite rates for *A. gambiae* and *A. funestus*, however these vary considerably in the same region depending on the facies and the disponibility of semi-permanent breeding places (Table II).

These results may suggest that the occurrence of permanent breeding places facilitates the oviposition by the female, but acts negatively on their survival rate. If this is true, then is the use of the parous rate for estimation of the survival rate not appropriate. In Papua New Guinea, Charlwood et al. (1988) suggest that the search of a permanent breeding place by *A. farauti* involves some form of memory of the mosquito. Similar studies do not exist for *A. 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. obs.). In these conditions we can imagine that environmental management for reducing *high* vector density may increase transmission by enhancing vector longevity.

Refractory strains of vectors – In the laboratory it has been possible to select refractory strains of *A. gambiae* (Collins et al., 1986). In the field, however, the consistent increase of the sporozoite rate with age of *A. gambiae* females imply 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 reached 14% after two weeks from capture, suggesting that no intrinsic refractory mechanism was involved.

RELATION BETWEEN TRANSMISSION, EPIDEMIOLOGY, MORBIDITY AND MORTALITY

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 is the VC close to this critical value, and relatively small changes in VC will produce large changes in prevalence. In a region with stable malaria is the VC far above the critical level and even large changes of VC will produce little changes in prevalence (in Molineaux, 1988).

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 centers 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 becomes difficult due to increasing drug resistance.

The basic question now is to know the relation between transmission (intensity, distribution)

TABLE II

Sporozoite rates (year average) according to breeding places in Burkina Faso (Robert et al., 1985)

	Savanna without subpermanent breeding places	Savanna with subpermanent breeding places	Rice fields
<i>A. gambiae</i> s.l.	4.8%	1.7%	0.5%
<i>A. funestus</i>	4.6%	2.1%	0.6%

and malaria related morbidity/mortality. Does vector control reduce malaria morbidity in areas with stable malaria? The principal difficulty is certainly to measure objectively specific malaria mortality/morbidity.

WHAT COULD BE EXPECTED FROM VECTOR CONTROL PROGRAMMES?

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 in two years with fenitrothion 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 antimalaria measures; a better medical and social coverage contributed probably to improved health in general (Carnevale & Vaugelade, 1987).

In the study area of Garki, Sudan Savanna, Nigeria, three to four spraying rounds a year 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 sporozoite bites were more successful in establishing patent parasitaemia than before intervention. In the control villages, infant mortality rate and parasitic incidence rate were strongly correlated throughout the year. In villages treated with propoxur only, the seasonal correlation of these two parameters disappeared, mortality decreased much less than the incidence (Molineux & Gramiccia, 1980).

The poor results on prevalence in Garki were attributed to the high initial transmission level and to non-uniform exposure of *A. gambiae* s.l. to the insecticide, which is explained by the exophilic behaviour of certain chromosomal variants. This was not the case in Kisumu, where the *A. 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) appears to be a

good predictor of the reduction of the man-biting rate by a residual insecticide, and this independent of the choice of the compound, fenitrothion or propoxur (Molineux et al., 1976).

In the rice field area of Burundi, with a transmission of 77 infective/bites/man/year, and a vectorial population with a low inversion polymorphism, only one spraying round a year with malathion (residual effect of two months) considerably reduced the prevalence (from 70% to 8%) after six years. High parasitaemias, responsible for malaria morbidity, were reduced to nil (Fig. 2). However these treatments have not affected the nuisance, since they cover only the end of the rainy season when the anopheline population naturally decreases together with an increase of transmission. These selective treatments of insecticide exert a minimal selective pressure on the anopheline population and sensitivity to malathion hasn't changed since the start of the operations. (Coosemans & Barutwanayo, 1989; Coosemans 1991, Barutwanayo et al., 1991).

During recent years, village scale trials were performed with impregnated bednets in areas of intense transmission. Different study designs of these trials make comparability of data difficult, however most of the authors came to the same results: a reduction of malaria transmission of about 90% and a reduction of malaria morbidity of about 60% without any change of endemicity (Carnevale et al., 1991). In a rural holoendemic area of The Gambia, insecticide-treated bed nets reduced the overall mortality and mortality attributable to malaria for children of 63% and 70%, respectively, while chemoprophylaxis gave no additional protection in preventing deaths. The decrease of mortality not directly attributable to malaria brings 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 bednets because they are quick-acting, highly insecticidal and stable. These compounds are now widely used in agriculture and appearance of resistance is not to be excluded. It's Achilles tendon of the impregnated bednets. But combination with other insecticides are now evaluated (Curtis, pers. comm.).

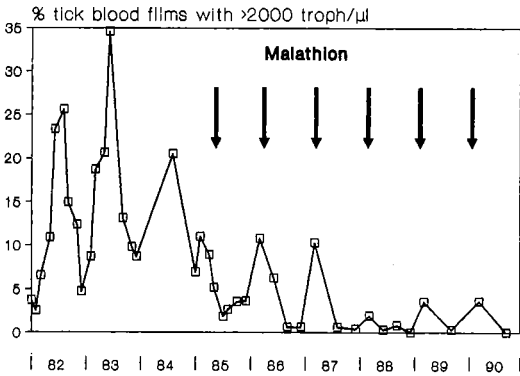


Fig. 2: percentage of positive children below 5 years for of high parasitaemia of *Plasmodium falciparum* before the intervention phase (1982-1984) and during the intervention phase in a rice field area of Burundi. The intervention is limited to one spray round a year with malathion (2 g a.i/m²) instead of four rounds. Treatments did not reduce the nuisance of *Anopheles gambiae s.l.*. Impregnated bed nets were introduced in August 1987 and protected about 40% of the population.

CONCLUSIONS

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

In tropical Africa, vector control is justified in regions with unstable malaria like high lands, sahel, where suppression of epidemics is feasible. The populations that could be protected in these areas are already considerable (Mouchet et al., 1991).

In areas with 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.

In regions with stable malaria, priority should be given to areas with a low chromosomal inversion polymorphism, like 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.

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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