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Malaria research in Africa:
new approaches to vector control (**) 

The statistics regarding malaria throughout the tropical and sub-tropical regions of the world are horrendous, persistent, and certainly demonstrate that it is the single most widespread vector-borne disease among the people of the developing tropical regions (Table 1). About 100 million cases occur annually. It is estimated conservatively that if minimal protection is to be provided for 60% of the population at risk in 1985, which is estimated to be about 1.5 billion people, such protection would cost U.S. $2.9 billion (McEvers, 1976) a year. Such an expenditure is a major burden to tropical developing countries, especially in Africa. For instance, in the Gezira province of the Sudan, which produces — through a major irrigation scheme — about 60% of the country’s export earnings through cotton production, a budget allocation of U.S. $40 million was earmarked for malaria control over the eight-year period, 1976-1984. This budgetary allocation represented a per capita investment of U.S.$ 17 in malaria control alone from a population whose overall per capita income is only about $ 112.

Such an investment in malaria control is undoubtedly heavy; it is, however, commensurate with the high profile this tropical disease occupies in the tropical developing regions of Africa and the world in general. Malaria, and other vector-borne tropical diseases, have serious social consequences:

— They cause high mortalities, especially among the young;

— They cause long-term debility: development of anaemia due to malaria infection, impairing the productivity of labour, lowering the qualitative output

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Table 1 - Malaria situation in all endemic areas world-wide, 1965-1985 (in millions).

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<tr>
<td>Number of people</td>
<td></td>
<td></td>
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<tr>
<td>At risk</td>
<td>1,041</td>
<td>1,088</td>
<td>1,191</td>
<td>1,293</td>
<td>1,459</td>
</tr>
<tr>
<td>Protected</td>
<td>635</td>
<td>650</td>
<td>840</td>
<td>900</td>
<td>1,021</td>
</tr>
<tr>
<td>Unprotected</td>
<td>406</td>
<td>438</td>
<td>351</td>
<td>393</td>
<td>438</td>
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of workers due to their impact on intellectual fulfilment; and leading to losses due to absenteeism;

— They cause waste of current resources invested in health care services (especially among the young), education, and agricultural production in the rural areas.

Thus, the control of malaria is seen very much in the context of national development objectives in Africa.

The cost of malaria treatment and control is colossal and persistent. Considerable rates of absenteeism among malarious school children in Africa, scholastic retardation, stunting of growth, and impairment of normal growth and development due to malaria in high endemic areas make the educational system in rural Africa relatively inefficient, while education as a whole enjoys an unprecedented priority in national development, utilizing about 40% of governmental budgets in most of sub-Saharan Africa. Among primary school children in Accra, Ghana, for instance, a study reported by Colbourne (1953) indicated that the high rate of absenteeism during the peak malaria transmission season was a major factor in the poor performance amongst the severely infected children. It will therefore not be possible to raise the productive input of the rural community in Africa without an effective, sustained, long-term control of malaria.

Yet, the conventional methods for malaria control are so inadequate that they cannot either reduce transmission or prevent repeated infection on a continuing basis.

Current malaria control strategies

The control of malaria in Africa has reached crisis proportions due to: development of resistance to conventional synthetic insecticides, unavailability of replacement insecticides without resistance problems, and the development by the main malaria agent in Africa (Plasmodium falciparum) of resistance to chloroquine, until recently the main chemotherapeutic anti-malarial drug used throughout Africa.
Resistance of the main mosquito vector of malaria in sub-Saharan Africa, *Anopheles gambiae* complex (now known to have 6 sibling species), was first recorded in Africa in Western Sokoto province of northern Nigeria in November 1955, where dieldrin had been used to spray the area 3 times over the previous 18 months. Incidents of resistance to dieldrin were then found rapidly in many parts of West and East Africa (Brown and Pal, 1971). Since then, one can state that dieldrin resistance is general throughout sub-Saharan Africa.

Resistance to DDT took much longer to become evident. Indeed, it is known that insofar as mosquito resistance to DDT worldwide is concerned, DDT-resistance develops more slowly (Brown and Pal, 1971). The first DDT-resistance case in Africa appeared 20 years after its use as a residual insecticidal spray in human homesteads, in 1967 at Bobo-Dioulasso (Burkina Faso) and Thies (Senegal). Part of this slowness of DDT-resistance development is due to the behavioural characteristic of *An. gambiae* mosquitoes of becoming highly irrigated by DDT and therefore flying away from sprayed surfaces (such as walls of houses) and flying towards the light, thereby escaping from further contact.

Much of insecticidal resistance reported in Africa (and elsewhere in the tropics) is a result, not of direct malaria control by insecticidal treatment, but of unrelated control of agricultural pests using insecticides. For instance, in Egypt’s Nile Delta, dieldrin-resistance was reported in 1959 in *Anopheles pharoensis*, the main malaria vector in this region, in spite of the fact that no residual house spraying had yet been undertaken. Dieldrin-resistance was in fact the result of extensive application of toxaphene and DDT for the control of cotton and rice pests. Similarly, in 1965, dieldrin-resistance accompanied by DDT-resistance was detected in Sennar, Kosti, Manasul and Gezira (all in the Sudan), all due to agricultural insecticides (Brown and Pal, 1971).

Such uncoordinated action, between plant protection practices and malaria control campaigns, have led to well documented near catastrophes, apart from insecticide-resistance arising in hitherto unexpected fashion, as recorded above. Most of these are related to the development of large irrigation schemes in order to increase agricultural production in Africa (and other tropical countries). In Kenya’s Athero Pilot Irrigation Scheme, for instance, the application of dieldrin (an organophosphate insecticide) to control rice stem-borers resulted in killing almost all aquatic life in the paddy fields. At the same time, there was an enormous resurgence of the principal malaria vector in the area (*Anopheles arabiensis*), which was one of the first re-colonizers of the paddy fields because of the absence of its normal predators (Service, 1984). Thus, the integration of such agricultural schemes, involving plant protection activities, needs to be integrated with those involving malaria control, and vice versa; this is an important part of the strategy to control vector mosquitoes in such a manner as to interrupt malaria transmission on a continuing basis.

We have presently few insecticidal agents which are effective against malaria vectors in Africa, except perhaps temephos (a larvicide) and fenitrothion (an adulticide). This major setback has been made more acute by the emergence
of chloroquine-resistant *P. falciparum* in Africa first noted some 10 years ago but unconfirmed. By 1984, WHO’s Malaria Action Programme was able to show on a map the extent to which chloroquine-resistance had spread in Africa; covering Angola, Rwanda, Burundi, Uganda, Tanzania, Kenya, Sudan, Zaire, Zambia, Namibia, Gabon, Seychelles, Comoros, Madagascar, Malawi and Mozambique. Mefloquine and mefloquine combinations (with sulfadoxine or pyrimethamine) have proved an effective chemotherapeutic drug in the transitional period before a longer-range drug treatment strategy is developed; but it cannot be used as a prophylactic because of the potential danger of the emergence of mefloquine-resistance.

The possibility of developing an anti-malaria vaccine is being held at the present time as the ultimate long-term solution of the malaria problem. Certainly, the World Bank/UNDP/WHO Special Programme for Research and Training in Tropical diseases is concentrating its research and development effort in immunological control of malaria. But this approach is still a long way from being a practical possibility, as evidenced by the wide-ranging NMRI/USAID/WHO workshop on the “Immunology of Malaria” held in October 1978 in Bethesda, Maryland, U.S.A. (WHO, 1979).

We are back to making do with vector control as still the most feasible method for large-scale malaria control for the foreseeable future. What are the characteristics of vector mosquitoes in sub-Saharan Africa which have made malaria control so difficult in the past? The short answer is to be found in the epidemiological characteristics of the *An. gambiae* complex, the major transmitters of malaria in this part of the world, although *Anopheles funestus* is another although minor vector.

**Epidemiological perspective**

*An. gambiae* plays the major role in the transmission of malaria, bancroftian filariasis (*Wuchereria bancrofti*) and oyong’nyong’ fever in tropical Africa; and there have therefore been considerable ecological and behavioural studies undertaken in respect of those elements which would give relevant information necessary for predicting breeding sites, host preferences, and resting sites vital for spraying larvicides (on breeding sites) and adulticides (in houses) for vector control. Much of this information was conflicting; and it was only in mid-1940’s that the first evidence was adduced that indicated that the ecologists were not dealing with a single homogeneous species. Further information was slow in coming; and it was only in the mid-1970’s that full information had been gathered to demonstrate that the *An. gambiae* in fact comprised six sibling species showing striking resemblances morphologically but exhibiting clear-cut sterility barriers in nature. The epidemiological consequences became apparent immediately then.

Barber and Olinger (1931) first noticed slight variations in appearance and breeding habits of a melanic coastal variety of an *An. gambiae* mosquito form in
West Africa, known to be associated with salt-water breeding sites. These distinctions were later utilized to separate, as distinct species, An. gambiae sensu stricto and An. melas: that is, physiological differences in salt-water breeding characteristics, and morphological differentiation provided by an extra dark band on the palps of adult females of An. melas and differences in larval pecten teeth (Ribbands, 1944a, b). These species distinctions were carried further by Muirhead-Thomson (1948), who demonstrated the fact that An. melas eggs are significantly larger than those of the freshwater-breeding An. gambiae s.s., and that on cross-fertilizing the two species they showed the presence of hybrid sterility. This resolution of the salt-water breeding species in West Africa raised the question whether the salt-water forms previously recorded in Mauritius and the coastal areas of East Africa also belonged to An. melas (Muirhead-Thomson, 1951). Crossing experiments made by Paterson (1962) confirmed that the East African salt-water form was indeed different from the freshwater-breeding species; crosses made between West African An. melas and the East African salt-water form showed that, indeed, the two salt-water forms were separate species (Davidson, 1962), later known as An. merus.

The freshwater An. gambiae mosquitoes themselves proved to be heterogeneous. Crossing experiments carried out in the early 1960's clearly demonstrated the existence of two other sibling species, apart from An. gambiae s.s. Crossing experiments reported by Davidson (1962) and Davidson and Jackson (1962) recognized the separate existence of An. arabiensis. Similar crossing experiments made by Paterson et al. (1963) differentially recognized An. quadrimaculatus, previously described from the high veldt of Transvaal, South Africa. A decade later, a fourth freshwater species, so-called species D, was found from Semliki Forest along the Uganda-Zaire border (White, 1973), and seems not to have been recognized from elsewhere in Africa.

This fascinating detective story was brought to a close by the masterly and comprehensive taxonomic revision by Mastingly (1977), which redescribed the 6 sibling species of the An. gambiae complex (Table 2), and provided their essential diagnostic characterization. Since then, these distinctions have been further added to by other techniques: enzyme polymorphism, cytogenetics, etc.

This painstaking taxonomic study, spanning over 30 years, opened up a new reassessment of the ecological and behavioural information critical to the epidemiological differential importance of the various components of the An. gambiae complex. For instance, a study of the distribution of the different sibling species was instructive: while An. gambiae s.s. and An. arabiensis are very widely distributed throughout sub-Saharan Africa, including the Indian Ocean islands, An. gambiae s.s. predominates in humid zones, while An. arabiensis is relatively more successful under more arid conditions; in some environments, the two species may even become sympatric, for example, in the lakeside area of Kisumu, in Kenya, where An. gambiae s.s. out-number An. arabiensis inside houses towards the end of the cool dry season, but the
Table 2 - Sibling species of the *Anopheles gambiae* complex in Africa (after Mattingly, 1977).

<table>
<thead>
<tr>
<th>Old name</th>
<th>New name, and where found originally</th>
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<tr>
<td>Species A</td>
<td><em>Anopheles gambiae</em> sensu stricto Giles, 1902. Material originally collected in Gambia</td>
</tr>
<tr>
<td>Species B</td>
<td><em>An. arabicus</em> Patton, 1905. Found in semi-arid and arid zones</td>
</tr>
<tr>
<td>Species C</td>
<td><em>An. quadrimaculatus</em> Theobold, 1911. Original material collected from Onderstepoort, South Africa</td>
</tr>
<tr>
<td><em>An. melas</em></td>
<td><em>An. melas</em> Theobold, 1903. Name unchanged. Species associated with West African brackish-water breeding sites</td>
</tr>
<tr>
<td><em>An. merus</em></td>
<td><em>An. merus</em> Donitz, 1902. Name unchanged. Species associated with salt-water breeding sites in East African coastal zones</td>
</tr>
<tr>
<td>Species D</td>
<td>Species D: still unnamed. Found in mineral water in Bwamba swamps</td>
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The reverse situation obtains in the hot dry weather following the short rains (Service, 1970; White, 1972). In contrast to the Africa-wide distribution of these two sibling species, *An. melas* is restricted to the West African coast from Angola to Senegal; and *An. merus* is confined to the East African coast from northern Natal (in South Africa) to lower Juba-land (in southern Somalia), including the Indian Ocean islands (Pemba, Mauritius and the Comoros), although this latter species has been recorded as breeding 50-120 km inland in Swaziland (Paterson et al., 1964) and coastal Kenya hinterland (Mosha and Subra, 1982). In this latter respect, Mosha and Muteru (1982) found that *An. merus* can occasionally breed in outdoor rain-water, and can even experimentally breed successfully in freshwater in the laboratory. It is therefore of interest to find that *An. merus* and two freshwater sibling species (*An. gambiae* s.s. and *An. arabiensis*) are found in sympatric association in certain villages along the Kenya coast of differing proportions. For example, in one village (Jimbo), 96% of the *An. gambiae* complex mosquitoes consist of *An. merus*; while in another village (Jogo), only 17.4% comprise *An. merus*, while *An. gambiae* s.s. constitutes 71.7%, and the rest *An. arabiensis* (Mosha and Petraruca, 1983). The remaining two sibling species of the complex, namely *An. quadrimaculatus* and species D, show a patchy and relict distribution: the first species seems to be confined to Zanzibar, and the highlands of Ethiopia and southern Africa; while the second has so far only been collected from Semiliki Forest in Bwamba (White, 1973).

The strong differences in distribution among the sibling species of the *An. gambiae* complex, considered together with other differences subsequently found in the differing vectorial capacities of these selfsame species, have strengthened the conviction that these characteristics are basic to the epidemiological
understanding of these malaria vectors in Africa. Muirhead-Thomson (1951) first showed that *An. merus* exhibits a lower vectorial capacity for malaria than *An. gambiae* s.str. White (1974) followed up these pioneer studies by demonstrating that the major vectors of malaria (as well as bancroftian filariasis) in Africa were in fact *An. gambiae* s.str., *An. arabiensis* and *An. melas*, even though the latter was confined to coastal areas of West Africa. It is unlikely that, because of its very restricted distribution, species D is epidemiologically important in terms of malaria transmission. Finally, *An quadriannulatus* may not be important epidemiologically either, because of its reported lack of anthropophily; indeed it shows a marked preference to animals as hosts, although it can bite man, especially when the latter are close to cattle.

The feeding behaviour of the different sibling species somewhat follows the pattern of findings from vectorial capacity studies. *An. gambiae* s.str. prefers human blood, and is normally caught feeding inside houses; *An. melas* also has strong preference for human blood, but bites both indoors and outdoors; while the third major malaria vector in sub-Saharan Africa, *An. arabiensis*, is a very opportunistic feeder, feeding where hosts are most abundant whether indoors or outdoors. *An. quadriannulatus* prefers animal hosts. Species D may yet prove a potentially important malaria vector, although restricted in distribution, as it feeds on man both indoors and outdoors. Finally, information on the feeding behavior of *An. merus* has only recently begun to be known (White, 1974). This species can readily feed on goats, sheep and cattle; but it can also feed on man exclusively, should other hosts be unavailable.

Information on resting behaviour of the different sibling species shows that the overall epidemiological picture is likely to be highly complex, while demonstrating clearly why *An. gambiae* s.str. is preeminently the leading malaria vector in sub-Saharan Africa. *An. gambiae* s. str. is the most endophilic of the sibling species, predominantly preferring to rest in houses or man-made shelters. Three other species (*An. arabiensis*, *An. quadriannulatus* and species D) rest either indoors or outdoors, depending on the availability of resting sites next to where feeding takes place. The two salt-water breeding species (*An. melas* and *An. merus*) are definitely exophilic. Thus, of those *An. melas* which may feed indoors during the night, 90% leave for outdoor resting sites by dawn (Gelfand, 1955), where they rest in rodent burrows, shaded earth banks, etc. Similarly, while only 2% of *An. gambiae* s.str. left houses after feeding, 35-40% of *An. merus* did so (Muirhead-Thomson, 1951); and the latter then go on to rest in crab holes, under fallen leaves, in shaded termite mounds, heavily shaded mangrove and mangrove trees, etc. (Iyengar, 1962), or coconut husks (Mutero, Mosha and Subra, 1984). Indeed, *An. merus* feeds mostly outdoors (Mutero, 1980; Mutero, Mosha and Subra, 1984), with peak biting activity between 2400 and 0100 hours, whether indoors or outdoors. If indoors, most biting occurs while the people are asleep, and then the *An. merus* mosquitoes move out shortly afterwards (Mutero, Mosha and Subra, 1984). This work shows clearly that residual insecticidal spraying of
houses at the Kenya coast may kill off *An. gambiae* s.str., but the largest proportion of *An. merus* population will escape the treatment.

The other major factor of epidemiological importance is the estimation of survival rates of field populations of the individual species of malaria vectors. The most thorough study so far done in Africa is that of Mutero (1985) undertaken at the ICIPE on the three sibling species sympatrically associated at the Kenya coast. In brief, his findings show that: (a) the dry season population of *An. gambiae* s.str. sustained a longer life than the wet season population; (b) there is a greater risk of malaria in Kenya within the distribution range of *An. merus*, but that because of the relatively restricted eco-geographical distribution of this species, the much more widespread *An. gambiae* s.str. is, on the whole, the more important vector of malaria, in spite of its vectorial capacity being 4 times less than that of *An. merus* (calculated on the basis of comparative survival rates alone); and (c) *An. arabienensis* exhibits a relatively low vectorial capacity, because of its high-altitude distribution, where the development of *P. falciparum* within the insect vector takes much longer.

The epidemiological perspective being adduced now since the elucidation of the taxonomic complexity of the malaria vectors in sub-Saharan Africa is rapidly giving us a better understanding of the vector-parasite-host transmission factors that might eventually lead to more rational integrated control of malaria. The biological control facet of this problem has not yet received much attention; and efforts are just beginning to be devoted to this facet of integrated vector control strategies in Africa.

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**Potential biological control of mosquito vectors of malaria**

More than 1,000 natural enemies of mosquitoes have been recorded worldwide. These include: larvivorous fish (such as the minnow, *Gambusia affinis*), which has been utilized for mosquito control since the early 1900's, but has lately declined in its effectiveness in some regions due to the advent of DDT and similar synthetic insecticides, predation by other fish, and decimation by fungal diseases; larvicidal plants, such as rooted algae of the family Characeae (especially *Chara* and *Nitella*) which exude toxin into the water, and other plants (such as *Phytolacca* and *Melia*) whose fruit contains anti-larval compounds; parasitic nematodes (especially mermithids) in larvae, for example *Roesimeris nielseni*; parasitic protozoans, especially spor-forming species, such as *Nosema stegovysae*, that kill larvae, pupae and adults, or reduce adult longevity; pathogenic bacteria, especially the spor-forming *Bacillus thuringiensis*; invertebrate predators, especially the predator larval mosquito of the genus *Toxorhynchites* living in tree-holes or other small containers, and feeding on mosquito eggs, larvae and pupae; and pathogenic fungi, particularly those belonging to the genus *Coelomomyces* (National Academy of Sciences, 1973).
There is recent resurgence of interest in the use of *Toxorhynchites* and *Coelomomyces* in Africa for malaria control.

*Toxorhynchites* is primarily a tropical genus, which takes no blood in the adult, and takes mosquito larvae and other aquatic arthropods as prey. The most studied species so far, *T. brevipalpis* (Theobald), breeds in tree-holes and leaf-axils, and has wide distribution throughout sub-Saharan Africa, where it is most abundant in forest vegetation, and not in peri-domestic situations or cultivated land (Lounibos, 1979). The latter author observes that this predator density is in contrast to the prey density (mainly consisting of *Aedes* mosquitoes), which is highest in the cultivated zone. Even though *T. brevipalpis* has been colonized in the laboratory, and mass production for field releases is now a practical possibility (Trpis and Gerberg, 1973), and prey population reduction by *T. brevipalpis* to the extent of 61% has been demonstrated (Lounibos, 1979), this predator species is not likely to be adopted as a malaria vector reduction option due to the disjunction between its population and that of its prey, and the fact that its mosquito diet is rather catholic, with *An. gambiae* complex being apparently only incidental to its usual menu.

The potential for the use of *Coelomomyces* in malaria vector control is somewhat higher. The genus, of which 40 species are known, is widespread in all the continents, except the Antarctica, but is virtually restricted to mosquito hosts, causing high mortality in infected larvae (Laird, 1967). Among the mosquito species it attacks, are *An. gambiae* s.lato. All *Coelomomyces* species require an intermediate crustacean host, usually a species-specific copepod or ostracod, and a definitive host, a mosquito larva. Because of this circumstance, it has been possible to have *in vivo* mass cultures of this fungus, since mid-1970’s, my maintaining separate cultures of the infected copepods and mosquito larvae (Federici and Chapman, 1977). So far, no successful attempt has been made for *in vitro* culture. If this were accomplished, and because of the obligate parasitic nature and restricted host range of *Coelomomyces*, the latter would have a high potential for the control of malaria vectors in Africa in at least two possible ways: as a microbial insecticide (the way *B. thuringiensis* toxin-bearing spores are presently being used); and as a suppressant of mosquito populations on a long-term basis when the fungus is introduced into areas in which it was previously absent.

That possibility has been raised recently by the discovery of epizootics of *An. gambiae* complex larvae being caused by a high infection by *C. indicus* in Kongowea and Rabai, at the Kenya coast (Otieno et al., 1980). Sampling throughout the years showed that infection varied between 33 and 100%. This fungus, and its copepod intermediate hosts, have been reared in the laboratory regularly, and it has been shown that the copepodid stage of the intermediate host can be made to emerge from soil of dried up pools within 18 hours of its flooding (Sabwa et al., 1980). There is still a long way to bring the *Coelomomyces* potential to the test; but a good start has been made.
Conclusion

It is imperative that the direction the current research in Africa on malaria control has taken should be pushed to the limit. It is much more sensitive to ecological and environmental issues, the coordination between plant protection and vector control, and the long-range goal of integrated vector and malaria control than during the era of exclusively insecticidal control regimens.
REFERENCES


