Malaria and dengue vector biology and control in Southern and Eastern Africa

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Abstract

Malaria vector control has been practiced in the eastern/southern half of the African continent since the beginning of the 20th century, from larval control in the north (Sudan, 1901) to adult control in the south (South Africa, 1931). The major vectors are Anopheles gambiae, An. funestus and An. arabiensis, with An. merus, An. bwambae and An. nili implicated in transmission in localized areas. Current vector control methods include indoor residual house spraying (± 9 countries out of 19), insecticide-treated bednets for personal protection (± 15 countries out of 19), larviciding under certain circumstances and very limited environmental management. Control programmes are faced with multifaceted problems such as service delivery, species diversity and identification, and insecticide resistance. Population-genetic studies are limited compared with West Africa and this gap in knowledge should be urgently addressed. Current evidence suggests far less polymorphism in all three major vectors, An. gambiae, An. arabiensis and An. funestus, than is seen in West-African populations.

As far as non-malaria disease vectors are concerned, both *Aedes aegypti aegypti* and *Ae. aegypti formosus* occur in East and Southern Africa. Genetic and disease-transmission studies provide strong evidence for the specific distinctness of these subspecies. Occasional cases of suspected dengue occur in Kenya, presumably transmitted by *Ae. aegypti*. Outbreaks of yellow fever, however, have been caused by other *Aedes* species and not the above two. No targeted control activities are carried out against these species.

Keywords: malaria; dengue; yellow fever; vector control; *Anopheles gambiae*; *Anopheles funestus*; *Anopheles arabiensis*; *Aedes aegypti*; *Aedes formosus*; insecticide resistance; population genetics

Malaria

The dynamics of malaria transmission are not simple, with many factors influencing individual situations. Major problems affecting malaria in Africa include funding and service delivery, political instability, poverty, drug and insecticide resistance, and extremely efficient (i.e. competent and long-lived) vector mosquitoes. Problems specific to vector control include species identification, population

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diversity, insecticide resistance and choice of control strategy. This paper provides an overview of the vector control situation in Eastern and Southern Africa and highlights issues specific to these regions.

Vector species

Anopheles gambiae complex

Six of the seven recognized species in the *An. gambiae* complex occur in Eastern and Southern Africa (Gillies and Coetzee 1987; Hunt, Coetzee and Fettene 1998). *Anopheles gambiae* and *An. arabiensis* are the major vectors, with *An. arabiensis* occurring throughout the region from South Africa to Sudan and Egypt, while *An. gambiae* is prevalent in the tropical belt only. The saltwater breeder *An. merus* is found in mainly coastal areas of Kenya and Tanzania, but also far inland in Zimbabwe and South Africa (Gillies and Coetzee 1987; Coetzee, Craig and Le Sueur 2000). It is an efficient vector in some areas (Temu et al. 1998, H.T. Masendu, unpubl. data). *Anopheles bwambae* is a minor vector, restricted to the Semliki forest of Western Uganda. The other two species, *An. quadriannulatus sp.* A and B, occur in Southern Africa and Ethiopia respectively. They are mainly cattle feeders and do not play any role in malaria transmission.

The identification of the above species is either by chromosomal inversion polymorphisms (Coluzzi, Petrarca and Di Deco 1985) or rDNA-PCR (Scott, Brogdon and Collins 1993). The occurrence of cattle-feeding species in a given area makes species identification essential so that control measures can target the actual vectors and not look-alike non-vectors. *Anopheles gambiae* is predominantly house frequenting, while *An. arabiensis* will feed on humans and rest indoors as well as feed on cattle and rest outdoors, making this a more difficult mosquito to control by conventional means. The resting and feeding behaviour of these two species, however, may vary considerably depending on locality and availability of hosts (Gillies and Coetzee 1987).

Anopheles funestus group

This group consists of nine morphologically similar species, of which only one, *An. funestus*, is a major vector (Gillies and De Meillon 1968). Species identification of the five most common members of the group is by rDNA-PCR (Koekemoer et al. 2002). *Anopheles funestus* is almost exclusively human biting and preferentially rests indoors, making it very susceptible to control by residual house spraying. It occurs in South Africa and extends northwards to Kenya (Gillies and De Meillon 1968). Early reports of *An. funestus* in Ethiopia have not been confirmed as the only species so far identified by PCR is the non-vector *An. parensis* (Weeto et al. 2004).

Insecticide resistance

Table 1 summarizes the status of insecticide resistance in the three major African malaria vector species (Zahar 1985; Hargreaves et al. 2000; 2003). In most cases the selection pressure has come from agricultural use of the insecticides and can be maintained without selective pressure in many of the mosquito populations through linkage to chromosomal inversion polymorphisms (Brooke et al. 2001).

Table 1. Insecticide resistance in East and Southern African malaria vector mosquitoes (situation in 2004)

Species	Insecticide	Region
An. gambiae	DDT	Zanzibar
	Dieldrin	Kenya and Madagascar
	Pyrethroids	Kenya and Zambia
An. arabiensis	DDT	Sudan, Ethiopia, Zanzibar, South Africa
	Dieldrin	Sudan, Ethiopia, Kenya, Madagascar,
	Organophosphates	Zimbabwe, Swaziland, Sudan
An. funestus	Dieldrin	Kenya
	Pyrethroids	South Africa, Mozambique
	Carbamates	South Africa, Mozambique

Population genetics

Chromosomal studies on both the *An. gambiae* complex and *An. funestus* group in Eastern and Southern Africa show far less inversion polymorphism than in West Africa (Ralisoa Randrianasolo and Coluzzi 1987; Petrarca and Beier 1992; Petrarca et al. 1984; 1986; 1990; 1991; Green and Hunt 1980; Kamau, Hunt and Coetzee 2002; Kamau et al. 2003). Population structure and gene flow studies have been carried out on *An. gambiae*, *An. arabiensis* and *An. funestus* but these remain few and more are needed (Donnelly et al. 1999; Donnelly, Licht and Lehmann 2001; Garros et al. 2004; Kamau, Hunt and Coetzee 2002; Kamau et al. 2003; Lehmann et al. 1996; 1997; Sinkins et al. 2000; Braginets et al. 2003; Temu, Hunt and Coetzee 2004). Population structuring in *An. funestus* has been demonstrated using microsatellite markers (Temu, Hunt and Coetzee 2004) and restriction-fragment length polymorphisms (RFLP) (Garros et al. 2004), providing evidence of distinct sub-populations. The situation in *An. arabiensis* is less clear with apparently significant gene flow over fairly large areas (Donnelly et al. 1999; Donnelly, Licht and Lehmann 2001).

Vector control

In East and Southern Africa, BHC (cyclodiene) resistance in *An. arabiensis* and pyrethroid resistance in *An. funestus* have had major impacts on control strategies. In the other areas, vector control was implemented in small areas only and discontinued after a few years for various reasons (Zahar 1985). The Zimbabwe and South-African experiences are highlighted here as examples of the problems of insecticide resistance faced by control programmes.

Zimbabwe

In 1974, the Zimbabwe residual house-spraying campaign used benzene hexachloride (BHC), an organochlorine closely allied to dieldrin. A malaria epidemic in the southeastern lowveld indicated problems with the control programme. At the time, the only species identification technique available was the banding pattern of the polytene chromosomes found in half-gravid female anophelines. This meant that only live females could be identified and not dead ones. The following year, an isoenzyme method was developed in Zimbabwe (Mahon, Green and Hunt 1976) that allowed identification of all adults collected. Insecticide susceptibility tests showed that the majority of dead mosquitoes were *An. quadriannulatus* while those surviving exposure to 4% dieldrin were all *An. arabiensis*. The Zimbabwe malaria control

programme changed their policy to DDT spraying and the epidemic was brought under control (Green 1981).

South Africa

In the early 1930s, De Meillon (1934) showed that the malaria vector *An. funestus* fed on humans indoors and rested inside houses until ready to lay eggs. Based on this information, the major epidemic of 1931-33 was brought under control by the use of pyrethrum flit pumps to spray indoors once a week (De Meillon 1936; Park Ross 1936). When DDT became available, South Africa began to implement a house-spraying campaign throughout the malarious areas of the northeast provinces with great success.

Malaria in South Africa is a notifiable disease with records of malaria case incidence kept since 1971. In 1995, a policy decision was taken to move from DDT to the more environmentally friendly pyrethroids. Coinciding with good rains, the number of malaria cases in 1996 almost trebled (Figure 1). Various reasons were postulated, such as cross-border movement of people from Mozambique carrying gametocytes, the weather, and deterioration of the control programme.

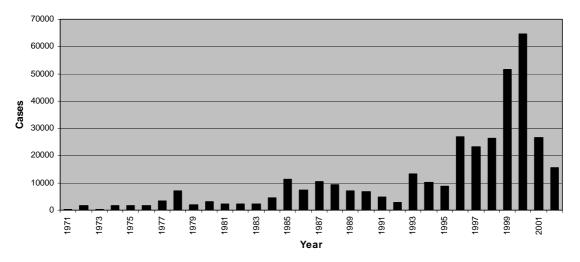


Figure 1. Malaria cases in South Africa, 1971-2001 (source: Department of Health, South Africa)

In 1999, the number of cases doubled again, reaching a peak of over 60,000 cases in 2000. Entomological surveys in December 1999 collected *An. funestus* in window exit traps in pyrethroid-sprayed houses. *Plasmodium falciparum* infection rates were >5% and susceptibility tests on papers treated with three different pyrethroids confirmed high levels of resistance (Hargreaves et al. 2000). Collections in Maputo, Mozambique, in 2000 showed that carbamate resistance was also present (Brooke et al. 2001). The malaria control programme policy was changed back to the use of DDT for traditional-style housing, with pyrethroids being used in the few western-style houses only. By 2002, the malaria case incidence had decreased by >70%.

A multicentre study in Southern Africa

In 2002 a partnership between five countries in Southern Africa (Namibia, Botswana, Zimbabwe, South Africa and Swaziland) was initiated, supported by the World Health Organization (WHO/AFRO), to obtain baseline information on insecticide resistance. Results showed complete susceptibility of *An. arabiensis* to

DDT and pyrethroids in Namibia, Botswana and Swaziland, with susceptibility to pyrethroids in South Africa and Zimbabwe as well (M. Coetzee et al., unpubl. data). Resistance to DDT was detected in South Africa (Hargreaves et al. 2003) and Zimbabwe (H.T. Masendu, unpubl. data). The impact of this resistance on malaria control is unclear, but at least in South Africa there appears to be no increase in transmission in the areas where the resistance was detected (National Department of Health, unpubl. malaria statistics).

Vector control in East Africa

Early pilot studies in the 1950s and 1960s using dieldrin, DDT and organophosphates for house spraying showed amazing success in many instances (Zahar 1985). Unfortunately, most of these studies were terminated after only a few years, presumably because of financial constraints. Table 2 gives a brief summary of control activities using indoor residual house spraying around the time of the WHO eradication campaign and later (see Zahar (1985) for a comprehensive summary).

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Locality	Dates	Insecticide	Outcome	
Sudan, Sennar	1956-59	Dieldrin	Transmission interrupted	
Gezira	1973-77	Malathion	Transmission reduced by 74%	
Uganda, Kigezi	1959-61	DDT	Transmission interrupted	
Kenya, highlands	1954-57	Dieldrin	Prevalence reduced to <2%	
Kisumu	1973-75	Fenitrothion	Transmission reduced by 73%	
Tanzania, Pare-Taveta	1954-59	Dieldrin	Transmission reduced by >90%	
Zanzibar	1958-61	Dieldrin	Transmission interrupted	
	1962-68	DDT	Transmission interrupted	
Zambia, Copper Belt	1945-70	DDT	Transmission interrupted	
Zimbabwe	1948-90	BHC, DDT	Transmission controlled, limited	
			to lowveld areas	
South Africa	1945-95	DDT	Transmission controlled, limited	
			to lowveld areas	
Swaziland	1960-04	DDT	Transmission controlled	
Madagascar	1949-69	DDT	Transmission interrupted on	
-			plateau	
Mauritius	1949-52	DDT	Eradicated	

The 1904-1910 Khartoum, Sudan, malaria control campaign using larviciding only, was successful in reducing malaria transmission within the city limits (Annual Reports of the Gordon Memorial Institute, Khartoum). However, the military precisions with which the campaign was run and the amount of manpower expended on the project were incredible. There was intense coverage of every available larval breeding site within Khartoum, each of them mapped on a monthly basis (the mapping exercise in 1902-04 equalled any modern geographic mapping system using GPS and GIS today!). The problem, however, was that it was impossible to cover all natural water bodies along the Nile rivers, thus enabling sufficient immigration of vector mosquitoes into the city. This, coupled with the constant influx of gametocyte carriers from outside the control area, ensured continued malaria transmission within Khartoum. Andrew Balfour reports (in Ross 1911, p. 530-542) that "... they have met with marked success, and doubtless will continue to do so, provided the work is carried out continually, thoroughly, consistently and with intelligence...", which

highlights the enormous amount of work and commitment that is required to carry out malaria vector control through larviciding even in a very small area. Khartoum today has a human population of over 1 million people compared with 41,000 in 1904.

Current vector control

- Indoor residual house spraying is being carried out to a greater or lesser extent in 9 of the 19 East- and Southern-African countries.
- Insecticide-treated bednets are being distributed or used in pilot studies in 15 countries.
- Larviciding is implemented on an ad-hoc basis where situations allow.
- Only very limited environmental management is undertaken.

Dengue and yellow-fever virus transmission

Both Aedes aegypti aegypti and Ae. aegypti formosus occur in East and Southern Africa. Genetic and disease-transmission studies provide strong evidence for the specific distinctness of these sub-species (Powell, Tabachnick and Arnold 1980; Failloux, Vazeille and Rodhain 2002). Occasional cases of suspected dengue have occurred in Kenya but these were not confirmed by virus isolation and PCR. Presumably, Ae. aegypti transmitted the virus. Outbreaks of yellow fever in East Africa, however, have not been transmitted by Aedes aegypti, but by other species such as Aedes simpsoni (see Chapter 8 for a more comprehensive summary).

No control activities are currently carried out against *Aedes* larvae, but where indoor residual house spraying is used for malaria vector control, this will presumably affect the adult populations of *Aedes aegypti*.

References

- Braginets, O.P., Minakawa, N., Mbogo, C.M., et al., 2003. Population genetic structure of the African malaria mosquito *Anopheles funestus* in Kenya. *American Journal of Tropical and Medical Hygiene*, 69 (3), 303-308.
- Brooke, B.D., Kloke, G., Hunt, R.H., et al., 2001. Bioassay and biochemical analyses of insecticide resistance in southern African *Anopheles funestus* (Diptera: Culicidae). *Bulletin of Entomological Research*, 91 (4), 265-272.
- Coetzee, M., Craig, M. and Le Sueur, D., 2000. Distribution of African malaria mosquitoes belonging to the *Anopheles gambiae* complex. *Parasitology Today*, 16 (2), 74-77.
- Coluzzi, M., Petrarca, V. and Di Deco, M.A., 1985. Chromosomal inversion intergradation and incipient speciation in *Anopheles gambiae*. *Bollettino di Zoologia*, 52, 45-63.
- De Meillon, B., 1934. Observations on Anopheles funestus and Anopheles gambiae in the Transvaal. Publications of the South African Institute for Medical Research, 6, 195-211.
- De Meillon, B., 1936. The control of malaria in South Africa by measures directed against the adult mosquitoes in habitations. *Quarterly Bulletin of Health of the Organization of the League of Nations*, 5, 134-137.

- Donnelly, M.J., Cuamba, N., Charlwood, J.D., et al., 1999. Population structure in the malaria vector, *Anopheles arabiensis* Patton, in East Africa. *Heredity*, 83 (4), 408-417.
- Donnelly, M.J., Licht, M.C. and Lehmann, T., 2001. Evidence for recent population expansion in the evolutionary history of the malaria vectors *Anopheles arabiensis* and *Anopheles gambiae*. *Molecular Biology and Evolution*, 18 (7), 1353-1364.
- Failloux, A.B., Vazeille, M. and Rodhain, F., 2002. Geographic genetic variation in populations of the dengue virus vector *Aedes aegypti*. *Journal of Molecular Evolution*, 55 (6), 653-663.
- Garros, C., Koekemoer, L.L., Kamau, L., et al., 2004. Restriction fragment length polymorphism method for the identification of major African and Asian malaria vectors within the *Anopheles funestus* and *An. minimus* groups. *American Journal of Tropical and Medical Hygiene*, 70 (3), 260-265.
- Gillies, M.T. and Coetzee, M., 1987. A supplement to the Anophelinae of Africa south of the Sahara (Afrotropical Region). South African Institute for Medical Research, Johannesburg. Publications of the South African Institute for Medical Research no. 55.
- Gillies, M.T. and De Meillon, B., 1968. *The Anophelinae of Africa south of the Sahara (Ethiopian Zoogeographical Region)*. 2nd edn. South African Institute for Medical Research, Johannesburg. Publications of the South African Institute for Medical Research no. 54.
- Green, C.A., 1981. Malaria epidemiology and anopheline cytogenetics. *In:* Pal, R., Kitzmiller, J.B. and Kanda, T. eds. *Cytogenetics and genetics of vectors:* proceedings of a symposium of the 16th international congress of entomology. Elsevier Biomedical Press, Amsterdam, 21-29.
- Green, C.A. and Hunt, R.H., 1980. Interpretation of variation in ovarian polytene chromosomes of *Anopheles funestus* Giles, *A. parensis* Gillies, and *A. aruni? Genetica*, 51, 187-195.
- Hargreaves, K., Hunt, R.H., Brooke, B.D., et al., 2003. *Anopheles arabiensis* and *An. quadriannulatus* resistance to DDT in South Africa. *Medical and Veterinary Entomology*, 17 (4), 417-422.
- Hargreaves, K., Koekemoer, L.L., Brooke, B.D., et al., 2000. *Anopheles funestus* resistant to pyrethroid insecticides in South Africa. *Medical and Veterinary Entomology*, 14 (2), 181-189.
- Hunt, R.H., Coetzee, M. and Fettene, M., 1998. The *Anopheles gambiae* complex: a new species from Ethiopia. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 92 (2), 231-235.
- Kamau, L., Hunt, R. and Coetzee, M., 2002. Analysis of the population structure of *Anopheles funestus* (Diptera: Culicidae) from western and coastal Kenya using paracentric chromosomal inversion frequencies. *Journal of Medical Entomology*, 39 (1), 78-83.
- Kamau, L., Munyekenye, G.O., Koekemoer, L.L., et al., 2003. A survey of the *Anopheles funestus* (Diptera: Culicidae) group of mosquitoes from 10 sites in Kenya with special emphasis on population genetic structure based on chromosomal inversion karyotypes. *Journal of Medical Entomology*, 40 (5), 664-671.

- Koekemoer, L.L., Kamau, L., Hunt, R.H., et al., 2002. A cocktail polymerase chain reaction assay to identify members of the *Anopheles funestus* (Diptera: Culicidae) group. *American Journal of Tropical Medicine and Hygiene*, 66 (6), 804-811.
- Lehmann, T., Besansky, N.J., Hawley, W.A., et al., 1997. Microgeographic structure of *Anopheles gambiae* in western Kenya based on mtDNA and microsatellite loci. *Molecular Ecology*, 6 (3), 243-253.
- Lehmann, T., Hawley, W.A., Kamau, L., et al., 1996. Genetic differentiation of *Anopheles gambiae* populations from East and West Africa: Comparison of microsatellite and allozyme loci. *Heredity*, 77 Part 2, 192-200.
- Mahon, R.J., Green, C.A. and Hunt, R.H., 1976. Diagnostic allozymes for routine identification of adults of the *Anopheles gambiae* complex (Diptera: Culicidae). *Bulletin of Entomological Research*, 66 (1), 25-31.
- Park Ross, G.A., 1936. Insecticide as a major measure in the control of malaria, being an account of the methods and organizations put into force in Natal and Zululand during the past six years. *Quarterly Bulletin of the Health Organization of the League of Nations*, 5, 114-133.
- Petrarca, V. and Beier, J.C., 1992. Intraspecific chromosomal polymorphism in the *Anopheles gambiae* complex as a factor affecting malaria transmission in the Kisumu area of Kenya. *American Journal of Tropical Medicine and Hygiene*, 46 (2), 229-237.
- Petrarca, V., Beier, J.C., Onyango, F., et al., 1991. Species composition of the *Anopheles gambiae* complex (diptera: Culicidae) at two sites in western Kenya. *Journal of Medical Entomology*, 28 (3), 307-313.
- Petrarca, V., Carrara, G.C., Di Deco, M.A., et al., 1986. Il complesso *Anopheles gambiae* in Mozambico. *Annali dell'Istituto Superiore di Sanità*, 22, 209-210.
- Petrarca, V., Carrara, G.C., Di Deco, M.A., et al., 1984. Osservazioni citogenetiche e biometriche sui membri del complesso Anopheles gambiae in Mozambico. *Parassitologia*, 26 (3), 247-259.
- Petrarca, V., Sabatinelli, G., Di Deco, M.A., et al., 1990. The *Anopheles gambiae* complex in the Federal Islamic Republic of Comoros (Indian Ocean): some cytogenetic and biometric data. *Parassitologia*, 32 (3), 371-380.
- Powell, J.R., Tabachnick, W.J. and Arnold, J., 1980. Genetics and the origin of a vector population: *Aedes aegypti*, a case study. *Science*, 208 (4450), 1385-1387.
- Ralisoa Randrianasolo, B.O. and Coluzzi, M., 1987. Genetical investigations on zoophilic and exophilic *Anopheles arabiensis* from Antananarivo area (Madagascar). *Parassitologia*, 29 (1), 93-97.
- Ross, R., 1911. The prevention of malaria. John Murray, London.
- Scott, J.A., Brogdon, W.G. and Collins, F.H., 1993. Identification of single specimens of the *Anopheles gambiae* complex by the polymerase chain reaction. *American Journal of Tropical Medicine and Hygiene*, 49 (4), 520-529.
- Sinkins, S.P., Hackett, B.J., Costantini, C., et al., 2000. Isolation of polymorphic microsatellite loci from the malaria vector *Anopheles funestus*. *Molecular Ecology*, 9 (4), 490-492.
- Temu, E.A., Hunt, R.H. and Coetzee, M., 2004. Microsatellite DNA polymorphism and heterozygosity in the malaria vector mosquito *Anopheles funestus* (Diptera: Culicidae) in East and Southern Africa. *Acta Tropica*, 90 (1), 39-49.

- Temu, E.A., Minjas, J.N., Coetzee, M., et al., 1998. The role of four anopheline species (Diptera: Culicidae) in malaria transmission in coastal Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 92 (2), 152-158.
- Weeto, M.M., Koekemoer, L.L., Kamau, L., et al., 2004. Evaluation of a species-specific PCR assay for the *Anopheles funestus* group from eleven African countries and Madagascar. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 98 (3), 142-147.
- Zahar, A.R., 1985. The vector bionomics in the epidemiology and control of malaria.

 Part I. The WHO African Region and the Southern WHO Eastern

 Mediterranean Region. World Health Organization, Geneva.