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MALARIA AT ITS SOUTHERN-MOST FRINGE IN AFRICA

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SUMMARY: A brief review of malaria in southern Africa is given. The first trials ever carried out using insecticides as a house spray for the control of adult mosquitoes, were conducted in South Africa in 1931 with remarkable success being achieved in the sugar-growing areas of Kwazulu/Natal province. An overview of the *Anopheles gambiae* complex is provided, with the implications of this complex containing morphologically similar yet biologically different species for malaria control programmes. The present situation, with increased malaria transmission in most countries, new species of *A. gambiae* complex being revealed and pyrethroid insecticide resistance appearing in some vector populations, is discussed.

KEY WORDS: Malaria, southern Africa, insecticide control, *Anopheles gambiae* complex, review.

INTRODUCTION

Malaria in southern Africa is largely thought of as a minor tropical disease simply because this area is at the very fringe of its distribution. Compared with Equatorial African countries, it does perhaps seem that malaria is a minor problem in the southern-most part of the continent. However, one needs to take into account the complexities of the disease, in particular the fact that the present-day southern African human populations have little immunity to malaria in those countries where vector control is practised, eg. Zimbabwe, Botswana, Namibia and South Africa. The result is that malaria is only a minor problem as long as the vector control programmes, case detection and treatment are efficient. Should these programmes be curtailed or fail for whatever reason, malaria would once again become a major scourge during transmission seasons that are suitable for the mosquito vectors.

HISTORICAL PERSPECTIVE OF MALARIA IN SOUTHERN AFRICA

The early 20th century

Malaria has always been recognised as a major problem for the economic development of the areas in which it occurs. It is interesting to read in ROSS (1911) that the estimated cost of malaria to the United States of America at that time was $100 million per annum and to the small Indian Ocean island of Mauritius, with a population of 383000 people, about 1 million rupees per annum. The earliest accounts of malaria and the vectors and preventive measures in southern Africa are to be found in HILL & HAYDON (1905), BOSTOCK (1911) and MURISON (1911), reporting on the situation in South Africa from 1903-1907. BOSTOCK (1911) and HOWARD (1911), detail the work carried out in Mozambique during the same period.

In recognition of the economic importance of malaria, the South African Institute for Medical Research established a Department of Medical Entomology in 1925 and appointed Dr. Alexander Ingram as its head. Dr. Botha de Meillon was appointed as assistant and together these two intrepid scientists undertook the task of researching malaria transmission in South Africa. As early as 1927, INGRAM & DE MEILLON (1927) reported on the efficacy of certain reagents as destroyers of Diptera when used in the form of sprays. Houseflies were released into a room and then sprayed with various chemicals, usually dissolved in kerosene. The most effective compound was found to be a solution of pyrethrum powder «saturated» in kerosene, which resulted in no flies surviving three hours after administration of the spray. At this time, control measures against mosquitoes were directed at the larvae, with Paris Green and oils being the usual chemicals applied to water surfaces. The insecticide work with pyrethrum was a rediscovery of work done around 1910 by G. Giemsa, who used it as a mist spray to kill hibernating culicine mosquitoes in the cellars of Hamburg, Germany (see HARRISON, 1978).

By 1930/31 it was common knowledge that the malaria vector mosquitoes could be found in human habitations (DE MEILLON, 1930, 1933 in South Africa; LEESON, 1931 in Zimbabwe; GARNHAM, 1929 and SYMES, 1930 in Kenya; GIBBINS, 1932 in Uganda; BARBER & OLINGER, 1931 in Nigera). Experiments carried out during the 1931/32 transmission season in two provinces of South Africa were to have a profound effect on the malaria control strategies of the future.

Work in the Letsitele Valley (also known as «death valley»), with infection rates in the mosquito vector *Anopheles funestus* as high as 27% (SWELLENGREBEL, ANNECKE & DE MEILLON, 1931) outside Tzaneen in the Northern Province of South Africa, demonstrated that *A. funestus* was entering houses to obtain a blood meal and then remaining indoors until ready to lay eggs (DE MEILLON, 1934). This basic biological discovery was achieved by erecting a bed net over the door of a traditional hut with the narrow top of the bed net pointing outwards (the forerunner of window traps), closing all other openings and collecting those mosquitoes leaving the hut in the morning. A total of 84% of the females collected were found to be fully gravid, i.e. they were leaving the hut to oviposit. As it takes about three days for a freshly fed female to reach the gravid stage, this was powerful evidence that the mosquitoes spent a considerable time inside the house, during which time they could be killed with a pyrethrum spray. Despite the excellent results reported in his 1934 paper and the results presented at the 1935 Pan African health congress (DE MEILLON, 1936), for many years De Meillon remained doubtful about the usefulness of spraying houses with pyrethrum as a general malaria control method (DE MEILLON, 1938). The reasons for this were probably three-fold. Firstly, he had a good understanding of the role that climatic conditions played in the presence and abundance of the malaria vector mosquitoes and thus the intensity of malaria transmission, preferring to attribute the drop in malaria incidence in the mid-1930's to «a return to normal climatic conditions» (DE MEILLON, 1938) rather than as a direct result of house spraying against adult mosquitoes. Secondly, he knew of the continued presence of «*A. gambiae*» in areas that were being sprayed. Finally, he possibly underestimated the residual effect of the pyrethrum deposited on the interior of the houses, seeing the presence of 1 *A. funestus* at 5 a.m. in a house sprayed at 8 p.m. the previous night (DE MEILLON, 1934) as an indication that the insecticide was short-lived and needed to be applied regularly throughout the night to be totally effective.

The summer of 1931/32 saw the most devastating outbreak of malaria in the province of Kwazulu/Natal, with 95% of the workers on sugar cane plantations not reporting for work because of infection with the parasite. Mortality estimates for this period were 22132 out of a population at risk of 985000 (see LE SUEUR, SHARP & APPLETON, 1993; SHARP & LE SUEUR, 1996). A senior health inspector in Natal, Mr. Sam Hamilton, a good friend of De Meillon's, was aware of the work that Ingram and De Meillon had carried out on the use of pyrethrum and on the biology of the mosquitoes in the Letsitele Valley, through regular training courses carried out by De Meillon in 1929-34 for provincial malaria control personnel. Under the supervision of the Chief Medical Officer for Natal, Dr. Park Ross, Hamilton carried out an experiment in northern Kwazulu/Natal that was later reported as being strikingly effective (LE SUEUR, SHARP & APPLETON, 1993). This was the first time that insecticides were used specifically for the indoor control of house resting mosquitoes to reduce the incidence of malaria. The success of the malaria control programme in Kwazulu/Natal was fully reported by Park Ross at the 1935 Pan African health congress where he concluded «.... we have no hesitation in recommending the spraying of every dwelling ....» (PARK ROSS, 1936).

Lieutenant-Colonel G. Covell, then with the British army in India, was so impressed with the results obtained by De Meillon that he implemented similar control measures in India with great success (COVELL, MULLIGAN & AFRIDI, 1938). GARNHAM & HARPER (1944) reported on the control of rural malaria by pyrethrum dusting in Nyanza Province, Kenya, where a 50% reduction in malaria incidence was obtained. There were others, however, who were even more sceptical than De Meillon himself. Dr. Fred Soper, regarded by some at the time as the leading authority on mosquito-borne diseases in the world, attended the Pan African health congress in Johannesburg in 1935 and visited Eshowe in Kwazulu/Natal. He was highly critical of the results, saying that killing mosquitoes indoors would not have any impact of the thousands of mosquitoes outdoors (GEAR, 1993). However, when it came to controlling a huge malaria outbreak in Brazil in 1938 transmitted by the African vector *A. gambiae*, Soper eradicated the vector in 2 years by instituting an intensive weekly house spraying campaign with pyrethrum insecticide (SOPER & WILSON, 1943).

The mid-20th century and the *Anopheles gambiae* complex

South Africa started manufacturing DDT in 1944 and in 1946 this insecticide replaced pyrethrum for indoor house spraying for malaria control. By 1958 all houses in the malarial areas of South Africa were being sprayed with DDT (SHARP & LE SUEUR, 1996) and in the mid 1950's the World Health Organization initiated its malaria eradication campaign based on indoor house spraying.

But all was not well with the spray programmes in the southern regions of the African continent. MASTBAUM (1954) had led a highly successful campaign to rid Swaziland of malaria by spraying houses with BHC. While transmission was successfully interrupted, the mosquito vector *Anopheles gambiae* nevertheless remained abundant although it now preferred to feed on cattle out of doors rather than humans indoors. This supposedly provided direct evidence for a change in behaviour of mosquitoes under selection by insecticides and became known as behavioural resistance. It was only in 1963 that Paterson and colleagues provided an explanation for this apparent change in behaviour: «*Anopheles gambiae*» in Swaziland feeding on cattle was a different species to that commonly found in houses transmitting malaria (PATERSON, PATERSON & VAN EEDEN, 1963).

The formal recognition that the taxon *A. gambiae* was comprised of at least five morphological species (PATERSON, 1964; DAVIDSON *et al.*, 1967) was as revealing for malaria epidemiology in Africa as was the recognition of the *A. maculipennis* complex for malaria in Europe (SWELLENGREBEL & DE BUCK, 1938). In southern Africa, in fact, the impact was probably more pronounced than in tropical Africa. This was because the zoophilic, and the only totally non-vector member of the *A. gambiae* complex, occurs in this region, i.e. *A. quadriannulatus* (COETZEE *et al.*, 1993; HUNT, COETZEE & FETTENE, 1998). Malaria control programmes in southern Africa are sometimes seriously hampered by the presence of this species which, while being mainly an outdoor-resting species, can also be found resting in houses when outside shelters are not available (HUNT & MAHON, 1986). The issue of correct identification of the vector species (i.e. «species sanitation» of SWELLENGREBEL & DE BUCK, 1938) is thus probably far more important in southern Africa than anywhere else. Professor M. Coluzzi once stated «I would not hesitate to say that separating *A. arabiensis* from *A. quadriannulatus* is more important in terms of epidemiological entomology than separating *A. arabiensis* from *A. funestus*. In fact, the pooling of *A. arabiensis* and *A. funestus*, two species that both show a high vectorial capacity ... would be in many respects less misleading to the malariologist than the pooling of *arabiensis* and *quadriannulatus*, i.e. the pooling of a vector species with a non-vector one» (COLUZZI, 1984).

Many researchers have worked on the problem of identification of the member species of the *A. gambiae* complex since the 1960's. Morphological characters were found to be mostly lacking (COLUZZI, 1964; COETZEE, 1989) so over the years various genetical methods were tried. While the banding sequences on the giant polytene chromosomes found in adult female mosquitoes and 4th stage larvae (COLUZZI *et al.*, 1979) remains the most accurate method, modern DNA technology has provided a more rapid technique for screening large numbers of mosquitoes at any stage of the life cycle (SCOTT, BROGDON & COLLINS, 1993). However, new members of the complex are still being discovered and neither of these methods has universal applicability (HUNT, COETZEE & FETTENE, 1998).

MALARIA TODAY

In the 50 years since control measures were implemented in South Africa, malaria has never again reached the proportions that it did in the 1930's. The number of cases and deaths from malaria from 1971 to 1997 are given in Fig. 1. The marked increase in the last two years are due to many factors. For example, the rainfall in the malarial areas was unusually high, following several years of drought. Also, the changed political situation in South Africa had resulted in an enormous increase in the movement of people across South Africa's borders, particularly in the potentially malarial areas bordering Mozambique, Zimbabwe and to a lesser extent Botswana. Human populations in these areas often have close family ties with people across the border living in situations of intense malaria transmission. Visits to and from such areas result in infections in South African citizens and in the infection of the residual populations of *A. ara-*

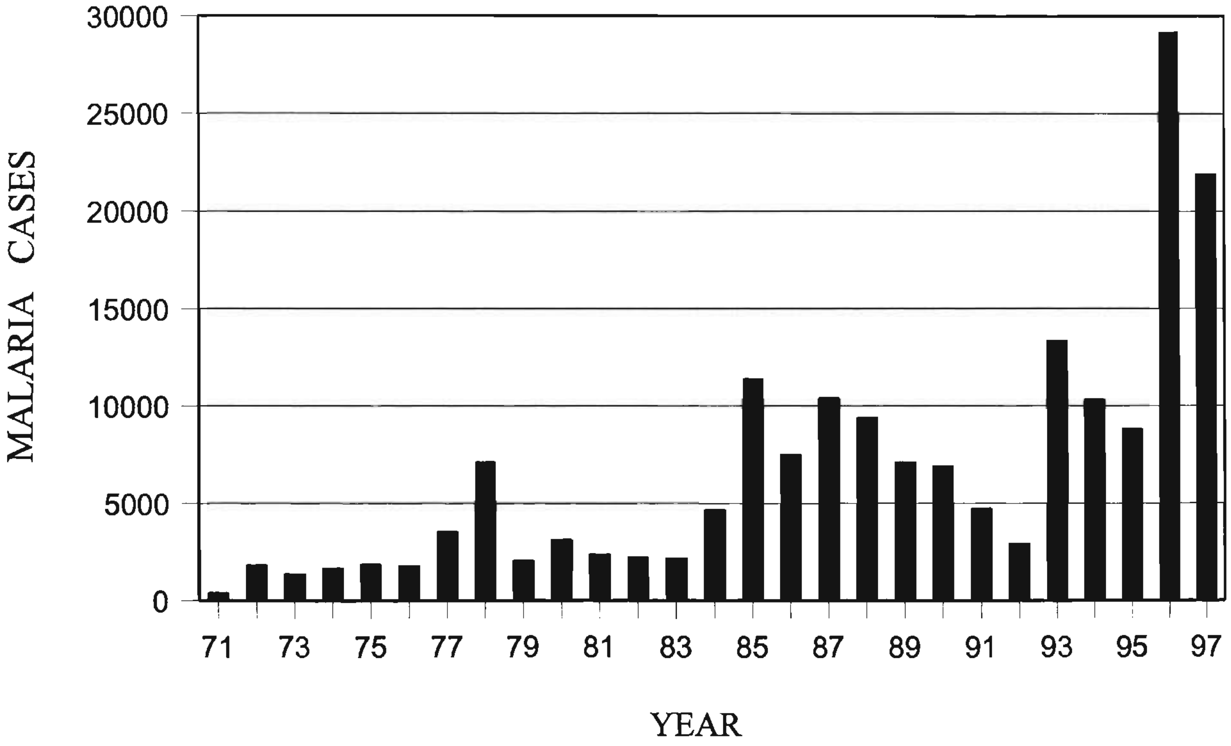

Fig. 1.– Annual number of notified cases of malaria in South Africa for the past 26 years.

biensis which survive the residual spray programme because of their exophilic behaviour. The epidemic of the 1995/96 summer was also evident in neighbouring Zimbabwe, where unconfirmed reports estimated the death toll from malaria as high as 10000. In Namibia it is estimated that 120000 new cases of malaria occur every year in children under 5 years of age (Namibian Ministry of Health Malaria Policy Document, 1995).

These figures serve to illustrate the tremendous importance of continued, sustainable malaria control measures once they have been implemented for any length of time. When drought conditions exist, as they often do in southern Africa, the importance of effective spray coverage may be forgotten because of the low incidence of the disease. However, as soon as conditions become favourable for the breeding of the mosquitoes, such lapses in control measures are immediately and devastatingly obvious. In the process of South Africa switching from DDT to synthetic pyrethroids for the spraying of houses, the monitoring of the spray programmes has become even more important, and more difficult. DDT deposits are visible on the walls of houses while synthetic pyrethroids are not, meaning that routine bioassay tests must be conducted to check on the efficiency of the spraying. More importantly, synthetic pyrethroids are widely used in agriculture in southern Africa and the reports from West Africa of resistance to these insecticides in *Anopheles gambiae* (MARTINEZ-TORRES *et al.*, 1998) give rise to grave concerns as to how long the use of this group of insecticides in malaria control programmes in South Africa will be effective.

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