Malaria in Sri Lanka

Current Knowledge an Transmission and Control

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ERRATUM
The second sentence at the top of page 24 should read:

In India, An. *culicifacies* B is believed **not** to play an important role in the transmission of malaria, while in Sri Lanka it is considered the most important vector and may be the only sibling species present (Subbarao 1988).

Flernming Konradsen, Felix P. Amerasinghe,
Wirn van der Hoek, and Priyanie H. Amerasinghe

IWMI
INTERNATIONAL WATER MANAGEMENT INSTITUTE

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/ malaria / risks / disease vectors / environmental aspects / human health / economic *impacts / social aspects / policy / Sri* Lanka /

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Photo credits: The photograph showing an IWMI staff member using a GPS device was taken by Flemrning Konradsen, IWMI. The photograph of the larvivorous fish was taken by Rohan Pethiyagoda. Wildlife Heritage Trust, Colombo 8. All other photographs were taken by Laxshmanan Nadaraja, Studio Times Limited, Colombo 5, Sri Lanka.

Contents

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Preface

It is now generally accepted that measures for malaria control must be based an the local epidemiological and transmission patterns using the right combination of methods at the right place, at the right time. Many of the studies done in Sri Lanka are of high scientific quality and can form the basis for the adaptation of the global malaria-control strategy to the Sri Lankan situation. However, there is no single text available that summarizes the malaria research efforts in Sri Lanka. Of the more than 150 references used for this review, many are from international journals that are not easily accessible to Sri Lankan students and researchers with very limited operational budgets. We hope that this book will fill the gap and that students in biological and medical sciences, researchers, and professionals involved in malaria control will find this book useful. The success and subsequent failure of the eradication efforts in Sri Lanka in the 1950s and **60s** are often used as an example in international textbooks and we think that much of the work done since then is also of interest to the international community engaged in research on and control of malaria. The text focuses on the current state of knowledge on transmission, epidemiology, and control and does not cover clinical aspects including the treatment of severe and complicated malarial disease. Globally, our knowledge about malaria has increased tremendously and continues to increase, especially because of developments in the field of molecular biology and genetic engineering. Sri Lankan researchers have significantly contributed to this knowledge. However, basic scientific research was not the focus of this review and certain specialized studies have not been included. Publications dealing with general aspects of health services or with research on health systems in Sri Lanka, whether from a policy, economic or management point of view are only included when they deal with malaria specifically. However, it should be realized that resource allocations within the health area as well as the national health policies play a major role in both the control of the disease and the impact of the disease on the individual and society in general.

Clearly, a number of papers and reports dealing with malaria in Sri Lanka have not been included in this review because they were not easily accessible. This might especially be true for studies undertaken as part of university degree programs, consultancy missions, conferences, or information contained in various restricted government documents.

The four authors are responsible for the main text. Others have provided text boxes that are interspersed throughout the book, and these give an overview of ongoing research or important issues in current control strategies that are yet to be published.

Acknowledgements

It took us over a year to prepare this book, involving a large number of people assisting with the identification of resource materials. Also, a number of colleagues at IWMI and at universities in Sri Lanka and overseas contributed valuable inputs to the preparation of the final output.

However, we especially thank Ms. Mala Ranawake for all the support she provided to this publication. Mala has been involved in the preparation of the photographs and graphical material of the book and has provided administrative support throughout the process. Our gratitude also goes to colleagues at IWMI, Ms. Sepali Goonaratne and Mr. Lal Mutuwatte for providing support with obtaining references and the generation of GIS-based outputs, respectively.

Of the people who provided input in the review process we especially wish to highlight the contribution made by Ms. Merete Bendixen.

Our most sincere gratitude goes to Mr. Laxshmanan Nadaraja for spending time, taking suitable photographs to illustrate fhis book.

We are most grateful for the collaboration extended to us by the Anti-Malaria Campaign of Sri Lanka.

Flemming Konradsen

Glossary, Abbreviations and Acronyms

AMC: Anti-Malaria Campaign.

Circumsporozolte protein: The major protein on the surface of spororoites.

Cytokines: Small proteins that are involved in intercellular communication during the immune response.

DNA probe: A strand of DNA that can be labeled and used to hybridize to a complementary molecule from a mixture of other nucleic acids.

Drug resistance: The ability of a parasite strain to survive and/or multiply despite the administration and absorption of a drug in doses equal to or higher than those usually recommended but within the limits of tolerance of the subject.

Ecology: The study of the relationship between communities of organisms and their environment.

EIR: Entomological inoculation rate. The number of infectious mosquito bites a person is exposed to in a certain time, typically a year. The EIR is the product of the human biting rate (HBR) and sporozoite rate.

ELISA: Enzyme-linked immunosorbent assay. **A** technique using the antigen-binding properties of antibodies *to* detect specific antigens or antibodies. Visualization is made possible by enzyme-induced color formation.

Environmental management for vector control: The planning, implementation and monitoring of deliberate changes of environmental factors, with the view to prevent the propagation of vectors and reduce human-vector-pathogen contact.

Epidemic: The occurrence in a community or region of cases of malaria clearly more than what is normally expected.

G6PD: Glucose-6-phosphate dehydrogenase. **A** key red blood cell enzyme

HBI: Human blood index. Proportion of female mosquitoes whose midgut contains human blood.

HBR: Human biting rate. Mosquito bites per person per unit of time.

IBN: Impregnated bed net. A bed net that is treated with an insecticide such as permethrin that is considered safe for humans.

IFAT: Indirect fluorescent antibody test

Incidence: New cases in a population over time.

MIV: Mean number of infective vectors per night.

PCR: Polymerase chain reaction. **A** method for amplifying **DNA** in vitro. involving the use of oligonucleotide primers complementary to nucleotide sequences in a target gene and the copying of the target sequences by the action of **DNA** polymerase.

Prevalence: Existing cases in a population (at a certain point in time). The proportion of individuals in a population having malaria parasites in the blood.

Recrudescence: Renewed manifestation of malaria attributed to survival of erythrocytic forms.

Relapse: Renewed manifestation of malaria attributed to development of hypnozoites, with subsequent invasion of red blood cells ***(Plasmodium*** vivax, *P. ovale* only).

Relative **risk** Ratio of the incidence of disease in the exposed group divided by the corresponding incidence of disease in the nonexposed group.

Sensitivity: Probability that a test is positive if the disease is truly present. Calculated by dividing the number of true positives by the sum of true positives and false negatives.

Sibling **species:** True species, which do not interbreed but are difficult to separate, based on morphological evidence alone.

Species complex: A species complex consists of a number of species with almost identical morphological features but with differences in certain aspects of their biology, behavior and distribution. In most cases, the distinction will have to be made using **PCR** techniques or studying the chromosome pattern.

Specificity: Probability that a test is negative if the disease is truly absent. Calculated by dividing the number of true negatives by the sum of true negatives and false positives.

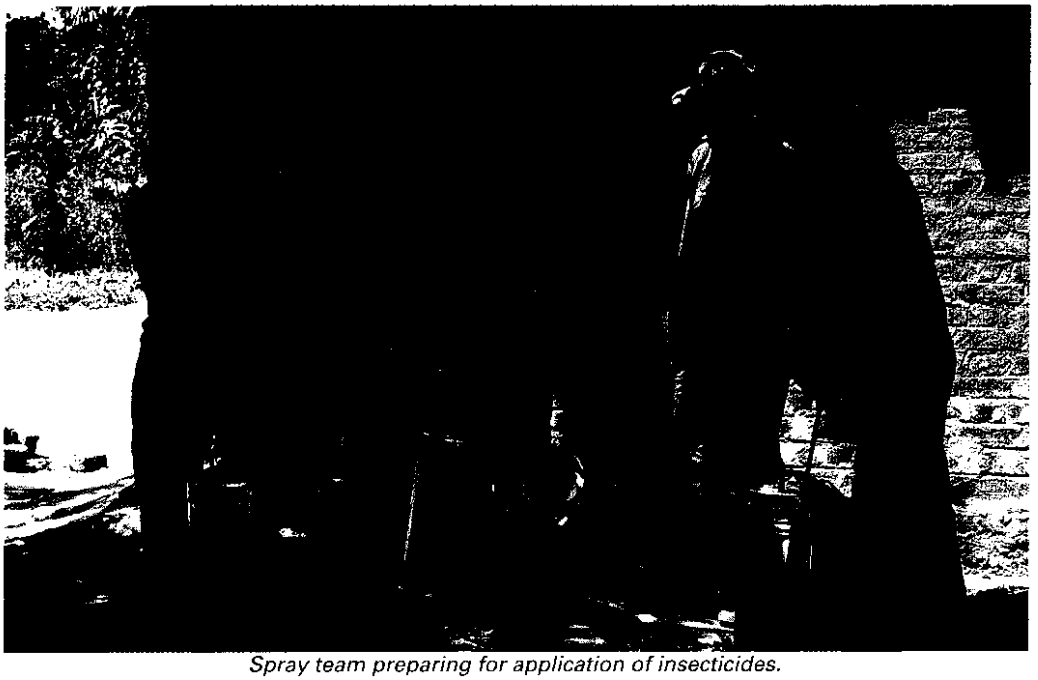
Sporozoite rate: Percentage of female anophelines with sporozoites in their salivary glands.

T cell: **A** white blood cell responsible for cell-mediated immunity.

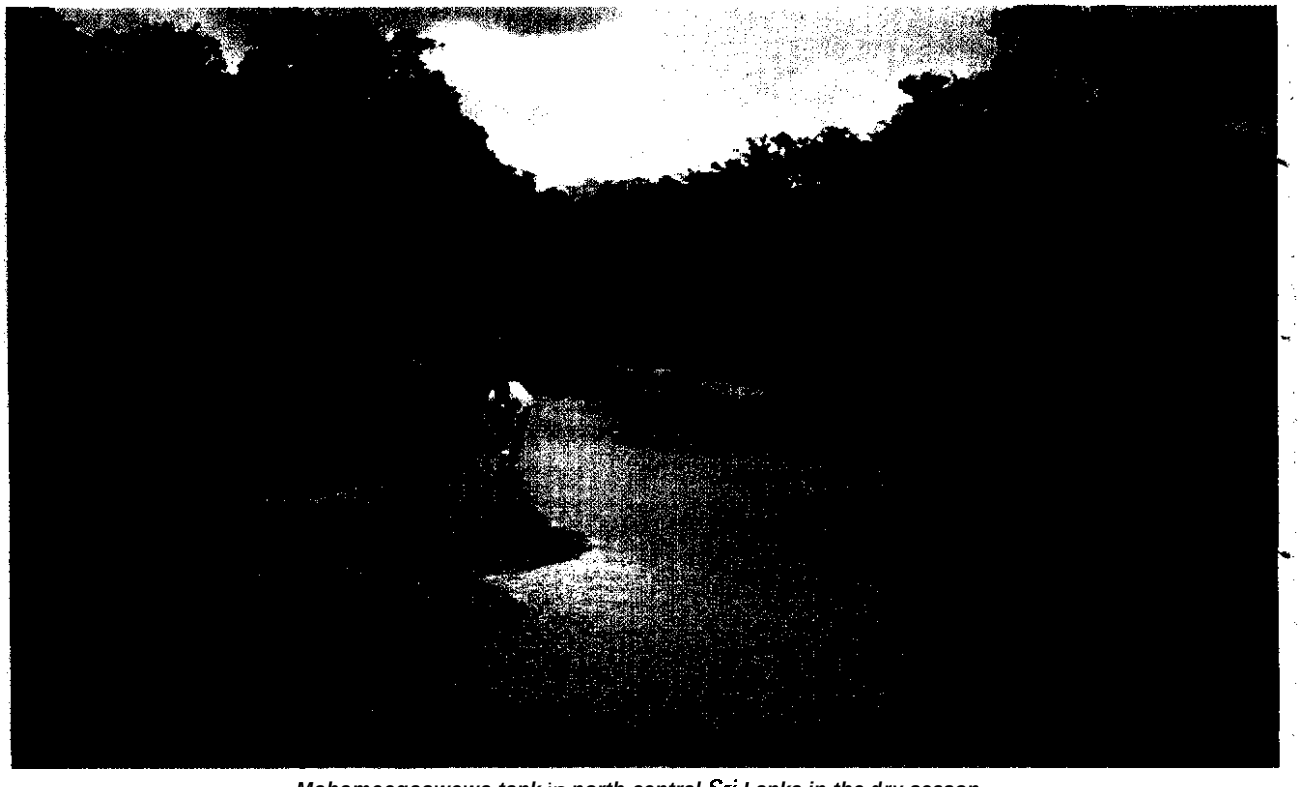
TNF Tumor necrosis factor. A cytokine that may contribute to the control of infection or to the development of pathology.

Vectorial capacity: The number of infective bites a person receives in a given period. **A** function of relative populations of mosquitoes and people, feeding frequency of the mosquito, duration of the latent period in the vector and the survival of the vector.

Community health worker preparing slide, with blood from patient.



Spray team preparing for application of insecticides.



Mahameegaswewa tank in *north-central Sri Lanka in the dry season*

Chapter 1

Introduction

Despite large-scale control efforts, malaria continues to be a major public health problem in Sri Lanka, which not only causes hardship to the patients and their families but also consumes a large share of the government's budget for health care. Over the years, a large pool of knowledge has accumulated on malaria in Sri Lanka. The present review includes a broad range of published literature **of** relevance for a description of malaria in Sri Lanka, including the control aspects of the disease. Based on the literature examined, a general overview of the status of research in Sri Lanka is given and areas where knowledge is lacking and further studies are required are identified. For the reader unfamiliar with Sri Lanka. figure **1** provides a map showing the districts of the country and major research sites referred to in the review. Many **of** the published papers, on which this text is based, focus on Kataragama in the southeast of the country where the Malaria Research Unit of the University of Colombo has been doing research since the mid-1980s. The authors have also drawn heavily on their own work in the northern dry zone. especially in the Anuradhapura District and in System C **of** the Mahaweli Development Project located in the northeast **of** the country.

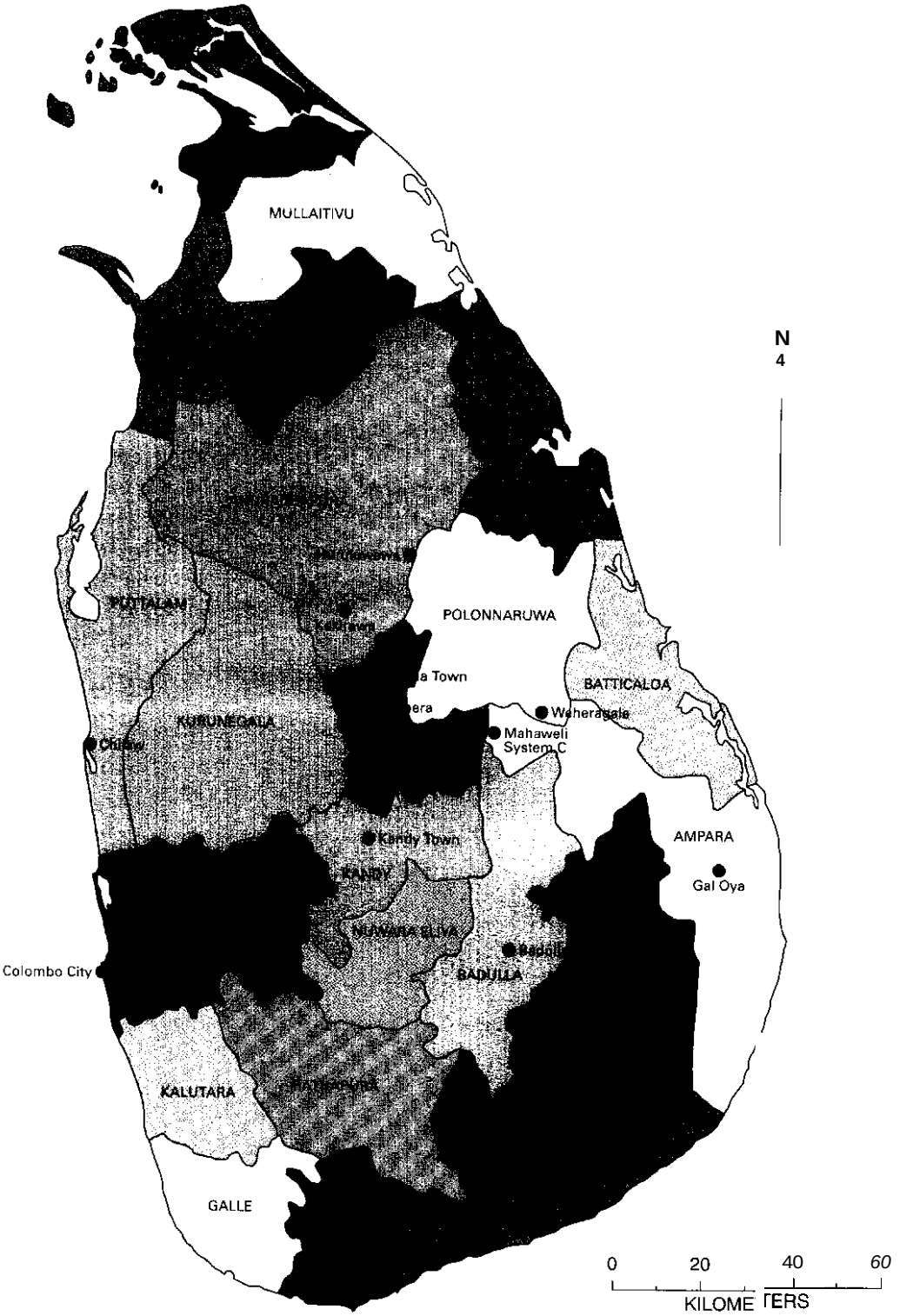


Figure 1. Administrative districts of Sri Lanka with selected malaria research sites

Chapter 2

Epidemiology of Malaria in Sri Lanka

Malaria and the Three Climatic Zones

Traditionally, Sri Lanka is divided into three climatic zones. The dry zone. covering the largest part of the country, receives less than 2,000 millimeters of rain per year, primarily from October *to* January during the northeast monsoon. The wet zone receives more than 2,500 millimeters of rainfall per year from October to January, and from May to July during the southwest monsoon. An intermediate zone lies between the dry and wet zones with between 2,000 and 2,500 millimeters of rainfall per year (see figure 2). Malaria has traditionally been endemic in the dry and intermediate zones where conditions for

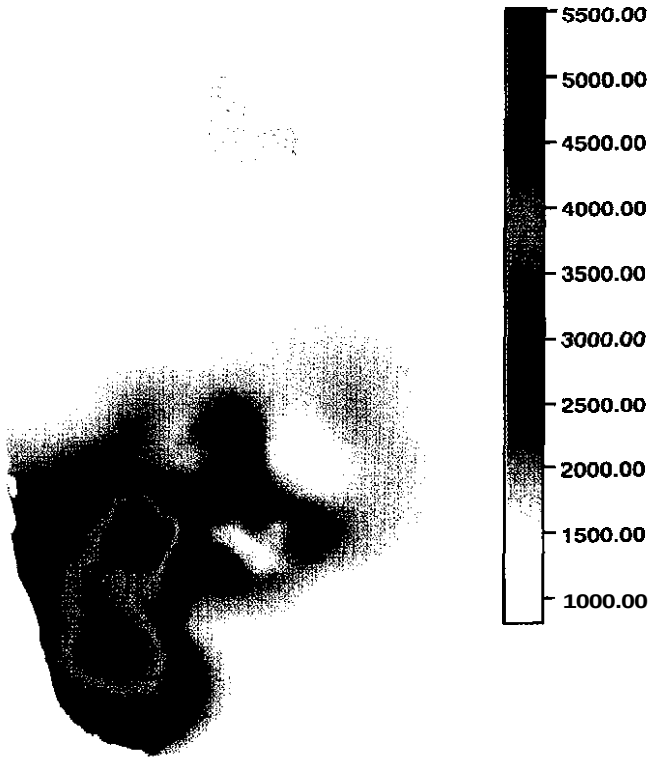


Figure 2. Average annual rainfall in *mm* ***from*** *1961* to *1990* recorded ***by*** ***146*** meteorological stations.
Source: IWMI Water **and** Climate Atlas.

malaria transmission are favorable for the larger part of the year with temperatures around 25 °C and a relative humidity of between 75 percent and 80 percent (Samarasinghe 1990; Nagendran et al. 1993). The peak-transmission season relates to the rainfall pattern and occurs from October to February each year with a moderate elevation in June (figure 3). However, even in the endemic parts of the country malaria transmission varies greatly from year to year. The abundant rainfall that normally occurs throughout the year in the wet zone is not conducive to the breeding of the malaria vector and malaria incidence remains low (Rajendram and Jayewickreme 1951a; Dissanaike 1984). However, in years with exceptionally low rainfall breeding opportunities are created in streams and rivers. The great epidemics of malaria in Sri Lanka have occurred, in fact, after the complete failure of the southwest monsoon. The only districts that have never been affected are Kalutara and Galle (Rajendram and Jayewickreme 1951a). Another area with consistently very low malaria incidence is the central mountainous wet zone of the country since malaria does not generally occur above 1,000 m (Gilles and Warrell 1993) (figure 4).

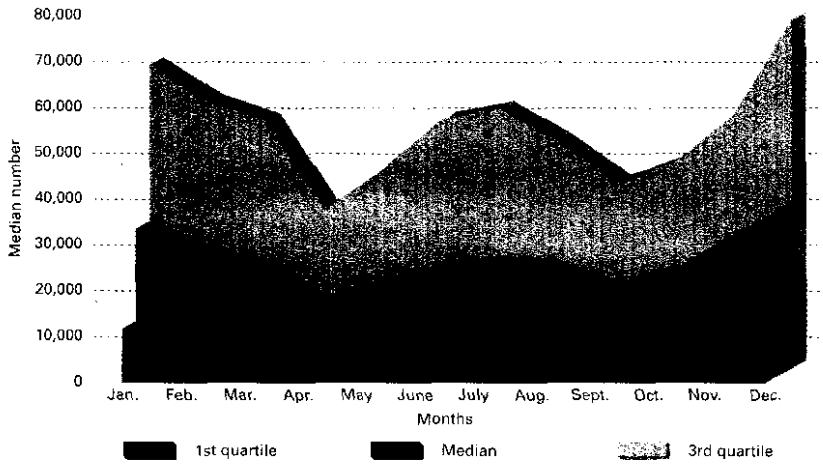


Figure 3. Seasonal pattern of malaria in Sri Lanka. Median number of laboratory-confirmed malaria cases with first and third quartiles over the period 1968–1990.

A Historical Reference

Early human settlements in the dry zone of Sri Lanka used constructed reservoirs (tanks) to sustain agricultural production and provide water for domestic use and other purposes. Eventually, irrigation engineering developed to such a technical perfection that historians often speak of a "hydraulic civilization." The first capital of this civilization was Anuradhapura, founded in 437 BC. Around 781 AD it was succeeded by Polonnaruwa, which reached its peak in the twelfth century. However, towards the end of the twelfth century, this civilization declined and many people migrated to other areas of the island. Some authors have attributed the decline of this civilization to the introduction of malaria from South India (Nicholls 1921). Others maintain that the anopheline vector and the malaria parasites should have been present long before but that the destruction of the irrigation infrastructure by foreign invaders caused people to leave the areas. The decaying tank and canal structures that followed the fall led to an increase in the vector abundance

by creating favorable breeding conditions and this prevented the return of people to the affected areas for many centuries (Edirisinghe 1988; Wijesundere 1989). There are also reports that the destruction of irrigation systems coincided with a gradual increase in aridity, creating an environment even more conducive to vector breeding (Tyssul Jones 1951a).

The few records that are available from the Portuguese and Dutch periods refer to the unhealthiness of certain areas because of periodic fevers (Uragoda 1987). After the British colonized the island and made inroads into the interior of the country, a large number of references were made to an illness which, most probably. would have been malaria. This included reports on ***a very*** serious epidemic in ***1803,*** which also affected the Kandyan kingdom in the central hill area of the country. Later, the disease had a severe impact on the Indian laborers brought in to work in the tea estates, especially since these people had to trek through the northern malarial dry zone to reach their place of work in the central hill country. The first systematic report on malaria from the island is found in an early administrative report of the Civil Medical Department in ***1867.*** At that time, the only type of antimalarial activity was the administration of quinine (Uragoda 1987).

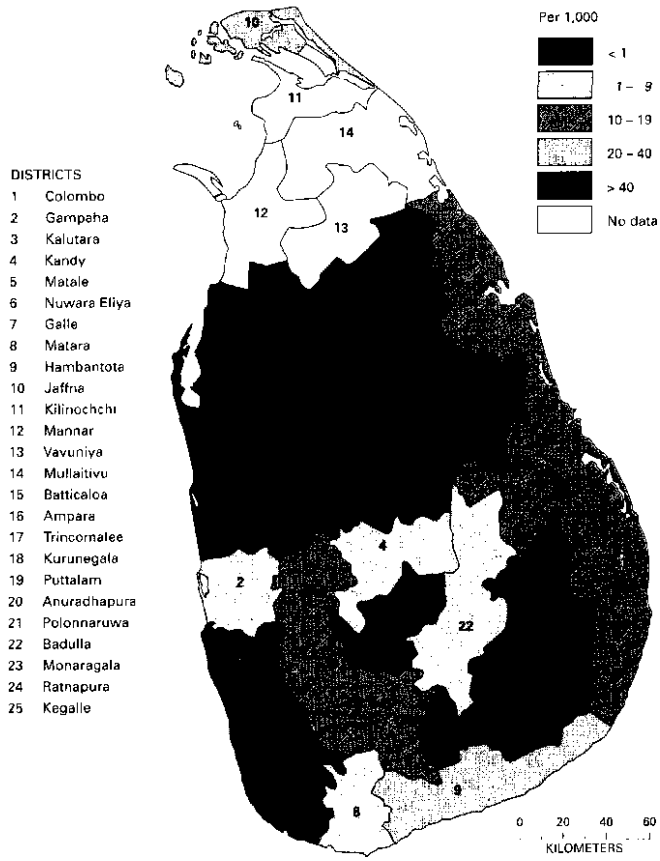


Figure 4. Average yearly number **of** ***microscopically confirmed malaria cases per*** *7,000* ***persons by district from 1989 to 1994.***

Milestones of Malaria Control in Sri Lanka

Punsiri Fernando

Malaria has been a major public health problem in Sri Lanka throughout the twentieth century. Over the years. there have been successes and reversals in the battle against this disease. Some of the highlights in this struggle are itemized below:

1911. The first antimalaria center in the country was set up at the town of Kurunegala in Sri Lanka (known as Ceylon before mid-1972).

1913. S.P. James and S.T. Gunasekera first incriminated the mosquito Anopheles culicifacies as the vector of malaria in the country.

1921. Henry F. Carter was appointed as the first malariologist in the country. Until his retirement in the 1950s, Carter made an enormous contribution to malariology in the country.

1921/22. The first comprehensive island-wide spleen and parasite surveys were carried out.

1927. Comprehensive reporting on the bionomics of anopheline species in the country commenced.

1928/31. Several antimalaria campaign units were set up in various parts of the country.

1934/35. A devastating epidemic of malaria occurred, with 5 million cases and 80,000 deaths.

1946. DDT spraying was introduced, followed by a dramatic reduction in malaria incidence.

1958. The Malaria Eradication Program was launched.

1963. Near eradication of malaria was achieved, with only 17 reported malaria cases.

1967/68. Resurgence of malaria occurred, leading to a countrywide epidemic.

1969. DDT resistance was detected in the vector mosquito Anopheles culicifacies.

1984. Drug resistance (to chloroquine) was detected in the malaria parasite Plasmodium falciparum in Sri Lanka.

1989. Activities of the Anti-Malaria Campaign were decentralized to the provinces.

1993. A new "Global Malaria Control Strategy" recommended by the World Health Organization (WHO)was introduced.

1999. A new WHO-sponsored global "Roll Back Malaria Initiative" was launched, with the target being the reduction of the malaria burden by 50 percent by the year 2010.

Punsiri Fernando,
Director, Anti-Malaria Campaign,
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Sri Lanka.

In 1897 in India, Ronald Ross demonstrated the role of mosquitoes in malaria transmission for the first time and this led to vector-control activities in several countries. In Sri Lanka. vector-control measures started in 1921 and consisted mainly of draining, filling, clearing and oiling of actual and potential breeding places and the introduction of larvivorous fish (Rajendram and Jayewickreme 1951a). Between the beginning of the twentieth century and the initiation of a DDT-based residual-spraying program after the Second World War, at least ten major epidemics occurred in the country. The most serious was the 1934–1935 epidemic with more than 5 million cases and 80.000 deaths (Edirisinghe 1988).

With the introduction of DDT in 1946, malaria morbidity and mortality declined steadily. In 1955, the World Health Organization (WHO) declared the goal of global eradication of malaria with a four-phase program: preparatory, attack, consolidation, and maintenance. In Sri Lanka, the malaria-eradication program started along these lines in 1958, and in 1963 the "attack" phase was successfully completed with only 17 malaria cases reported islandwide during that year. In 1964, the "consolidation" phase was started and most of the DDT spray teams were disbanded (Wickramasinghe 1981). The discontinuation and weakening of the vector-control program led to a resurgence of malaria with a massive epidemic in 1968, now considered the classical example of a post-eradication epidemic (Nájera, Kooznetzsov, and Delacollette 1998). Malaria had reestablished itself as a major disease especially in the dry zone of the country. Throughout the 1970s, there were a constant relatively high number of malaria cases although morbidity never reached the levels that existed before the eradication period (figure 5). The reintroduction of DDT had limited effect due to vector resistance. Although no detailed controlled studies have been carried out it is likely that the replacement of DDT by malathion as the insecticide of choice in the residual spray program was a contributing factor leading to the significant reduction

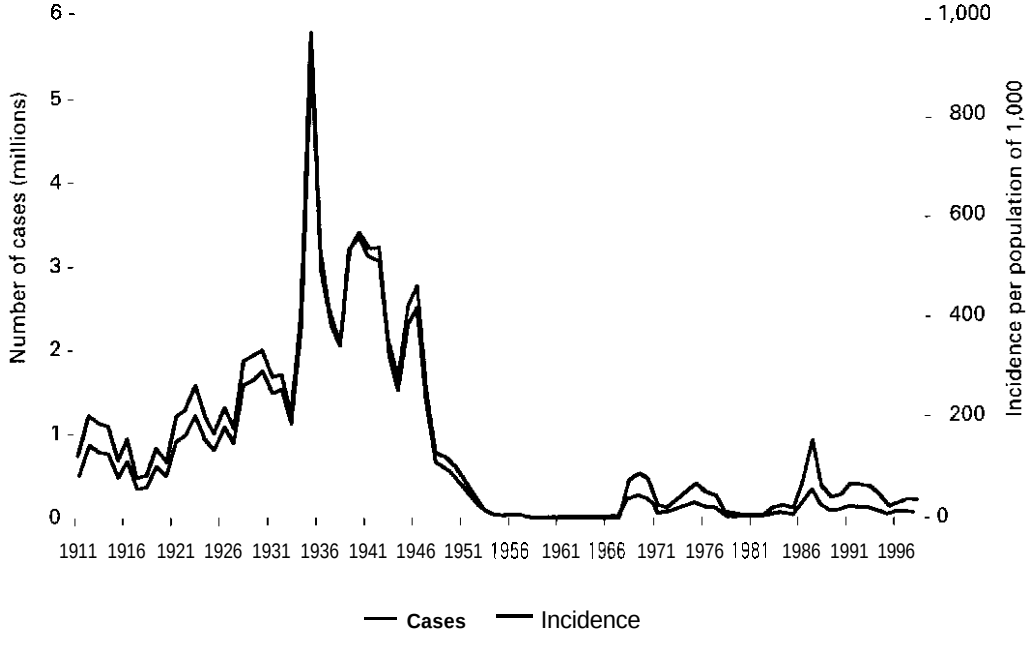


*Figure **5.** Annual incidence of malaria in **Sri** Lanka from 1911* to *1998.*

in the incidence of malaria observed in the late 1970s. From more than 200,000 cases in 1977 it went down gradually to only 38,000 cases in 1982 and was maintained at a low level until the mid-1980s (Samarasinghe 1990).

Mortality due to malaria was very high during the epidemics in the first half of the twentieth century. After the Second World War, overall mortality rates and mortality due to malaria went down sharply. Interestingly, the overall decline in mortality in Sri Lanka has been attributed to the introduction of DDT spraying, although this is disputed by others (Langford 1996).

Recent Trends in the Number of Malaria Cases

The most recent peak in the number of malaria cases occurred in 1987 with 56 cases per 1,000 persons, followed by a smaller peak in 1991 with 23 cases per 1,000 persons. In the years since 1991, malaria incidence has ranged between 9 and 23 cases per 1,000 persons for the island as a whole. At the peak in 1987, the incidence was comparable to that experienced in the previous epidemics of 1968-1970 and 1973. Nevertheless, it was considerably lower than the annual incidence of 200-500 per 1,000 persons, typically seen in the 1930s and 1940s before the initiation of DDT spraying. Although treatment-seeking behavior and recording of malaria cases have changed, this should still be considered as a very important real decline in incidence.

Mortality due to malaria is now very low. Only 18 deaths due to malaria were reported countrywide in 1996. Alles, Mendis, and Carter (1998) reported a case fatality for *P.* falciparum of 0.01 percent in endemic areas against 1 percent in Colombo, a non-endemic area. Delay in diagnosis and treatment in non-endemic areas explained the hundredfold higher case-fatality rate although lack of acquired immunity could also play a role.

During the epidemic in 1987, the ratio of male to female cases was 1.4:1 but it gradually declined to a ratio of 1.1:1 in 1994 (Graves, Fernando, and Attanayake 1995). Differences in treatment-seeking behavior or differences in exposure could explain the larger number of cases among men than among women. However, this is difficult to verify since only one study has analyzed the gender differences in treatment-seeking behavior (Konradsen et al. 2000).

In recent years, the ratio of *P.* vivax to *P.* falciparum cases has gone down from 33:1 in 1980 to 3:1 in 1989 (Samarasinghe 1990). According to the government Annual Health Bulletins the *P. vivax* / *P.* falciparum ratio for the first half of the 1990s fluctuated between 4:1 and 5:1 for the country as a whole. Plasmodium falciparum is highly pathogenic and causes more severe clinical symptoms. Also, the relative increase in the number of *P* falciparum cases may increase the epidemic potential often associated with this form of malaria in Sri Lanka (Gilles and Warrell 1993). Most epidemics reported in Sri Lanka were mixed, with *P.* vivax occurring before *P.* falciparum (Tyssul Jones 1951b). Plasmodium malariae constituted up to a few percent of all malaria cases before the Second World War. Since 1984, this species has not been found anymore (Samarasinghe 1986).

Cyclical Pattern of Epidemics

Gill (1936) studied malaria data from 1906 to 1934 and described the epidemic nature of malaria in Sri Lanka. He found that epidemics in the island occurred at 5-year intervals. Gill also carried out an analysis of the relationship between rainfall patterns and the occurrence of epidemics. He concluded that in the wet zone of the country, a deficiency of rainfall in the "spring" was favorable for the occurrence of a "summer" epidemic, and a deficiency of rainfall from July to September was favorable for the occurrence of a "winter" epidemic. It was the opposite in the dry zone where excessive rainfall during the "winter" was favorable to the occurrence of a "winter" epidemic. It was also suggested that malaria epidemics were closely related to an abrupt rise in atmospheric humidity during the pre-epidemic period. Bouma and van der Kaay (1996) correlated malaria epidemics with the El Nirio weather pattern between 1867 and 1943. Epidemics were significantly more prevalent during El Nino years, when the southwest monsoon tends to fail, confirming Gill'sfindingsforthewetzoneofthecountry. Inthis way, advances made in predicting El Nirio events may be used to forecast high-risk years. One study assessed the possibility of using routinely collected meteorological information to predict outbreaks of malaria at district level. Van der Hoek et al. (1997) correlated monthly rainfall and monthly malaria incidence in Kekirawa, in the northern dry zone of the country for the period 1979 to 1995. The correlation was weak and only significant when a 2-month time lag was observed. The study concluded that the relationship between higher-than-average seasonal rainfall and higher-than-average seasonal malaria incidence was not very strong and, despite the statistical significance of the correlation, its practical relevance for the planning of malaria control seemed limited. The finding is in contrast with the results of Gill for the dry zone. However, it is possible that the many environmental changes and malaria-control efforts have affected malaria transmission and local climate conditions enough to weaken and complicate the relationship between rainfall and malaria.

There isconcern worldwide that future malaria epidemiology will be influenced considerably by global climate change. Global warming could be important in areas where low temperature is currently an important limiting factor for effective malaria transmission. Most of Sri Lanka already has an optimum temperature for malaria transmission and a slight increase would not have a large impact. Mutuwatte et al. (1996) modeled the impact of climate change on malaria under the scenario of a doubling in CO_2, one of the major greenhouse gases. It was concluded that the endemicity of malaria in the dry zone of Sri Lanka is likelyto remain unchanged or decrease slightly, provided that other conditions remain the same.

Risk Factors and Protective Behavior

A number of studies have been done to identify the vulnerable groups and the risk factors for the disease. Also, information on knowledge of the disease among at-risk communities and on the preventive measures taken by households has been collected to support the planning of control activities.

Age

Graves, Fernando, and Attanayake (1995) calculated the age-specific incidence in six different malarial districts of the country over the period 1986 to 1994 including both *P.* vivaxand *P. falciparum* cases. From 1986 through 1990, incidence rates were lowest in infants below 1 year, increasing sharply to 20–30 cases per 1,000 in the **1-4** year-olds, and then showed a gradual decline through the older age groups. In the 1992–1994 period this had changed somewhat with the highest incidence rates in the 1–4 year olds and the 10–14 year olds. However, it was clear that, for the entire 19861994 period, the highest incidence was among children and not adults. A similar trend in age-related incidence pattern has been recorded from a different study site in the Southern Province of Sri Lanka where the endemicity for malaria is low. In this site too, the incidence was highest among the youngest age groups (Mendis et al. 1990). The difference in age-related incidence has been explained by differences in exposure and by age-related immunity.

Example *of a relatively good* house *in* the *dry zone of Sri* Lanka.

House Construction and House Location

Since early this century, it has been known that Anopheles culicifacies, the main vector of malaria in Sri Canka hides itself in cracks and crevices within houses. Wattle and daub houses, thatched with the interwoven leaf of the coconut palm provided many opportunities for the mosquitoes to hide (Rajendram and Jayewickreme 1951a). The percentage share of permanent houses using durable construction has increased over time. At the last census in 1981, 42 percent of the houses in Sri Lanka were permanent units constructed of durable materials such as cement, bricks, tiles or asbestos sheets. However,

Example ***of a*** poor ***house in which higher*** *mosquito* ***densities can be expected.***

the other 58 percent still used perishable materials alone or with some durable products (NARESA 1991). Especially in rural areas, walls and floors of houses are often constructed from mud, and roofs from perishable materials such as cadjan. Mosquito densities are expected to be higher in such temporary houses than in permanent houses and this increases the risk for malaria for its inhabitants. An epidemiological study undertaken over a 17-month period during 1986–1987 in Kataragama showed that the risk of being infected with malaria was greater for inhabitants living in the poorly constructed houses (Gamage-Mendis et al. 1991a). In the same area in 1992–1993, the risk for malaria was found to be 2.5-fold higher among people living in poorly constructed houses than among those living in well-constructed houses (Gunawardena et al. 1998).

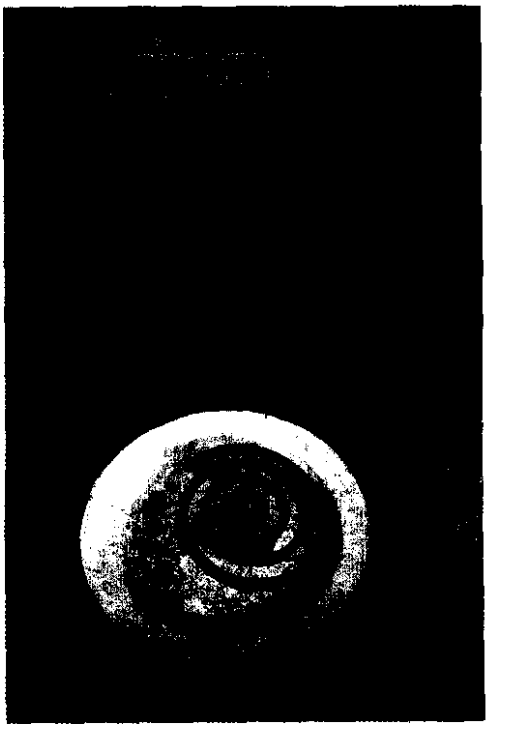
In Huruluwewa, living close to an An. culicifacies breeding site was associated with an increased risk for malaria (Van der Hoek et al. 1998a). The study emphasized the importance of making a detailed temporal risk analysis because of the changes in breeding preferences over the year and stressed the need to make the association with established vector-breeding sites rather than with potential breeding sites.

Gender Aspects

In *a* study in four purana (traditional) villages in the northern Anuradhapura District a slightly higher incidence of malaria was recorded for men than for women. This was explained by the fact that women's clothing covered more of their body. **Also** women often spend the hours at dusk preparing food in the smoky environment of a kitchen, which has a possible repellent effect on the mosquito. Another factor was that women. as a rule, sleep inside the house while the men often sleep outside or spend nights guarding their crops in

The burning of neem leaves is a traditional method for protection against mosquitoes.

the fields where they will be highly exposed to mosquito bites (Silva **1990).** Although it seems that gender is not an important risk factor in Sri Lanka. the specific gender-related risk factors have not been quantified and most information is anecdotal.



*Pyrethrum mosquito coils are widely available in Sri **Lanka.***

Mosquito Repellents

In traditional villages, Silva (1991) found that the habit **of** burning herbal ingredients as a mosquito repellent was still widely practiced. The burning of special leaves for protection against mosquitoes was also found to be practiced regularly among ***69*** percent of the households surveyed in five villages in the Huruluwewa watershed located in the Anuradhapura District (Konradsen et al. 1997a). In an epidemiological study in one of the five sample villages it was found that burning of leaves was protective and reduced the risk of contracting malaria by approximately twofold. Another common practice in the village, burning of

commercially produced pyrethrum mosquito coils, was not found to provide protection (Van der Hoek et al. 1998a). The commercial mosquito coils are relatively expensive and most families used only one per night, which may not be enough to provide effective protection. In contrast, in the households where the traditional fumigants were used, excessive smoke was generated throughout the house at time of dusk and into the night. Most of the international evidence of the repellent effect of certain chemicals is based on entomological data. There is still a lack of epidemiological evidence that this repellent effect also leads to lower malaria incidence and it is therefore difficult to appreciate the role they could play in malaria-control strategies. Locally available citronella and neem oil are cheap and culturally acceptable in Sri Lanka and their role in malaria control should be further investigated (Perera et al. 1998).

Knowledge

In the northern dry zone, a household survey showed that the people there had a very good knowledge of malaria, including route of transmission. means **of** diagnosis and medication needed for treatment (Konradsen et al. 1997a). The community knowledge of malaria has not been documented systematically for other parts of Sri Lanka. However, the general opinion is that this knowledge is very good compared with that of most other countries and this is important as a basis for planning disease-control programs.

Migration

Large-scale population movements can increase the transmission of malaria when nonimmune individuals move into an endemic area. Some of the migrating groups identified by Silva (1995) are the communities that have been resettled in the dry zone of the country in relation to large-scale irrigation development, members of the security forces, refugees, pilgrims and seasonal farm workers. The problems associated with the resettlement of large populations from non-malarial areas, where they have had no experience with the disease, to the endemic dry zone has been highlighted by Jayawardena (1993). In another study in a low-endemic area in the Badulla District, migrant workers were also found to have a high risk for malaria (Mutuwatta et al. 1998). However, it is not yet clear if the vulnerability of the migrants was due to extreme exposure linked to their living and working conditions. the lack of immunity or possibly their limited ability to cope with the illness. Some parts of the north and the east of the country cannot be covered by the government health services because of the ongoing armed conflict. There were an estimated 603,000 internally displaced people because of this conflict in 7998 (www.unhcr.ch 1998). In many cases, international aid organizations have taken up responsibility for malaria-control activities. Military personnel stationed in the northern jungle areas are at high risk of contracting malaria, especially if they are from non-endemic areas. They can also carry parasites back to their home areas. Large-scale population movements, both permanent and seasonal, also increase the opportunity of spreading resistant parasite strains from ***one*** region to another. A clear health policy with regard to preventive measures is needed for migrating groups.

Bed Nets, Sleeping Behaviors and Malaria incidence in an Endemic Area of Sri Lanka

K.N. *Mendis, R.* Carter, **S.** Bandara, A.B. Herath and M.W.A. de *Silva*

A longitudinal study was carried out to test the efficacy and acceptability of impregnated bed nets (IBNs) in the Kataragama and Buttala Divisional Secretary Divisions of the Monaragala District. The study utilized a quasi-experimental, test and control design. The intervention commenced with the distribution of bed nets to experimental areas. The net distribution and selection of types of nets were entirely based on the judgement of the householders. Malaria infections were monitored in both test and control villages through diagnosis and treatment posts, and hospitals located in the areas.

Following the intervention, the incidence of malaria in the test areas was drastically reduced, particularly in the 2-5 and 6-15 year age groups. The unintended changes in sleeping arrangements and sleeping behavior in the households consequent to the introduction of IBNs significantly contributed to a change in age and gender distribution of malaria incidence in the test areas. The analysis suggests that a) there has been a change in sleeping patterns in test households subsequent to the introduction of IBNs, and b) these changes are correlated with malaria incidence in the test areas. The study confirms that an analysis of household composition and sleeping arrangements can help better planning and reduce the cost of malaria control with IBNs.

Table *1.* Malaria incidence from October 15, *1993* to April *14, 1995* in test and control areas.

Age group in years	Test population			Control *population*			Test control difference
	N	Malaria cases	*Cumulative* incidence	N	Malaria cases	Cumulative incidence	
		NO.	%		*NO.*	%	%
1	74	9	12.1	80	18	22.5	10.3
2 - 5	245	74	30.2	210	241	114.7	84.5
6 - 15	555	116	20.9	526	554	105.3	84.4
16 - 25	406	94	23.1	333	215	64.5	41.4
26 - 50	639	150	23.4	598	402	67.2	43.7
> = 51	152	25	16.4	146	62	42.4	26.0
Total	2,071	468	22.5	1,893	1,492	78.8	56.2

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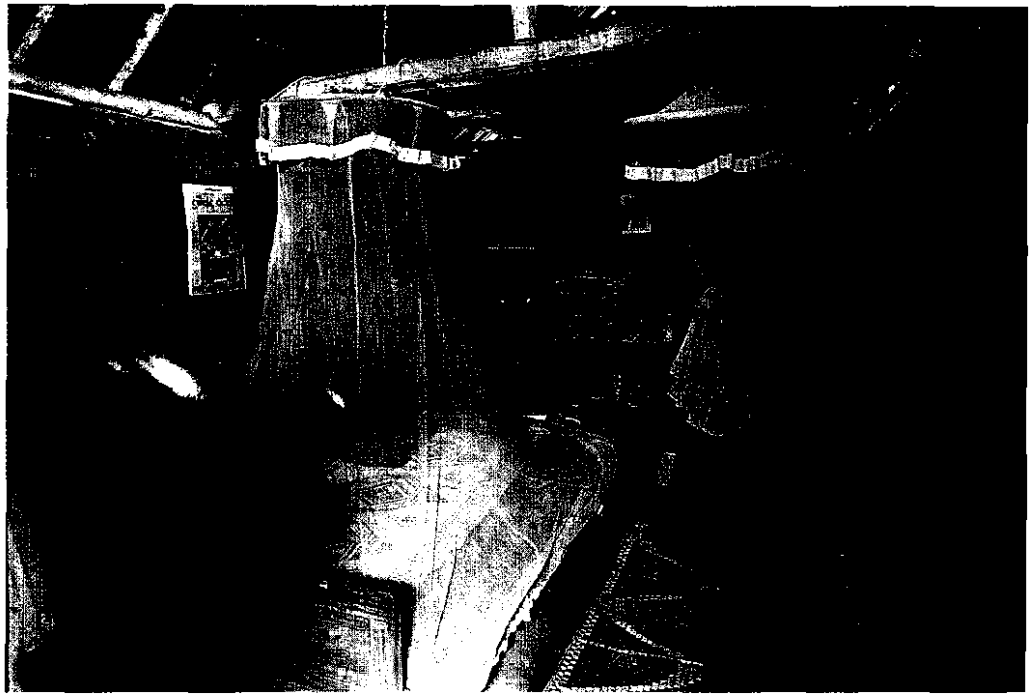


Mosquito ***bed nets*** in *a* typical ***house*** *in* ***the dry zone*** *of* ***Sri Lanka.***

Mosquito Bed Nets

There is no clear information available on the extent to which mosquito nets are in use in the country. However, they are sold from normal commercial outlets and promoted by organizations active in the field of health. In a study done close to the Kirindi Oya resettlement scheme in the southern part of the country, the use of bed nets was found to be very low although this was not quantified. The main reasons given by the local community for its limited use related to discomfort, the cost involved, the difficulty of using the net in temporary dwellings and the assumed ineffectiveness (Pinikahana 1993). Konradsen et al. (1997a) found that in 23 percent of the surveyed households one or more members were using bed nets. However, this relatively high coverage was influenced by the fact that **2** years prior to the survey a bed-net promotion program had been conducted in the area. A series of studies linked **to** bed-net use have been conducted in a community close to Kataragama. **A** permethrin impregnated bed-net trial was carried out in three test units with one test and control village each. It was found that in two of the three units the test villages had a very significant reduction in the malaria incidence but no significant reduction was observed in the test village in the third unit. In the villages where the bed nets provided protection it was significant among the school age group (6 1 5 years) and in the 26 to 50 years group. Young adults (16–25 years) and the elderly (above 50 years) were not significantly protected by the use of bed nets (Bandara et al. 1994). However, it is not clear if this lack of protection reflects the bed-net use. Entomological surveys carried out in one of the units found a significant reduction in indoor resting densities in the test village compared to the control village for An. *culicifacies* but not for An. *subpictus* (Bandara et al. 1995). In a dry-zone village in the Anuradhapura District it was found that the use of bed

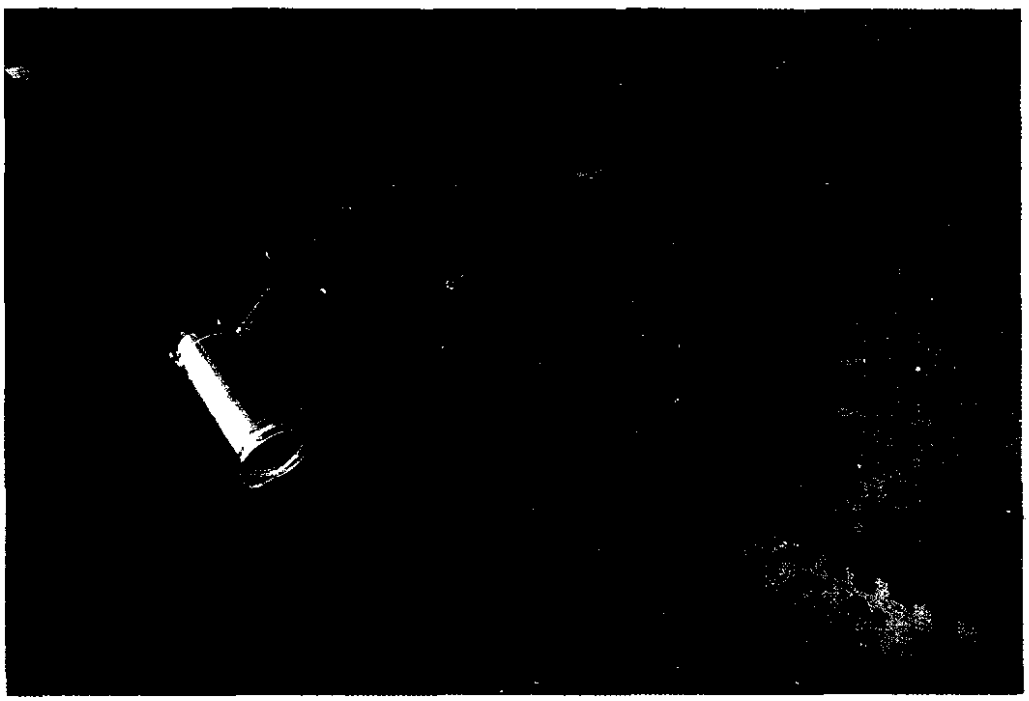
nets reduced the risk of malaria significantly, an approximately sixfold reduction compared with people not using bed nets, even though no effort had been made to promote their use in the previous 2 years and no recent impregnation had taken place (Van der Hoek et al. 1998a).

The last population census of 1981 found that only 15 percent of all housing units had electric lighting, When electricity is introduced in a village, people go to bed later and this might reduce the impact of impregnated bed nets in malaria control (Dewit et al. 1994).

Residual Insecticide Spraying

Routine records of the health authorities provide a lot of information on the use of residual spraying as a protective measure and the number of targeted houses covered.

The coverage of the 900,000 to 1,200,000 houses targeted for spraying throughout the 1980s and until 1993 has always been above 50 percent and often close to 60 percent. Since a program of more Selective spraying began in 1994 and malathion was replaced by other insecticides, the coverage has been close to 75 percent according to the Annual Health Bulletins of the Ministry of Health. In the study by Konradsen et al. (1997a) the coverage of houses sprayed as part of the residual spraying program reached more than 90 percent in a rural community. However, there is a large variation between the different districts. In some areas, the coverage has been reduced due to the ongoing armed conflict in the country or due to specific religious or cultural values in certain segments of the community. In some Muslim households non-kin males cannot enter houses when only women are present making it difficult for the all-male spray teams to work. The same problem has been



A staff member of the Anti-Malaria Campaign spraying a residual insecticide

Heterogeneous Transmission of Malaria

Arjuna *De Zoysa* and *Lal Mutuwatte*

It is well known that the distribution of malaria within an endemic community is clustered and hence nonhomogeneous. The observed variation of the mosquito densities in malarious regions, variations in susceptibilities and response of humans to disease are the major causes of this heterogeneity. However, most quantitative studies on the transmission of malaria have assumed homogeneous conditions. This is mainly due to two reasons: lack of adequate field data to represent heterogeneous transmission conditions, and the lack of a viable computation methodology to deal with this.

Therefore. a project was initiated to develop a mathematical model to describe the heterogeneous transmission of malaria. This model, in addition to the usual parameters assumed under homogeneous conditions, considered the following factors:

- mosquito/human density variations (due to environmental factors)
- variations in susceptibility to disease within the human population (age, immunity, and social factors);
- asymptomatic carriers of the malaria parasite

In the mathematical approach, a generalized version of the vectorial capacity and inoculation equations were derived, as used by Dietz, Molineaux and Thomas (1974). For the purpose of modeling heterogeneity, an endemic region was divided into several 'strata.' Within each stratum the transmission conditions were assumed homogeneous, while they differ between the various strata. These strata may coincide with geographical areas, or be merely a set of human-related categories such as age. These generalized equations account for the impact of transmission to and from adjacent areas having different transmission conditions. A geographical information system (GIS) was used to model the relevant topographical features, and relevant entomological parameters were superimposed as attributes.

The model was used to simulate malaria transmission with field data taken from a study done around a village in southern Sri Lanka. The results showed a close agreement with observed malaria case incidence. It was also decided to do a number of further simulations to study the behavior of the model, and thereby to gauge its ability to describe transmission under different Conditions. The model could be an important starting point for the use of mathematical analysis for the selective control of malaria. This has become important today, for economic reasons, and due to the biological adaptation Qroblems, which have resulted from the use of blanket-control strategies.

Appreciation is given to the Malaria Research Unit of the University of Colombo and Dr. D.M. Gunawardena of the Anti-Malaria Campaign for their help in allowing the use of some of their valuable research data.

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reported from some Tamil households where "high caste" families have denied entrance to sprayers if they were of a "low caste" for fear of ritual contamination (Ault 1983; Pinikahana 19921. In a study in southern Sri Lanka it was reported from a Sinhala community that when the householders refused spraying it was most often due to their fear of getting their house contaminated, bad odor, impact on household pets, discoloration of walls and the inconvenience of having to remove all the furniture (Pinikahana 1993).

There is certainly a need for more detailed epidemiological studies to identify and quantify the importance of the risk factors associated with malaria for the different regions of the country. To improve the design of health education campaigns, additional studies are needed for areas not covered previously to obtain information on the community knowledge of malaria. This should include communities living in the intermediate zone and in urban areas of the dry zone.

Preliminary epidemiological studies indicate that traditional fumigants are protective and they should be further assessed in future epidemiological studies. Additional survey information on the preventive measures taken by the households would be of value, especially if it also identifies the attitudes and receptiveness to different control interventions. Although the promotion of mosquito nets and the support of a bed-net impregnation program are still not a core activity of the government health services there is an urgent need for operational research into deriving the most cost-effective means of undertaking large-scale implementation of such activities in the Sri Lankan context.

Malaria transmission in humans is a dynamic process that continues to confound those who attempt to bring it under control. Despite the vast information available on the interaction of the parasite and its host, the underlying mechanisms of its success are far from clear. In nature, this successful functional dynamism has selected parasite populations to adjust to the micro and macro environments that are in continuous flux. Thus, the immunity of the host, evasion strategies and use of therapeutic drugs on the one part and the availability of its susceptible mosquito vectors on the other, in fact support and maintain this protozoan parasite through its sojourn in the vertebrate and invertebrate hosts.

Relapse of Plasmodium vivax

One of the factors that is likely to have an impact on the occurrence of malaria cases outside the normal transmission season is the relapse of *I?* vivaxcases. These relapses are due to the persistence of dormant forms **of** the parasite (hypnozoites) in the liver. Although primaquine is normally given against the liver stages of the parasite, drug compliance is never complete. In a study of malaria patients at the General Hospital in Colombo, 82 patients with *P.* vivax were identified whose disease seemed definitely a relapse. The time period from the primary attack to the relapse ranged from 8 to 44 weeks (Fonseka and Mendis 1987). This long survival of *I?* vivaxoutside the normal transmission season could play a part in maintaining transmission.

Infectious Reservoir

The infectious reservoir of *P. falciparum* and *P.* vivax in Sri Lanka was established by direct feeding of *An.* tessellatus on infected individuals followed by an examination of the development of oocysts (Gamage-Mendis et al. 1991b). The study concluded that patients in the **6-25** years age group made the largest contribution to the *P.* vivax reservoir. Patients in the youngest and oldest age groups contributed least to the infectious reservoir. This is in sharp contrast to studies from hyperendemic areas of Africa where children below 5 years contribute most to the infectious reservoir. The usefulness of using *An. tessellatus* to assess the infectious reservoir was supported by other studies in Sri Lanka where it was found that the presence of oocysts provided a fairly reliable indication of the potential infectivity of the vector (Gamage-Mendis et al. 1993).

Farmers can be highly exposed to ***mosquito bites when they sleep in tree huts*** to ***guard their crops against wild animals.***

Research assistants sampling a tank bed pool for mosquito larvae.

Chapter 3

Entomology of Anopheline Mosquitoes in Sri Lanka

Anopheline Vectors of Malaria

Carter (1925) prepared keys for the identification of adults and larvae of Sri Lankan anophelines and later (Carter 1950) published a list of the island's mosquitoes. Jayasekera and Chelliah (1981) produced a revised checklist of the Sri Lankan mosquito fauna. This was updated by Amerasinghe (1991) to include changes resulting from taxonomic revisions during the ensuing decade, and listed a total of 22 species of anopheline mosquitoes. Amerasinghe also developed new keys for the identification of anopheline mosquitoes in Sri Lanka for adults (1990), for larvae (1992) and for pupae (1995).

Chalmers first drew attention in 1905 to the association between ***An.*** culicifacies and malaria outbreaks (Wickramasinghe 1981). However, James and Gunasekera (1913) were the first to incriminate ***An.*** culicifacies as a vector of malaria transmission in Sri Lanka and Carter confirmed this finding in the 1920s. Between 1925 and 1928, Carter carried out investigations into natural infection of anophelines with malaria parasites in five localities throughout the island. He found that ***An.*** culicifacies was the most abundant species and of eight different anophelines he found that only ***An.*** culicifacies was infected (Carter and Jacocks 1929). In a later sample in 1927-1929, close to Chilaw town, Carter (1930) again found that only ***An.*** culicifacies was infected (sporozoite rates of 6.1%). Subsequently, 14 anopheline species have been shown to be capable of supporting sporogonic development of malaria parasites under experimental laboratory conditions (Abhayawardana and Herath 1994; Herath, Abeywardena, and Padmalal 1983). Field studies that used enzyme-linked immunosorbent assay (ELISA) techniques or dissection have shown ten anopheline species in addition to ***An.*** culicifacies to be infected with human malaria parasites (table 2).

The locations in Sri Lanka where malaria-infected anophelines have been detected, based on findings from James and Gunasekera's time to the present, are shown in figure 6. It is striking that ***An.*** culicifacies has been incriminated in every locality where studies have been done, ranging from the south to the western, northwestern, central, north central and eastern regions of the island. It is also noteworthy that ***An. subpictus*** has been implicated in five areas ranging from the south to the north central region of the island. An evaluation of the malariogenic potential of Sri Lankan amophelines is provided in table 3.

Due to the armed conflict in the north and east of the country only very little entomological research has been carried out in these areas for the past 14 years. A survey of peri-domestic mosquito species in the town of Jaffna is one of the few recent reports available from this area (Rajendram and Antony 1991).

Table 2. Secondary anopheline vectors of human malaria in Sri Lanka (*P.v. = P.* vivax, *P.f. = P. falciparum).*

Mosquito species	*Reported* by	Type of evidence in wild populations
An. subpictus	Mendis et al. (1990)	ELISA P.v. 210
	Amerasinghe et al. (1991)	ELISA: P.v. 210 and P.f.
	Arnerasinghe et al. (1992)	ELISA and dissection: P.v. 210 and P.f.
	Amerasinghe et al. (1994)	ELISA P.v. 210 and Pf.
	Amerasinghe et al. (1999)	ELISA Pv. 210. P.v. 247 and P.f.
An. vagus	Mendis et al. (1990)	ELISA: P.f.
	Amerasinghe et al. (1991)	ELISA P.f.
	Amerasinghe et al. (1999)	ELISA: P.v. 210 and P.f.
An. varuna	Arnerasinghe et al. (19911	ELISA: P.v. 210
	Amerasinghe et al. (1994)	ELISA P.f.
	Amerasinghe et al. (1999)	ELISA: P.v. 210, P.v. 247
An. aconitus	Amerasinghe et al. (1991)	ELISA P.v. 210
	Ramasamy et al. (1992b)	ELISA: Pv. 210
An. *annularis*	Amerasinghe et al. (1991)	ELISA P.v. 210 and P.f.
	Ramasamy et al. (1992b)	ELISA. P.v. 210
An. tessellatus	Mendis et al. (1990)	ELISA: P.f.
	Arnerasinghe et al. 119911	ELISA P.v. 210
An. barbirostris	Amerasinghe et al. (1999)	ELISA: P.f.
An. *hyrcanus* group*	Mendis et al. (1990)	ELISA: P.v. 210
An. nigerrimus	Mendis et al. (1992b)	ELISA parasite species not specified
An. pallidus	Mendis et al. (1990)	ELISA P.f.
An. peditaeniatus	Amerasinghe et al. (1999)	ELISA P.f.

* A mixture of An. nigerrimus and *An.* peditaeniatus.

Note: Two polymorphs of *P. vivax* are *known* to exist in *Sri* Lanka. On available evidence, *P.v.-210* appears to occur more commonly than *P.v.-247.* The *two* polyrnorphs are antigenically dissimilar but there is no information as to whether rhey can be distinguished on the basis of clinical manifestarions.

Table 3. Selected characteristics of anophelines implicated in malaria transmission (overall comparative assessment based on published *data* sources).

Species	Indoor resting habit	Human biting habit	Seasonal abundance	Major breeding habitats	Malariogenic potential
An. aconitus	+	+	+	Rice fields	+
An. annularis	+	++	++	Marshes, tanks, canals	++
An. barbirostris	+	+	+	Marshes, tanks, pools	+
An. culicifacies	+++	++	+	Riverlstream pools	+++
An. *jamesii*	–	+	+	Marshes, tanks	+
An. nigerrimus	+	+	+	Marshes, tanks, pools	+
An. pallidus	–	+	+	Pools	+
An. peditaeniatus	+	+	++	Rice fields, pools	+
An. subpictus	+++	+	++	Pools	++
An. tessellatus	+	++	+	Pools	+
An. vagus	+	+	+++	Pools, rice fields	++
An. varuna	+	+	+	Streams, pools	+

+ = low; ++ = moderate; +++ = high: – = *not* recorded.

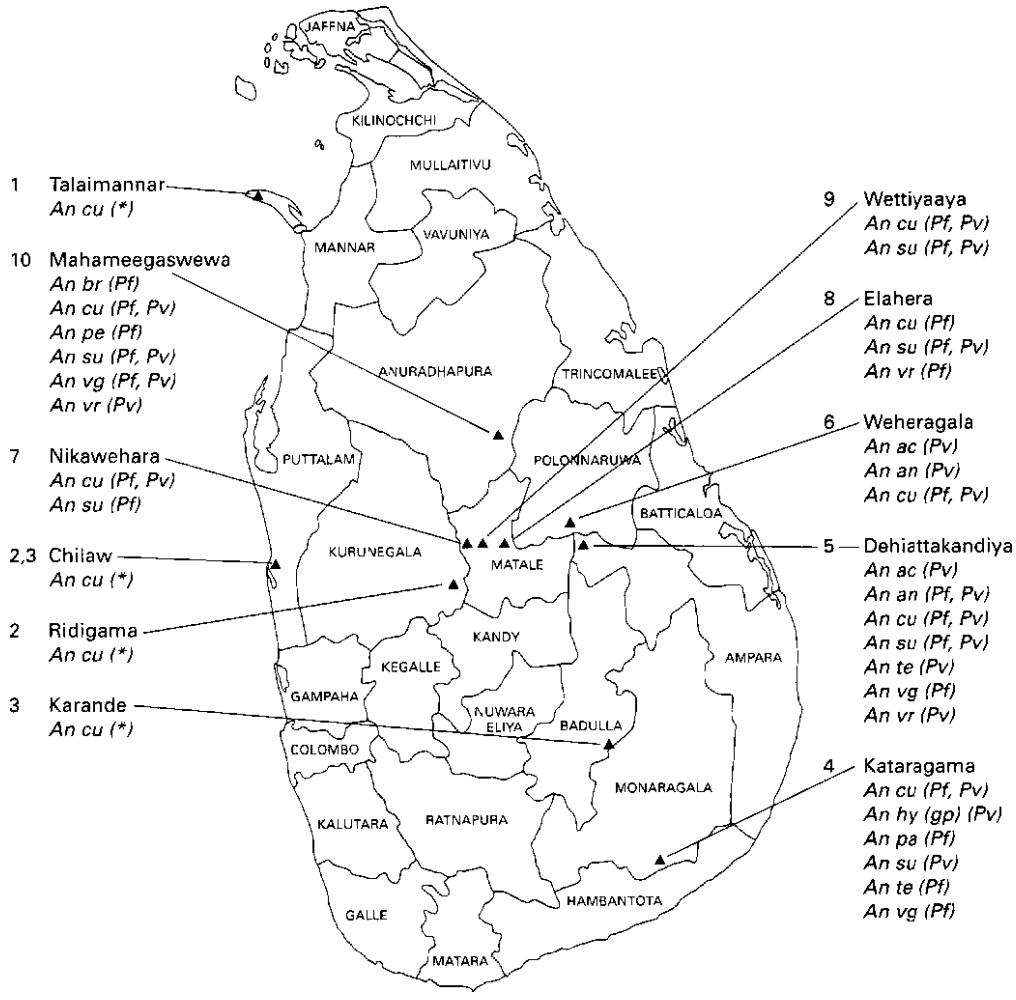

Figure 6. Sites of vector incrimination studies.

An.ac = Anopheles aconitus, An.an= Anopheles annularis, An.br = Anopheles barbirostris, An.cu = Anopheles culicifacies, An.hy (gp) = Anopheles hyrcanus (group) spp., An.pa = Anopheles pallidus, An.pe = Anopheles peditaeniatus, An.te = Anopheles tessellatus, An.vg = Anopheles vagus, An.vr = Anopheles varuna, Pf = Plasmodium falciparum, Pv = Plasmodium vivax.

(1) James and Gunasekera 1913; (2) Carter and Jacocks 1929; (3) Carter 1930; (4) Mendis et al. 1990; (5) Amerasinghe et al. 1991; (6) Ramasamy et al. 1992b; (7) Ramasamy et al. 1992a; (8) Amerasinghe et al. 1994; (9) Amerasinghe 1998; (10) Amerasinghe et al. 1999; (*) Infected guts and glands, determined by dissection only.

Anopheles Species Complexes in Sri Lanka

An. culicifacies is a species complex consisting of at least four different sibling species designated A, B, C, and D. In India An. culicifacies B is believed to play an important role in the transmission of malaria, while in Sri Lanka it is considered the most important vector and may be the only sibling species present (Subbarao 1988). Anopheles subpictus is also a species complex consisting of at least four sibling species, A, B, C, and D (Suguna et al. 1994). In an islandwide study (that excluded the war-torn northern region) Abhayawardana, Wijesuriya, and Dilrukshi (1996) and Abhayawardana. Dilrukshi, and Wijesuriya (1996) found that, on the basis of chromosome analysis, only An. culicifacies sibling species B was present whereas sibling species A and B of An. subpictus were identified. A similar islandwide survey of An. culicifacies using DNA probes, which could differentiate sibling species A from B and C, also demonstrated the absence of sibling species A (De Silva et al. 1998). A limited number of specimens screened cytogenetically in that study conformed to sibling species B. Sibling species can show differences in ecology, behavior, vectorial capacity, insecticide resistance, etc., and it is therefore important to confirm that An. culicifacies sibling species B is the only type present in Sri Lanka. It is also important to find out if the population characterized as sibling B in Sri Lanka is genetically identical to the sibling species B found in India. For this purpose modern molecular studies are needed. Anopheles annularis and An. *maculatus* are also known to exist as sibling species in Nepal and Thailand, respectively (reviewed in Subbarao 1984). The status of sibling species of these mosquitoes in Sri Lanka is unknown.

Biting and Resting Behavior of Sri Lankan Anopheline Mosquitoes

The preferred biting times for the different anopheline mosquitoes have been documented since this is important to the community exposed to the bites and their ability to use protective measures. Likewise, the place of biting and where the mosquito digests its blood meal will be of importance for control.

In the intermediate zone of the country, Dewit et al. (1994) found the peak biting time for An. culicifacies to be between 20:00 and 23:00. A different study in the same region found a peak biting time between 18:00 and 23:00 (Ramasamy et al. 1994). Amerasinghe and Indrajith (1995) studied the nocturnal biting rhythms of a number of anophelines. Peak biting times of An. barbirostris and An. vagus were immediately after sunset. Peak biting 2–4 hours after sunset was found for An. aconitus, An. annularis, An. jarnesii, An. tessellatus, An. *nigerrimus* and An. peditaeniatus. For An. subpictus the peak time was found to be during the first quarter of the night. Amerasinghe and Munasingha (1994) confirmed a peak biting preference immediately after sunset for An. vagus. Additional full-night collections from different geographic areas, and in wet and dry seasons, would be useful to better document biting times of An. culicifacies. Additionally. the data on *An.* subpictus s.l. are scanty, and further studies on the biting behavior of the different sibling species of An. subpictus will be important, since available evidence points to at least one of these siblings being the most important secondary vector in the island.

It is generally believed that An. culicifacies bites outdoors as well as indoors (Gilles and Warrell 1993). Herath and Joshi (1989) and Dissanaike (1984) report that An. culicifacies mainly rests inside houses and sheds after taking a blood meal. However, there is no information on outdoor resting habitats, and no detailed studies have investigated the relative proportions of indoor and outdoor resting females of this species in Sri Lanka. The same is true of An. subpictus, especially in the context of at least two sibling species being present in the island.

Dispersal

There have been only two published studies on the dispersal and flight range of malaria vectors in Sri Lanka. In a series of mark-release recapture experiments on An. culicifacies, Curtis and Rawlings (1980) showed that this species could travel at least 500 m in one night. In further experiments it was found that 2–7 percent of An. culicifacies mosquitoes had flown a distance of 2 km to a recapture village within 4–7 days of marking and release from a capture village, and that the tendency for dispersal was greater in young adults unencumbered by blood or eggs than in the physiologically older segment of the population (Rawlings et al. 1981). Thus, a rapid and wide dispersal of freshly emerged young adults could be expected during periods of population buildup associated with intensive breeding in pooled rivers and streams. No further research on dispersal in this or other malaria transmitting Sri Lankan anophelines has been done since Rawlings' studies. There is a need for such studies, especially in the context of the trends in human population increase, mass-scale resettlement, increasing contiguity of village settlement areas, decreased wilderness areas and increased urbanization that have taken place in the malaria-endemic regions of the country during the past 20 years.

Age Structure

Information on the age structure of vector populations is extremely scanty. The physiological age of a vector population is generally assessed by determining parous rates, i.e., the proportion of females that have oviposited previously, and are thus likely to be in a position to transmit disease. Herath et al. (1986) reported parous rates of 50–75 percent for An. culicifacies from two dry-zone sites in the north central and northwestern provinces, respectively. Values for other anopheline species ranged from 30 to 80 percent. Dewit et al. (1994) found a 60 percent parous rate for An. culicifacies at a site on the dry-intermediate zone border. They also found that the parous rates of the early (18:00–23:00) and late (23:00–06:00) biting segments of the population were similar, and that malathion spraying did not prevent the increase of the parity index during the transmission season. This led to a suggestion that the spray scheduling should be adjusted so as to achieve a reduction in both vector density per se and in the parity index (Dewit et al. 1994). There is a need for further studies on seasonal changes in the age structure of vector populations, and the effects of insecticidal spray regimens on the age structure. Another aspect that deserves attention is more detailed determinations of parity status in terms of the actual number of completed oviposition cycles in parous females, which give a better measure of the capability of a given population to transmit disease than simple parity determinations.

Human Biting Index and Human Biting Rates

The extent to which a mosquito species prefers human blood is clearly of importance for the transmission of disease. It is generally believed that *An.* culicifacies are attracted to cattle and other domestic animals rather than to man (Gilles and Warrell 1993). Dewit et al. (1994) found that the proportion of freshly fed female *An.* culicifacies whose midgut contained human blood (human blood index, HBI) was on average 0.389 over a transmission season in the intermediate zone. Using the gel diffusion test on females caught from various regions of the island during 1989–1991, Abhayawardena (1995) determined that, on average, 35 percent (range 19–69 percent) of engorged *An.* culicifacies contained human blood, a value similar to that of Dewit et al. (1994). For *An.* subpictus s.l., the HBI rate was 0.5 percent (Abhayawardena 1995). The preference for human blood has been found to be much lower in ELISA-based studies. In a study conducted in the Huruluwewa watershed (a dry zone area), the HBI for the total number of *An.* culicifacies collected over a period of 2 years and *6* months was 9.5 percent. However, even with this relatively low HBI *An.* culicifacies was still the species with the highest preference for human blood of all the **11** anophelines analyzed (Amerasinghe et al. 1999). A study on indoor-resting *An.* subpictus in the Mahaweli System C area, done over three sampling periods in April–June 1989, November–December 1989 and April–June 1990, detected human blood in only 4.3 percent, 0.8 percent and 5.2 percent, respectively of analyzed meals from the three sampling periods (Amerasinghe et al. 1992). A subsequent study in the Huruluwewa area revealed an HBI of **1.6** percent (Amerasinghe et al. 1999). It might be difficult to compare HBI across studies since it is dependent on the type of collection methods practiced, the type of blood-analysis method used and the availability of alternative hosts to humans in the study area.

The mosquito–human contact can be quantified with the human biting rate (HBR). The rate is normally given as bites per person per night but in some of the studies in Sri Lanka the authors prefer to indicate it as bites per person per hour (see below).

Very low "human biting rates" (presumably numbers biting per man-hour of collection effort) for *An.* culicifacies, ranging from <0.001 to 0.01, were recorded by Herath et al. (1986) in three dry-zone study sites located in the north central and northwestern provinces. Values for other anopheline species, too, fell within this range.

Mendis et al. (1990) found, over a 17-month study period, that although *An.* culicifacies constituted only 3.0 percent of the total number of Anophelescollected, its HBR was the highest among all species with 0.7 bites per person per night. For the same study, the average human biting rate of all anopheline species was 2.5 bites per person per night. Another study over a 6-month period in Nikawehera, a village in the intermediate zone of the country found the HBR for *An.* culicifacies to increase from 1.9 bites per person per night in October to *5.5* bites per person per night in January. But extremely high biting rates for *An.* culicifacies of up to 26.3 were observed in the sample locations close to a stream during the month of January (Dewit et al. 1994).

A study in the intermediate zone of the country found peak biting rates for *An.* culicifacies in November and December 1990 to be 2.53 and 3.00 bites per man-hour, respectively. The

only other infected mosquito vector found in the area, An. subpictus, had a peak biting rate of 0.94 in November and a lower rate for the rest of the period (Ramasamy et al. 1992a). Another study undertaken in the same village (Nikawehera) found a maximum HBR for An. culicifacies at 1.35 bites per person per hour in December 1991 (Ramasamy et al. 1994). Ramasamy et al. (1992b) found a record high human biting rate of 12.25 bites per person per hour for An. annularis in a village (Weheragala) in the eastern part of the country. Human biting rates of 0.15 and 0.12 per man-hour for An. *culicifacies* were reported from a dry-zone forest of Sri Lanka during the dry and post-monsoonal periods, respectively (Amerasinghe and Munasingha 1988a). Rates of 0.26 and 0.27 per man-hour were recorded during the monsoonal season for An. vagus and An. varuna in the same study. When a rice irrigation system was established in this same area, the human biting rates per man-hour recorded during the first year under irrigation were 0.70 for

Physiological Aspects of Multiple Blood Feeding in the Malaria Vector An. tessellatus

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Factors such as vector density, man biting rate and vector longevity influence the rate of malaria transmission in a community. In turn, these factors depend on the physiological characteristics of the different anopheline vectors of malaria in the country. We have investigated the influence of several physiological aspects of the malaria vector An. tessellatus on its ability to take several blood meals during a single gonotrophic cycle. While An. tessellatus is a significant vector of malaria in the southern dry zone. it is probably less important countrywide than An. culicifacies and An. subpictus and possibly even An. annularis.

The rate of oogenesis and oviposition in An. tessellatus is not influenced by multiple blood meals. Multiple blood feeding in the first gonotrophic cycle does not increase fecundity. However, multiple blood feeding in the first gonotrophic cycle serves to increase fecundity in the second gonotrophic cycle. When larvae are reared at different densities, adults of different sizes categorized as large, medium and small mosquitoes according to the wing lengths, are produced. While all sizes of An. tessellatus are able to take multiple blood meals, the smallest mosquitoes have a greater requirement for a second blood meal. The first blood meal in the smallest mosquitoes is apparently utilized for oogenesis and egg maturation and not for building up maternal reserves as in other anopheline mosquitoes. This is attributed to the availability of at least 0.465 calories of lipid in even the smallest An. tessellatus. Irrespective of body size, mosquitoes that take a multiple blood meal have digested their previous blood meal and show oogenesis in progress. Multiple blood feeding in An. tessellatus appears to be driven by the completion of digestion of the previous blood meal and other endogenous factors. The ability of An. tessellatus to feed several times within a single gonotrophic cycle increases vector-human contact and vectorial capacity and, therefore, malaria transmission rates.

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Multiple Blood Feeding in Field Vectors of Malaria in Sri Lanka

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It is generally believed that a female mosquito feeds to repletion only once during an egg-laying cycle (gonotrophic concordance), and estimates of vectorial capacity are based on this principle. However, recent research has demonstrated that female mosquitoes may engorge more than once during a gonotrophic cycle, a phenomenon known as gonotrophic discordance or, more simply, as multiple feeding.

We investigated this behavior in a field population of An. culicifacies and An. *subpictus* in a malaria-endemic area in the dry zone of Sri Lanka by catching engorged females, serially sectioning them, and mounting the histological sections on microscope slides. We observed that multiple meals were physically distinguishable, and that their age could be estimated by observing the degree of digestion that had occurred. Nearly 4.000 mosquitoes were observed in this manner, to make estimates of multiple feeding that occurred in the field.

On average, 30–34 percent of blood-engorged females of these two species were multiple-fed (see illustrations on page 29). Roughly half of these multiple meals had been taken on separate nights and the rest on the same night. High rates of feeding on separate nights suggested that multiple feeding was partly due to a nutritional requirement for protein and/or energy (see text box by Ramasamy et al.). Several meals taken during the same night could be attributed to interruption of feeding due to defensive reactions of the host. Using a laboratory technique known as an enzyme-linked immunosorbent assay (ELISA) in conjunction with histology, we estimated that multiple feeding involving a human host occurred in 7 percent of the An. culicifacies sample investigated. Multiple feeding could be one reason why the endophilic but mainly zoophilic Sri Lankan An. culicifacies, which is often present at low population densities, can still act as an effective transmitter of malaria,

Our data for An. culicifacies showed that the percent of multiple feeding was significantly positively related to temperature. Higher temperatures would trigger greater multiple feeding by increasing blood digestion and energy utilization rates. Our study estimated that a 2°C rise in mean temperature would result in a 6-percent increase in multiple feeding and a 5°C rise in temperature, in an 18-percent increase in multiple feeding in An. culicifacies. If this holds true for other malaria vectors as well, global warming trends could impact on malaria transmission by influencing greater host-feeding activity simultaneously with the vectors extending their geographic ranges.

Greater host-feeding frequency will increase the capacity of a vector to transmit malaria. If a mosquito has one meal per gonotrophic cycle and the cycle lasts 3 days, the feeding frequency is 1 meal every 3 days (=0.33). However, a combination of gonotrophic discordance and interrupted feeding could greatly increase the number of meals taken during a gonotrophic cycle, and the feeding frequency value could equal or exceed unity. To obtain a more accurate estimation of vectorial capacity, it will be necessary to determine not only the mean duration of the gonotrophic cycle but also the mean number of blood meals taken during the cycle.

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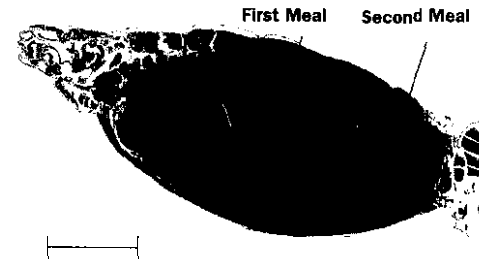
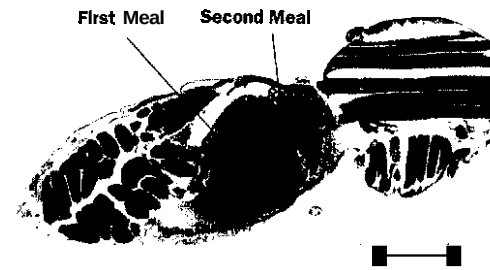
An. annularis, 0.16 for An. culicifacies. 0.13 for An. subpictus, 0.05 for An. *tessellatus,* 0.20 for An. vagus and 0.39 for An. *varuna* (Amerasinghe and Ariyasena 1991).



Sagittal section *of* An. culicifacies showing the *presence of two* physically *discernible blood* meals in the midgut. The first meal is at *6-12 hr. age and* the *second meals* at ≤ 6 *hr.* age. Scale bar represent *0.5* mm.



Sagittal section *of An.* culicifacies showing the Presence of two *physically* discernible blood meals in the midgut. The first *meal* is *at 24 hr.* age and the second meal at ≤ 6 *hr.* age. *Scale bar represent 0.5 mm.*

Entomological inoculation Rates

The risk of getting malaria depends not only on the biting rate on a person but also on the percentage of anophelines with sporozoites in their salivary glands. The product of the biting rate on man and the sporozoite rate is the entomological inoculation rate (EIR). This is a useful parameter to indicate the risk of human infection for different areas, for different time periods and can be used as an indicator of the impact of an intervention.

In a study in southeastern Sri Lanka, the EIR of the Anopheles species was estimated at 0.0029 infectious bites per person per night for *P.* vivax and 0.0109 for *P.* falciparum (Mendis et al. 1990). In another study in the eastern part of Sri Lanka in 1989 and 1990, the EIR for An. subpictus ranged from 0.00006 infectious bites per person per night to 0.007 for *P.* vivax and from 0.0002 to 0.005 for *P.* falciparum (Amerasinghe et al. 1992). In the same area of the country, Ramasamy et al. (1992b) found in March 1990 an EIR for An. culicifacies at 0.06 infectious bites per person per hour and a corresponding EIR for An. annularis at 0.12 both related to *P.* vivax. In a study in the intermediate zone of the country, Ramasamy et al. (1992a) found an EIR for An. subpictus at 0.03 infectious bites per person per hour for *P.* falciparum in the month of January, 1990 but zero for the eight other months where samples were carried out. In the same study An. culicifacies reached a maximum of 0.12 infectious bites per person per hour for *P.* vivax and 0.06 for *P.* falciparum.

The relatively low human-biting rates and sporozoite rates make the traditional entomological parameters of transmission difficult to calculate and, often, a less-useful tool for the assessment of the degree *of* transmission compared with countries with stable malaria. However, indirect estimates of EIR have been used in Sri Lanka where the human biting rate is derived from the number of freshly human blood-fed anopheline mosquitoes found in a bedroom divided by the number of individuals sleeping in the room (Amerasinghe et al. 1992). A further extension of the indirect approach was developed by Amerasinghe et al. (1999). Here female anophelines from various sampling methods were pooled per collection night and multiplied by the ELISA-based human blood index (HBI) and the

sporozoite rate to derive at a mean number of infective vectors per collection night (MIV). Based on the MIV it was possible to compare the transmission potentials of different anophelines, and *to* compare trends in the infectivity rate with trends in human malaria cases. Mendis et al. (1992b) derived a mathematical expression to estimate the relative malaria-transmission efficiency of an anopheline species with respect to a standard well-characterized species for which all vector parameters could be sufficiently determined. The reference species used was An. subpictus. a vector species for which properties are studied more easily in Sri Lanka than, for example, An. culicifacies. The expression was used to estimate the relative contribution made by the different species to the transmission of human malaria in an area of southeastern Sri Lanka from 1986 to 1988. Of the total contribution of all anopheline species An. culicifacieswasfound to contribute 52 percent and 54 percent of the total human malaria transmission in the wet season and the dry season, respectively. However, a significant part of dry-season transmission was attributable to An. subpictus.

An approach to estimate the degree of transmission in an area was proposed by Del Giudice et al. (1990). On the basis of studies undertaken in the southeastern dry zone of Sri Lanka. it was found that anti-sporozoite antibody prevalence in humans would provide useful information to analyze the exposure of a population to infectious bites and to estimate levels of transmission.

Even though a large number of Anopheles species have been incriminated as vectors the available information suggests that An. culicifacies is the primary vector with a range of less-important vectors supporting transmission at a low level. This is best documented in a recent study looking at both Anopheles larvae and adult abundance, as well as the number of human malaria cases. It was here concluded that An. culicifacies was the epidemiologically most important vector responsible for outbreaks of the disease (Amerasinghe et al. 1999).

Further studies of the EIR or estimates thereof are needed to determine the importance of the different secondary vectors and to assess the risk of infection in different areas of the country. If possible, this should become part of the routine monitoring system. It is important that the entomological based transmission studies pay increased attention to the temporal analysis, includes a monitoring of human-malaria incidences, and continues to relate the entomological parameters with ecological changes in agricultural practices and human habitation. Estimates of vectorial capacity would be useful; alternatively, techniaues used to measure transmission should be modified to suit local conditions.

Main Breeding Sites of *Anopheles* culicifacies

The knowledge of breeding sites for the different vectors opens opportunities for control and gives insights into the seasonality of transmission. In this section only An. culicifacies is dealt with. For other species, one can consult Carter and Jacocks 1929, Herath et al. 1986, Amerasinghe and Munasingha 1988b, Amerasinghe and Ariyasena 1990, Amerasinghe and Indrajith 1994, Amerasinghe, Indrajith, and Ariyasena 1995, Amerasinghe et al. 1997, and van der Hoek et al. 1998b.

Pool in tank bed, *highly productive* for anopheline mosquitoes.

In a study undertaken in a jungle area in the east of the country in 1948, along the Gal Oya river, Rajendram, Cader, and Visvalingam (1950) established that An. culicifacies was not purely a domestic species living in close proximity to human habitation. This was confirmed by Amerasinghe and Munasingha (1988a, 1988b) who found larval and adult An. culicifacies in an uninhabited dry-zone forest area.

The breeding habits of the Sri Lanka An. culicifacies differ from those in India where substantial paddy breeding takes place (Herath and Joshi 1989). In Sri Lanka, the preferred breeding sites of An. culicifacies are drying-up rivers with pools of sandy bottoms or rocky formations (Gill 1936). A similar finding has been reported by Carter and Jacocks who, on the basis of a study in 1927–1929, found that An. culicifacies was primarily found in slow-flowing water or in pools established in rivers or trenches (Carter and Jacocks 1929). This finding was further supported by Amerasinghe and Munasingha (1988b) and Amerasinghe and Ariyasena (1990). Carter and Jacocks (1929) concluded that An. culicifacies could be found in abundance in exposed rather than in shaded habitats, a finding supported again by Amerasinghe and Munasingha (1988b). However, a study conducted

Pool in riverbed, highly productive ***for*** anopheline mosquitoes.

in an area with a diverse number of habitats showed that An. culicifacies was able to exploit exposed tank-bed pools as well as shaded stream pools including both clear and turbid water (Amerasinghe et al. 1997; Van der Hoek et al. 1998b). Amerasinghe et al. (1997) found a clear progression in breeding habitat use from streambed pools and the slow-flowing stream to new rain-generated tank and drainage pools established after the onset of the pre-monsoonal rains. These findings may indicate that An. culicifacies has a more diverse habitat preference than is generally assumed in Sri Lanka.

Van der Hoek et al. (1998b) did not find a statistical correlation between An. culicifacies and the presence of vegetation, fauna or culicine mosquitoes in the breeding habitats. The only published study that has linked breeding preference with physico-chemical water-quality characteristics was carried out in System C of the Mahaweli Project in 1986. In this study it was found that An. culicifacies positively correlated with dissolved oxygen, phosphate and temperature and negatively correlated with carbon dioxide (Amerasinghe, Indrajith, and Ariyasena 1995).

No published studies have assessed the vector breeding in the peri-urban or urban areas of the dry zone. Additional studies on vector breeding are needed along with the EIR estimates to support the development of malaria risk maps for the country. Focused entomological studies should support the epidemiological-based research looking at land use and malaria risk. Such studies could, with advantage, be linked with the use of remote sensing and geographical information systems. Further emphasis should be given to the study of the vector breeding in the diverse ecosystems linked to the small and medium tank-irrigation systems in the dry zone. This agro-ecological system with its 15–20,000 tanks constitutes a significant proportion of the total irrigated area of the country and a major land use (Steele, Konradsen, and Imbulana 1997). Detailed field and experimental based larvae ecological studies are needed to give insights to the species habitat preference and larvae survival.

Vector Resistance against Insecticides

The Anti-Malaria Campaign (AMC) of the Government has, on a routine basis, collected information on the susceptibility of a range of potential vectors to the insecticides being used by the health authorities. This has led to changes in dosages, coverage and frequency of insecticide application as well as a change to new insecticides. In 1969, the first reports of resistance to DDT by An. culicifacies was reported (Pinikahana and Dixon 1993). Since then a number of potential vectors in Sri Lanka have developed resistance to DDT including An. subpictus, An. vagusand An. nigerrirnus (Gilles and Warrell 1993). From 1981 to 1987, adult anophelines were sampled from localities selected randomly in the malarial areas of Sri Lanka, to assess the level of resistance towards insecticides. Anopheles subpictus and An. nigerrirnus showed a broad spectrum of resistance towards organophosphates and An. nigerrirnus towards carbamates. For both species the frequency of resistance to malathion and fenitrothion increased between 1980 and 1987. Of the organophosphates An. culicifacies showed resistance only to malathion and at a lower frequency than for the two other species. A possible explanation to the higher level of resistance reported among An. subpictus and An. nigerrirnus is the fact that these two species, more often

than An. culicifacies, breed in paddy fields and are, therefore, exposed to agricultural insecticides. The selection pressure on An. nigerrimus from the residual spraying program is likely to be minimal due to the exophily expressed in this species (Herath and Joshi 1989). The use of malathion and fenitrothion for agricultural purposes was banned in the mid-1980s. A study assessing the persistence of the effect of malathion on An. *culicifacies* in palm-leaf huts showed that a 3-month spraying regime, as recommended in Sri Lanka.

Insecticide Resistance in *An. culicifacies* and *An. subpictus*

S. H. P. Parakrama Karunaratne

Recent studies on insecticide resistance of the malaria vectors, An. *culicifacies* and An. subpictus, in a rural area in Sri Lanka, have shown that both populations have a high level of resistance to organochlorines and organophosphates.

Log-probit mortality lines for malathion, propoxur, permethrin and chlorpyrifos obtained using adult and larval bioassays produced LD50 percentages of 4.45, 0.002. 0.16 and 0.001, respectively, for An. culicifacies and 0.66, 0.004.0.004 and 0.04, respectively, for An. subpictus. Adults were also tested for WHO discriminating dosages of malathion, propoxur, permethrin, DDT, cypermethrin, deltamethrin and lambda cyhalothrin. Both populations were highly resistant to DDT. An. culicifacies was more resistant to malathion and An. subpictus to cypermethrin and lambda cyhalothrin. Adult mosquitoes were individually tested for their insecticide detoxifying enzyme activities and altered target-site, acetylcholinesterase. Results showed that almost all mechanisms analyzed were present in both species. Native gel electrophoresis resolved one elevated esterase isoenzyme, with high affinity to organophosphates, from each species. Synergistic studies showed the possible involvement of monooxygenases in resistance of both species. When interacted with a standard dosage of propoxur, both populations showed greater than 80 percent remaining activity of acetylcholinesterase, the target site of organophosphates and carbamates. Resistance to inhibition with this dosage indicates the presence of altered acetylcholinesterases in most anopheline species (Penilla et al. 19961. However, the level of resistance to the carbamate propoxur was very low, especially in the An. culicifacies population. Low resistance to carbamates shows that the impact of agricultural pesticides is not significant in the development of resistance. Pyrethroids, other than permethrin, can be successfully used in vector-control programs. Carbamates will be an alternative.

Studies on resistance mechanisms (Herath 1997) have shown both vector species to possess metabolic resistance to malathion by means of altered carboxylesterases, to organophosphates and carbamates by means of elevated carboxylesterases, to DDT by means of glutathione-S-transferase enzymes and to DDT, organophosphates, carbamates and pyrethroids by means of oxidases. Resistance to organophosphates and carbamates by means of altered target sites to acetylcholinesterase also has been demonstrated for both species.

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would immediately give a great selective advantage to any resistance gene arising in the population (Rawlings, Goonatilaka, and Wickramage 1983). More recently, Abhayawardena and Wickramasinghe (1995) have reported An. culicifacies to demonstrate variable susceptibility to malathion ranging from a high of 90–98 percent of tested samples from the Uva and Southern provinces, to a much lower range of 40–67 percent in the West, Central, North Central, North West and Sabaragamuwa provinces.

There is no doubt that the development of resistance to malathion is well under way in An. culicifacies in many regions of the island and this will reduce the effectiveness of the insecticide in controlling malaria. A constant monitoring of vector resistance against insecticides is needed. This should be supported by population studies assessing the underlying nature and causes of resistance development whether genetic, biological or due to specific operational practices.

Major mechanisms of insecticide resistance involve alterations in the rate of insecticide detoxification by enzymes or mutations of the target site of the insecticide (Karunaratne 1998). Relatively few studies have been done on Sri Lankan malaria vectors, but they have mainly revealed the operation of mechanisms of metabolic resistance. There is evidence that metabolic resistance to malathion in *An. culicifacies* is based on nonelevated esterases that hydrolyze the ester bonds in the insecticide (Herath et al. 1987). In An. culicifacies and An. subpictus, resistance to DDT appears to be based on **glutathione-S-transferase** enzymes (Herath et al. 1988) that are involved in the dehydrochlorination of the insecticide. These enzymes may **also** be involved in dealkylation **of** organophosphate insecticides in general (Karunaratne 1998), and thus could potentially contribute to malathion resistance in these species. Organophosphate resistance in An. subpictus also has been shown to be mediated by a mixed function oxidase mechanism (Cytochrome P450) (Hemingway et al. 1987), which results in the oxidative degradation of the insecticide. **As** for insensitivity of target site, there is evidence for altered acetylcholinesterase (which is the target site of organophosphate and carbamate insecticides) as a basis for insecticide resistance in Sri Lankan An. *nigerrimus* (Hemingway et al. 1986) but so far, this mechanism has not, been detected in An. culicifacies and ***An.*** subpictus (Hemingway et al. 1987).

Malaria and Environmental Change

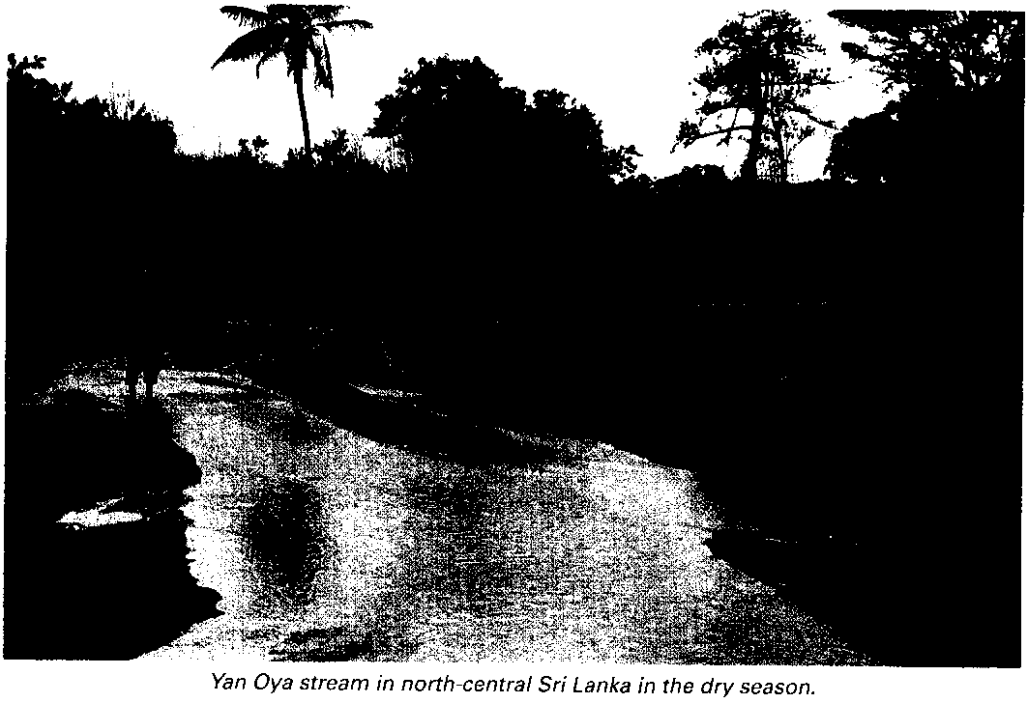
Urbanization, changes in agricultural practices, infrastructure development, resettlement programs, etc.. can, in one way or another, increase or decrease the risk of malaria. **To** be able to assess the health impacts and opportunities of different development activities on malaria transmission it is necessary to study the interactions between development and disease in detail.

In 1930, Carter argued that man-made changes linked to jungle clearance and agricultural development would increase the risk of malaria epidemics (Carter 1930). The most significant study undertaken in Sri Lanka assessing the impact of irrigation development on the malariogenic potential of an area was done in the Eastern Province of the country in System C of the Mahaweli Project from 1984 to 1990. In 1984 and 1985, both adult and immature mosquitoes were collected in the forest area during a period before the

development of the irrigation system took place and these found a very diverse mosquito fauna (Amerasinghe and Munasingha 1988a and 1988b). Larval surveys undertaken in the area over a 12-month period in 1986–1987 made it possible to assess the impact on vector breeding as a result of irrigation development. The study found that the habitat simplification and niche reduction created as a consequence of the development activity decreased species richness and increased abundance of only a few species that found conditions suitable for exploitation. The Anopheles species that increased as a result of irrigation development were An. annularis, An. subpictus. An. nigerrirnus and An. jarnesii, all potential vectors of malaria in Sri Lanka. However, the development had only a minor effect on the breeding of An. culicifacies. The majority of species that did increase after the development were associated with the new breeding habitats created by the rice irrigation system (Amerasinghe and Ariyasena 1990). Adult collections in the area from 1986 to 1989 confirmed that An. subpictus and *An.* jarnesii increased in abundance but An. annularis, An. culicifacies, An. *barbirostris* and ***An.*** varuna decreased. Anopheles nigerrimus and An. vagus did not change substantially (Amerasinghe et al. 1991). Whilst An. culicifacies was implicated in malaria transmission throughout the study, other species were implicated more focally: An. annularis during the pre-irrigation land-clearing and settlement period and An. subpictus after irrigation development (Amerasinghe et al. 1991). Another study carried out in Mahaweli System C focused ***on*** irrigation management and design, and their impact upon vector breeding. The same study found that where maintenance of the system was neglected, or inefficient water management was practiced, increased vector-breeding sites could be created through waterlogging, seepage from canals, excess water in the drainage system, reduced velocity of canal water and water rotations favoring the propagation of vectors (Speelman and van den Top 1986).

In another study related to the Mahaweli Project, Wijesundera (1988) describes the epidemic of malaria that occurred close to Kandy town in 1987. The epidemic was related to the hydrological changes brought about by the development of hydropower dams on the Mahaweli river. Close to the town of Kandy the river is highly susceptible to pool formation with an alternating sandy and rocky nature creating perfect breeding sites for, especially, An. culicifacies. The construction of a series of dams on the river reduced the discharge below the reservoir favoring the formation of pools that can be sustained for a long period unless rainfall or intermittent dam releases flushed the river. It is believed that the dams, in general, have increased the potential for outbreaks of malaria along the river.

Additional studies are needed to assess the impacts and opportunities linked to the very extensive ongoing small-scale irrigation rehabilitation programs, the rapid expansion in the number of agro-wells, small town developments, the reduction in the number of livestock in certain areas and the changes in forest cover.



Yan Oya stream in north-central Sri Lanka in the dry season.

Chapter 4

Immunity

Due to the unstable malaria transmission pattern in Sri Lanka, it is assumed that the population does not have high levels of immunity unlike the situation in highly endemic regions such as sub-Saharan Africa. Thus, the disease manifests as an acute febrile illness in both adults and children with few asymptomatic carriers. In Sri Lanka. studies on malarial immunity started about two decades ago in parallel with the increasing world focus on the development of a vaccine against malaria. Research has taken place in several areas amongst which the elucidation of immunity in endemic and non-endemic populations and antigenic diversity of malarial parasites stand out. Although the actual mechanisms of immunity and the success of parasite survival are far from clear, studies carried out in Sri Lanka have contributed to the understanding of some aspects of host parasite interactions that exist in nature.

This chapter deals with acquired immunity. Innate immunity is also important in malaria, especially in relation to certain red blood cell characteristics, of which glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency is important in Sri Lanka.

Naturally acquired immunity to malaria in humans manifests as antidisease or clinical immunity, which is characterized by less-severe clinical symptoms due to tolerance to the parasite, and as an antiparasite immunity, which results in lowering of the parasitaemia (Karunaweera et al. 1992). Different types of immune responses of the host, protective and transmission blocking, are important in the control and regulation of the malaria parasites.

Anti-Disease Immunity

A study conducted in Kataragama showed that clinical tolerance to malaria infection increased as a result of successive *I? vivax* infections taking place within a few months. Clinical tolerance however, did not increase with age (Gunewardena. Carter, and Mendis 1994). Karunaweera et al. (1998) found important differences in the intensity of clinical symptoms between patients from Kataragama, an endemic area, and patients from Colombo. Colombo is located in an area where malaria transmission does not occur and therefore malaria patients from Colombo had acquired their malaria during travel to an endemic part of the country. They had more intense symptoms than patients from Kataragama even when controlling for parasite density. This indicates a tolerance to parasites in the patients from endemic areas. Anti-disease immunity to *I?* vivax malaria was also assessed in this study by measurement of haematologic indicators of pathology such as erythrocyte sedimentation rate, serum bilirubin, reticulocyte count, tumor necrosis factor-alpha (TNF-α), and blood glucose levels. At any given parasitedensity, the underlying pathology as measured with these indicators was significantly lower in the endemic

population, suggesting a true toleranceto parasites. TNF-a is a cytokine which is presumed to be a mediator of clinical disease in malaria. Its levels were elevated in both groups of patients but significantly higher in the non-endemic patients from Colombo. However, at comparable levels of TNF-a the non-endemic population had a higher level of clinical disease and underlying disease pathology, suggesting that the people living in endemic regions were more tolerant to the effects of TNF-a (Karunaweera et al. 1998).

In the same study area a transient increase in $CD3^{+}$T-cells in the peripheral blood of nonimmune individuals was observed in association with *P.* vivax malarial paroxysms (Perera et al. 1994). The absence of such a response in endemic patients with lesser disease intensity points to the involvement of these cells in the pathology of malaria.

Karunaweera et al. (1992) demonstrated the association between the period of febrile paroxysms in *P.* vivax malaria and parasite-killing factors in the serum such as TNF. Further studies have found that one of the parasite-killing complementary factors is **of** parasite origin in its native form (toxins), short-lived in circulation, i.e., 4 hours and species-specific (Wijesekera et al. 1996). Similar responses were not seen with *P.* falciparum. The differences may be attributed to the differences in the pathogenesis of the two species. Abolishment of this killing-effect due to the presence of antibodies in the serum of convalescing individuals indicates another strategy employed by parasites for survival.

Anti-Paraslte Immunity

Protectlve Immunity

The lower incidence of malaria among the adult population as described in the chapter on risk factors and protective behavior may indicate some form of age-related immunity, especially since this group is likely to be more exposed than the younger age groups. Several studies have assessed this age-related immunity. Other investigations have looked at antibodies **as** a measure of exposure. Anti-sporozite antibodies are now considered a good surrogate to estimate the intensity of malaria transmission in an area. This is useful in countries such as Sri Lanka where it is difficult to estimate the entomological inoculation rate (EIR) because of very low sporozite rates in the vector mosquitoes.

Mendis et al. (1992a) did repeated measurements of antibodies to the circumsporozoite protein of *P* vivax and *P.* falciparum in a group of individuals close to Kataragama. The population had a lifelong exposure to *P.* vivax but not to *t?* falciparum, one of whose epidemics occurred in the study area a few months prior to the beginning of the study. The prevalence of naturally occurring anti-fl vivaxand anti-fl falciparum circumsprozoite protein antibodies was never more than 20 percent. While malaria incidence was highest in the age group of 6–15 years, the prevalence of anti-circumsporozoite antibodies was higher in the older age groups. This pattern was the same for both parasite species. Given that antibodies to circumsporozoite proteins are assumed to be short-lived and are lost in the absence of reinfection (Wijesundera et al. 1990). it was argued that the increase in prevalence of antibodies with age was associated with repeated inoculations rather than with a cumulative effect over time. However, the lack of a clear correlation between sero-

conversion and malaria infections in individuals made it difficultto explain the precise role of the antibodies.

A study carried out at Nikawehera, in the intermediate rainfall zone showed that the prevalence and concentrations of specific antibodies to repetitive epitopes of *I?* vivax and *I?* falciparum circumsporozoite antigens and surface proteins of *I?* falciparum merozoites were in general higher in adults than in the age group of 7–15 years. This correlated with malaria transmission in the region as measured by entomological assessments and against hospital records (Ramasamy, Nagendran. and Ramasamy 1995). In Weheragala, located in the dry zone just 70 km from Nikawehera, the prevalence of anti-circumsporozoite antibodies was much higher with 97 percent of the population having antibodies to the circumsporozoite antigen of *I?* falciparum (Ramasamy, Nagendran, and Ramasamy 1994). Asignificant number had antibodiesto *I?* vivaxcircumspororoite epitopes and *I?* falciparum merozoite antigens. The antibodies to circumsporozoite proteins of both species lasted only during the transmission season. Thus, this study confirmed that the anti-circumsporozoite antibodies were short-lived. The study could not find a significant difference in antibody levels between parasitemic and nonparasitemic persons (Ramasamy, Nagendran, and Ramasamy 1994). The results show that antibody prevalence in the dry-zone site was higher than in the site in the intermediate zone nearby. Such low immunity regions lying adjacent to high transmission regions could become epidemic foci when environmental conditions are favourable.

Additional studies in a non-endemic malarial area showed that antibodies to *I?* falciparum circumsporozoite antigen in a primary infection were lost within a year in the absence of reinfection. No correlation was found between the prevalence of circumsporozoite protein antibodies and blood-stage antibodies (*Wijesundera* et al. 1990). Persistence of antibodies was related to the intensity of the initial antibody response (Mendis, David, and Carter 1991).

The studies in Sri Lanka have confirmed that immunityto parasite antigens varies between populations. This was to be expected as inoculation rates, immunological status of individuals, attitudes towards use of drugs and protective measures will differ between the different populations. The fact that the prevalence of the disease is clustered even within a microenviroment of an endemic situation brings about another dimension to the assessment **of** immune response at an individual level.

The responses to malaria infection and its impact on age-related incidence levels or clinical tolerance to infection are still not fully worked out. The available information indicates that an increased clinical tolerance and possibly a reduced parasitaemia develop with increased exposure.The immune response is, therefore, likely to be higher in adults than in children, due to the increased exposure with age. However, the immunity seems to be short-lived and will require continued exposure to be maintained. It is also possible that increased antibody levels among adults could be due to other factors such as a more-complete immune system able to produce more antibodies than a child's at the same level of exposure. It is important to point out that the cited studies have been undertaken at a limited number of sites and possible islandwide differences might not have been captured.

Transmission-Blocking Immunity

Sexual stages of the malaria parasite are ingested by the mosquito when it takes a blood meal. At the same time, antibodies are also ingested that could act on the parasite stage in the mosquito to interfere with transmission. This has raised the question of whether immunity to sexual stages could be the basis for a transmission-blocking vaccine. Studies in Sri Lanka have shown that *P. vivax* is highly susceptible to anti-gamete transmission-blocking immunity (Munesinghe, Mendis, and Carter 1986). Natural immunity to sexual stages of *P. vivax* was readily induced in humans but was observed to be short-lived, i.e., 4 months (Mendis et al. 1987a). If reinfections were to occur at short intervals, immunity was boosted to high levels. Thus, it was concluded that maintenance of such immunity required frequent infections (Ranawaka et al. 1988). Though short-lived in nature, the impact on the transmission dynamics and effect on the parasite incidence has been shown by using field-collected data in a mathematical simulation model (De Zoysa et al. 1988). The simulations indicate that in an epidemic situation, naturally occurring anti-gamete transmission-blocking immunity has a controlling influence on malaria incidence.

The prevalence and the transmission-blocking effect of naturally occurring *P. falciparum* anti-gamete antibodies was compared between Sri Lanka and Papua New Guinea where malaria transmission is more intense (Premawansa et al. 1994). Although the prevalence of anti-gamete antibodies was similar, the prevalence of a transmission-blocking effect of these antibodies was 56 percent in Sri Lanka against 75 percent in Papua New Guinea. It was suggested that the functional efficacy of sera differed and may be related to the number of malarial attacks the patient would have had, which would have been comparatively higher in Papua New Guinea.

Studies have also shown that a *P. vivax* febrile paroxysm of nonimmune individuals releases cytokines and other non-antibody factors, that mediate death of sexual stages in the blood. In contrast, endemic individuals with age-acquired anti-disease immunity exhibit clinical symptoms that are mild and parasite-killing factors are not induced (Carter and Mendis 1991). Thus, it is possible that these individuals from endemic regions could act as reservoir hosts of parasites in nature, should such cases go untreated.

Parasite Antigens and Prospects for Vaccine Development

Antigens of sporozoites, asexual erythrocytic stages, and gametocytes stimulate antibody production and could therefore, in principle, be used in vaccines. The dynamics of cellular and humoral immunity in humans and laboratory animals to different parasite antigens of *P. vivax* and *P. falciparum* have been assessed in a number of studies in Sri Lanka. While populations of B-lymphocytes secrete antibodies, T-lymphocytes IT-cells) are central to the cell-mediated immunity. Investigating the T-cell proliferation in response to specific malarial antigens and nonspecific mitogens is done to establish the importance of the T-cells in immune mechanisms. T-cell responsiveness to different *P. vivax* malarial antigens and cloned antigens that are potential vaccine candidates (PV200 and GAM-1) was investigated in two groups of adults from endemic and non-endemic areas convalescing after an acute infection (Goonewardene et al. 1990). The T-cell response was lower in individuals residing

in the malaria-endemic area compared with those from the non-endemic area. It was argued that this was due to antigen-specific immunosuppression that has resulted after long-term exposure to the parasites in endemic situations. What was noteworthy was the lack of a proliferative response to the cloned malarial antigens. This has implications in the selection of candidate vaccine-constructs suitable for different endemic situations and therefore should be studied further. In general, experiments have utilized either synthetic peptides or parasite stages collected from infected patients or experimentally infected primates. In these studies, while cultures of *P. falciparum* have been successfully maintained in laboratories, the lack of long-term in vitro culture tecniques for *P. vivax* has made it necessary to constantly utilize parasites collected from infected humans.

Antigens of *P.* vivax parasite isolates from Sri Lanka have been characterized by immunochemical methods as well as on their ability to render infectivity to the mosquito vectors (Munasinghe. Mendis and Carter 1986; Premawansa et al. 1990; Udagama et al. 1987). Some of these antigens are vaccine candidates, such as the schizont surface antigen PV200, the gamete antigen GAM-1 and repetitive domains of circumsporozoite antigens.

It has been found that gamete surface proteins of varying sizes were immunogenic while only a few were important in the transmission of parasites to the mosquito vector. The use of monoclonal antibodies to test the presence of target antigens in 30 isolates from nature revealed that there were differences between isolates that could be attributed to polymorphism of the antigens (Premawansa et al. 1990). In contrast, a single protein designated GAM-1, an antigen shared between asexual stages and gametes, was conserved in all isolates tested (Udagama et al. 1987; Snewin et al. 1997). While GAM-1 is reported to be poorly immunogenic in nature its presence in all isolates highlights its usefulness as a candidate vaccine antigen. The biological importance of the antigen to the parasite warrants further study.

Thus, antigenic polymorphism in nature is a drawback for selection of vaccine candidates. Antigens that are conserved among different parasite isolates could be used as vaccines to maximize the immunity.

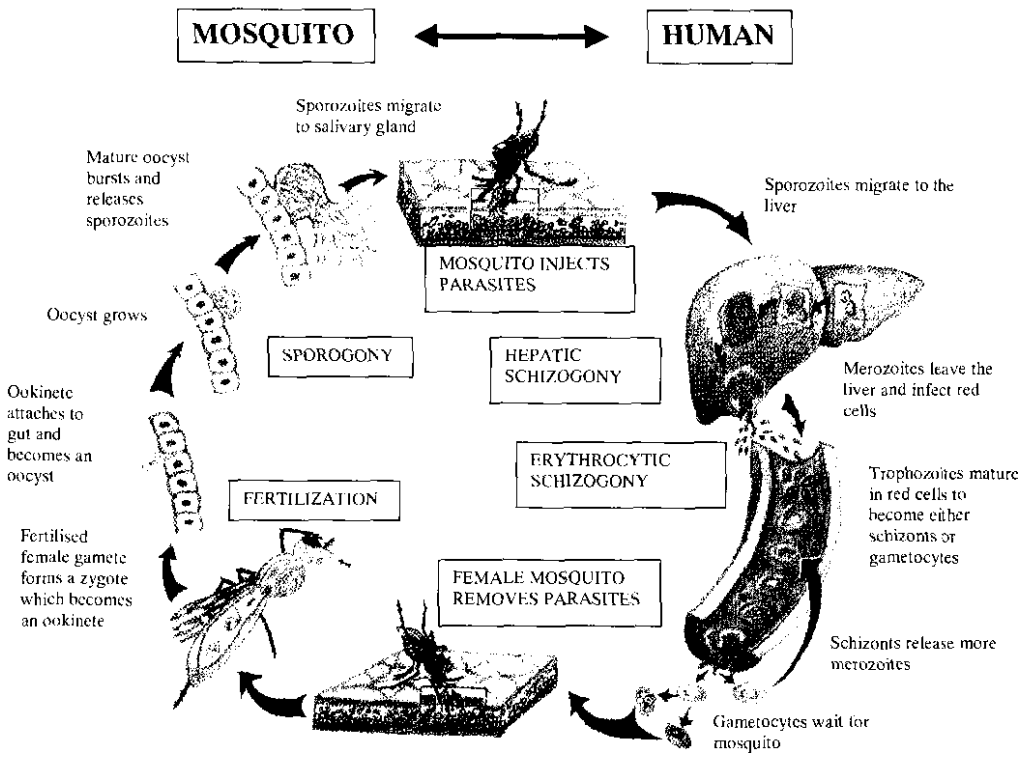
Studies have also shown that antibodies to sexual stages of *P.* vivax malarial parasites could either enhance or suppress infectivity to mosquitoes (Mendis et al. 1987b; Peiris et a1.1988). Two *P.* vivax gamete surface antigens important in transmission-blocking immunity have been defined by using monoclonal antibodies (Mendis et al. 1987b). The infectivity was enhanced when anti-gamete antibodies occurred at low concentrations of either monoclonal antibodies or polyclonal human antibodies collected from immune sera (Peiris et al. 1988).

In the field of malaria immunology, surface proteins and other molecules of the different stages of the parasites are the focus of attention, as measures are being taken to control parasite propagation in nature. This approach would be useful in the discovery of protective mechanisms involving humoral and cellular responses that are hitherto not unraveled. Antigenic variation that allows the parasites of both species to survive against the immune responses of the host in endemic situations needs further study. While the presence of polymorphism in selected antigens has been established, longitudinal studies looking at

parasite isolates in nature might prove useful in understanding how antigenic variation occurs in a given population *of* parasites from season to season in a local context. However, the more interesting and challenging question would be to address the issue of genetic switching that takes place during this expression of the antigenically different molecules. This would not only be useful in the ultimate treatment approach but will contribute to the vaccine effort at large.

Now it is accepted worldwide that there need to be different types of vaccines to combat malaria in contrast to other infectious diseases. While the relative merits of the different strategies of vaccination adopted for the management of the parasite could only be assessed in relation to the degree of the problem in any given country, research should continue to focus on the biology of the human malarial parasites, which have had a long and successful association with their mammalian host.

The Life Cycle of Malaria



Source: Singapore Polytechnic, Chemical **Process** & Biotechnology Department, reproduced with permission.

Immune Evasion by Merozoites: A Conundrum for Malaria Vaccine Development against Asexual Blood Stages

R. Ramasamy, S. Yasawardena, *R.* Kanagaratnam and M.S. Ramasamy

There is considerable worldwide interest in developing a vaccine against malaria based on sporozoites\liver stages, asexual blood stages and the sexual stages. Effective vaccination directed against asexual blood stages of *P. falciparum* is expected to prevent serious malaria. Immunity against asexual stages is believed to be largely mediated by antibodies acting to block merozoite invasion of red blood cells. We have produced antibodies against several merozoite proteins to investigate the efficacy of the antibodies in blocking merozoite invasion and parasite growth in vitro. The 40–50 kDa merozoite surface antigen (MSAZ) is a candidate molecule for use in such a malaria vaccine. The gene for MSAZ from the 3D7 isolate of *P.* falciparum was PCR-amplified and cloned into the bacterial expression vector pGEX-3X to obtain a fusion protein of MSAZ with Schistosoma *japonicum* glutathione S-transferase. The recombinant fusion protein was used to immunize rabbits. After four injections, the sera had Western blotting and immunofluorescence titers of 10^{-6}. Immune sera, and IgG, $F(ab)'_2$, F(ab) prepared from the immune sera, were assessed for their effects on the growth of 3D7 parasites in vitro by microscopy and an $[H^3]$-hypoxanthine incorporation assay. The antibodies did not significantly inhibit red blood cell invasion and parasite growth when added to cultures as 10 percent v/v serum or as immunoglobulin preparations at concentrations up to 200 µg ml^{-1}. However in the presence of IgG or $F(ab)'_2$, but not F(ab), antibodies to MSAZ. the proportions of red blood cells invaded by more than one merozoite increased significantly. Multiple invasion is attributed to merozoites cross-linked by bivalent antibodies, attaching to and subsequently invading the same red cell. The results clearly demonstrate that the merozoites are able to avoid complement mediated lysis in this in vitro system. Similarly, antibodies generated against the N-terminal portion of a different 185kDa merozoite surface protein, MSA1, with titers of 10^{-3} were unable to inhibit parasite growth in culture. These observations have a bearing on the evasion of host-immune responses by the parasite and the use of full-length recombinant MSAZ protein in a malaria vaccine.

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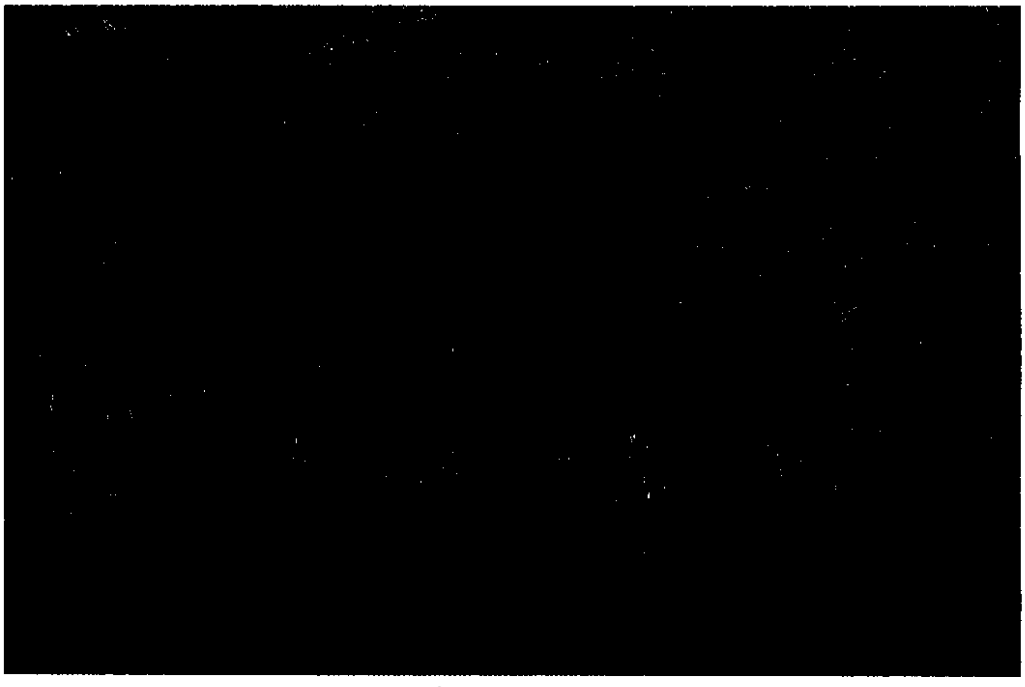

Vegetation in shallow edges of tanks can provide refuge to mosquito larvae.

Chapter 5

Malaria Control

Diagnosis and Treatment

The early diagnosis and prompt treatment of malaria patients constitute the mainstay of the Global Malaria Control Strategy (WHO 1993), which has also been accepted by Sri Lanka. However, presumptive treatment of malaria is highly discouraged in Sri Lanka and all patients who present themselves at a government facility should, in principle. have a blood slide taken for confirmation by a microscopist at the facility or at a central laboratory (passive case detection). Early detection and treatment are also pursued through fever surveys and mobile malaria clinics (active case detection). The malaria-control program is supported by the large network of family health workers engaged in the distribution of chloroquine for prophylaxis of malaria in pregnant women.

Microscopist of the Anti Malaria Campaign

The standard method to diagnose malaria is still the microscopic examination of a blood film for malaria parasites. However, other diagnostic methods have been tested, based on detection of parasite antigen or using molecular techniques such as the polymerase chain reaction (PCR). Kodisinghe et al. (19971 tested the use of the ParaSight™-F dipstick test for the diagnosis of *P. falciparum* malaria among outpatients at government facilities. When the ParaSight™-F dipstick was compared with microscopical examination done under strict laboratory conditions it had a sensitivity of 90 percent and a specificity of 99 percent. However, the ParaSight™-F dipstick gave negative results when there were only gametocytes in the blood. The time taken for a patient to revert to a negative ParaSight™-F dipstick test was up to 14 days. This makes it difficult to check the response to antimalarial treatment and it could lead to unnecessary secondary treatment after self-medication. **Also,** the cost of dipsticks is still too high for routine use.

The standard treatment regime promoted by the Anti-Malaria Campaign is chloroquine and primaquine for all cases of *P.* vivax and *P. falciparum*. So far there have been no reports of chloroquine-resistant *P.* vivax infections in Sri Lanka. The first *t* falciparum chloroquine-resistant case was reported from a survey in the Dambulla District in August 1984 (Ratnapala et al. 1984). In vitro tests showed chloroquine resistance at the RI and RII

Treatment of Uncomplicated Malaria

Chloroquine is a cheap and safe drug and is still the treatment of choice for uncomplicated malaria in Sri Lanka. The recommended dose for adults is 600 mg chloroquine base on the first and second days and 300 mg on the third day. Children are given 10 mg/kg on the first and second days and 5 mg/kg on the third day.

The second-line drug in case of chloroquine-resistant *f? falciparum* is sulfadoxine-pyrimethamine (Fansidar) given as a single dose.

Primaquine is added to chloroquine treatment because it is active against the hypnozoite stage that occurs in *P.* vivax infections. The recommended 5-day course is a trade-off between optimum effectiveness, which would require a longer duration of treatment, and the potential serious side effects of the drug. In people who are deficient in the enzyme glucose-6-phosphate dehydrogenase (G6PD), primaquine can cause serious destruction of red blood cells (hemolysis). The action against hypnozoites prevents relapses of *f?* vivax. This is useful in low-transmission areas but not *so* much under conditions of intense transmission when reinfection will be common. Primaquine also kills the sexual stages of *P.* vivax as well as *P. falciparum.* This was considered important in the eradication era, to reduce the human reservoir of malaria. It is now only recommended during epidemic conditions, when a single dose is sufficient to eliminate gametocytes. A policy on primaquine use should be based on the local level of malaria transmission, and the local prevalence of G6PD deficiency.

Resistance to Antimalarial Drugs

For more than 20 years WHO has recommended standard in vivo tests to monitor drug resistance. It distinguishes the following responses to an antimalarial drug:

- Sensitive: clearance of asexual stages by day 6 (day 0=first day of treatment) without subsequent recrudescence until day 28.
- RI resistance: clearance of asexual stages for at least 2 consecutive days. the latest on day 6 after the initiation of treatment, followed by a recrudescence.
- RII resistance: reduction in asexual parasitaemia to less than 25 percent of pretreatment counts within 24 hours of initiation of treatment, but no subsequent disappearance of asexual parasites.
- RIII resistance: only a moderate reduction, no change, or even an increase, in asexual stages during the 48 hours following the initiation of treatment.

A new standard field test is under development, which is of shorter duration and makes use of clinical response in addition to parasitological response (WHO 1994).

level. For resistant cases the drug of choice is sulphadoxine-pyrimethamine (Fansidar). In 1992, the first Fansidar-resistant case of *P.* falciparum was reported from a patient who had been infected in Chilaw (Handunnetti et al. 1994). The official policy is to restrict the use of Fansidar to government health facilities to avoid further spread of resistance against this second-line drug. However, parallel imports of Fansidar sold through local pharmacies and prescribed by private practitioners may undermine the government policy.

In 1991, the Anti-Malaria Campaign reported 15 percent chloroquine resistance among *P.* falciparum cases (Ministry of Health 1991). Graves, Fernando, and Attanayake 11995) examining the Anti-Malaria Campaign information for 1992 found a relatively high level of chloroquine resistance with approximately 40–50 percent of isolates tested resistant in vitro and 1617 percent showing the highest level of resistance in vivo (RIII). Handunnetti et al. (1996) studied malaria patients over the period 1992–1994 and found in vivo RI chloroquine resistance of 30 percent and 55 percent from patients living in endemic and non-endemic areas, respectively. The study also found that the recrudescent infections had significantly lower peripheral parasitaemia. Also, the recrudescence of chloroquine-resistant infections gave rise to clinical signs and symptoms of markedly reduced severity, resulting in a lower probability that recrudescent infections would be diagnosed and treated. This, linked with the fact that chloroquine-resistant *P.* falciparum infections were significantly more infective to mosquitoes due to higher gametocytaemia, might support a buildup of a *P.* falciparum reservoir.

The formulation of a revised policy to reduce the spread of *P.* falciparum-resistant cases should receive high priority. Based on the available information a review of the existing monitoring activities and a reinterpretation of the data on the spread of antimalaria-drug resistance should be carried out. This should include a discussion on patient groups to be included in the monitoring program, parasitological and clinical parameters used for the assessment and the geographical coverage needed. Investigations need to be carried out to assess the possibility of using a combination of drugs to treat malaria infections that would reduce the development of drug resistance. The different antimalaria-drug policies need to be evaluated against potential side effects to the patient, long-term impacts on transmission and cost to both the government and the individuals. The drug policy has to be updated regularly to maintain an effective treatment response and low levels of malaria-related morbidity. Apart from the consequences of resistance against the first-line antimalarial drugs, the role of primaquine in the drug policy should be reassessed. There is no clear evidence that the effects of primaquine on liver stages of *P.* vivax and on gametocytes of *P.* vivax and *P.* falciparum reduce transmission. The policy of early diagnosis and treatment might be more sustainable with better patient compliance when treatment is simpler, only including one schizontocidal drug.

Treatment-Seeking Behavior

The treatment-seeking behavior of the population is not fully documented and is likely to vary considerably between the districts and between urban and rural settings. However, the studies that have been done indicate a generally high preference for government services against prtvate facilities (Mendis et al. 1990; Ramasamy et al. 1992c; Pinikahana 1993;

Jayawardene 1993; Konradsen et al. 1997a). In contrast, a survey in southeastern Sri Lanka found an almost equal number of malaria patients seeking treatment at government and private facilities (Abeysekera et al. 1997).

In Huruluwewa, the community-perceived advantages and disadvantages of government and private malaria-treatment services were documented (Konradsen et al. 2000). The population in that area was seeking treatment at the government hospitals since this service was free of charge, a blood-film was normally taken to confirm infection, in-patient facilities were available if necessary and the staff members were seen as highly qualified, especially at the larger facilities. However, the long queues were seen as a major disadvantage at the government facilities causing hardship, especially for the elderly and mothers with sick children. In addition, the time and attention given to each patient at a government hospital were often seen as being inadequate. This was in contrast to the private facilities, often serviced by the government doctors after their normal duty hours, where the attention given to the patients was seen as much more thorough and service-oriented. In addition, the drugs prescribed were perceived as of a better quality, often modern equipment was available but most importantly, the patient did not have to wait as long as at the government facility. A disadvantage with the private facility was the fact that it was often not possible to have a blood film taken and the service was costly. However, for a segment of the community the fact of paying for treatment was seen as a guarantee for better service and quick recovery. The use of traditional medicine for perceived malarial signs and symptoms is generally found to be very low (Wolffers 1989; Silva 1991; Konradsen et al. 1997a). Over time, there has been a change in health-seeking behavior from indigenous to Ayurvedic, from Ayurvedic to modern western services provided by the government, and recently from government services to private health-care providers.

A study in two hospitals, one in the wet zone and one in the dry zone, found that people were seeking treatment from 3 to 6 days after onset of malaria symptoms (Ramasamy et al. 1992c). Mendis et al. (1990) found a similar pattern in the southeastern dry zone where 50 percent of the people would seek treatment within 2 days and 90 percent within 4 days of the onset of symptoms. Among the community in five villages in the northern dry zone, treatment was sought, on average, 1.2 days after the onset of symptoms (Konradsen et al. 1997a). In contrast, a study of illness behavior in two villages in the southern Hambantota District found that, in remote settlements, a certain number of malaria patients do not take medical treatment and a larger number of patients delay seeking treatment (Pinikahana 1993). The reasons for the delay in seeking treatment were linked to the cost involved, the distance to the treatment facility and the lack of knowledge. The only study assessing the gender and age differences in response-time for seeking treatment found a very fast response-time for small children, most often taken directly to a larger government facility or mobile clinic by their mothers or grandmothers 1–2 days after experiencing high fever. The adult population, irrespective of gender, would often wait for 2–3 days before seeking treatment. A small segment of the population, especially the elderly or handicaped, would at times wait 5–7 days before seeking treatment since they sometimes had to wait for someone to accompany them to the facility or had financial dificulties (Konradsen et al. 2000). Both in poor and relatively more well-off communities self-treatment at home is often practiced before going to the hospital (Pinikahana 1993). However, unlike in many

other countries self-treatment is mainly with analgesics, especially paracetamol and rarely with antimalarial drugs. Konradsen et al. (1997a) found that 85 percent of the surveyed households used paracetamol as the first treatment at home.

With the need for prompt diagnosis and treatment, it has been suggested to train health volunteers in the diagnosis and management of malaria on clinical grounds. Health volunteers were employed to dispense drugs on a large scale under the Mahaweli Development Project, when large numbers of people migrated to new settlement areas before an adequate health-care infrastructure was in place. Also among refugee populations, health volunteers fulfilled this role (Van der Hoek, Premasiri. and Wickremasinghe 1997). However, health volunteer programs are only succesful if adequate supervision and support can be provided. While this is possible in small-scale, well-managed projects, it has been described that these programs lose most of their effectiveness once they grow too big, mainly due to failures of training, supervision, and logistics (Walt, Perera, and Heggenhougen 19891. Also, diagnosis by health volunteers is presumptive and leads to overtreatment with antimalarial drugs, thereby accelerating the development of drug resistance. Overtreatment could be limited if a simple protocol based on clinical signs and symptoms could accurately identify malaria patients. However, for most of the common symptoms and signs of malaria either the sensitivity or the specificity is very low and implementation of such a protocol would still lead to unnecessary treatment for many while denying treatment to others who have malaria (Van der Hoek, Premasiri, and Wickremasinghe 1998). The use of health volunteers or nonmedically qualified staff is also complicated by the relatively high frequency of glucose-&phosphate dehydrogenase (G6PD) enzyme deficiency that has been found in the North Central Province, especially among the communities living in the ancient villages (Abeyaratne et al. 1976). Primaquine has a

Village-level diagnosis and treatment center operated at Horulowewa.

haemolytic effect in patients with G6PD deficiency and the administration of primaquine should, therefore, be confined to qualified medical practitioners in these areas.

Van der Hoek, Premasiri, and Wickremasinghe (19971 undertook one of the few studies comparing different health delivery systems for the diagnosis and treatment of malaria among a refugee population in Kalpitiya. This study concluded that the best option would be to upgrade the existing health facilities available for the refugee community instead of training and supervising the large number of health volunteers that would be needed to service the refugee population.

To test new approaches in health-care management, in particular malaria, a study was initiated in seven villages to assess the community response to the introduction of a village-level treatment center. The center was initially established with the support of the Anti-Malaria Campaign (AMC) and the researchers involved, but was increasingly managed by trained assistants from the local community. The center quickly took over the role as the main center for diagnosis and treatment of malaria from the government facilities. The center did not improve the response-time in seeking treatment for young children since the mothers continued to use the distant government facility to a large extent. However, the response-time for the adult population was reduced by 1–2 days. Generally, the center was of most benefit to the elderly, handicapped and financially disadvantaged segments of the community. The study found that the effective population coverage of the center was, among other things, influenced by the selection procedure and training of the assistants and the history of the relationship between the different villages serviced by the center (Konradsen et al. 2000).

The generally good coverage of health facilities in most parts of the country is likely to encourage a speedy treatment-seeking response from the community. But there is a need to experiment and research new strategies of health delivery, especially in remote areas and among the refugee community involving community-based organizations or the private sector. Government policies and administrative procedures will need to be adjusted to facilitate new approaches in health care.

Health Information System

The routine health information system of the AMC provides the basis for the planning of malaria-control activities and guides researchers in their work. It is therefore important to assess the quality of these data on a routine basis. Only blood-slide-confirmed positive cases are included in the malaria statistics. This underestimates the total number of cases since most government institutions at the periphery do not have laboratory facilities. In 1994, in four of the major malarial districts of the country (Kurunegala, Matale, Polonnaruwa and Anuradhapura) only approximately 40 percent of the medical institutions had microscopists attached to them (Graves, Fernando, and Attanayake 1995). Although a number of the institutions without a microscopist will have their slides checked at neighboring institutions, the number of fever patients that will get a blood slide taken is still far below 100 percent. Another important factor in the underreporting of malaria cases is the use of private health facilities that do not keep records.

Overall, the information available indicates that annual trends and district-wide fluctuations are captured in the government data and the information is likely to be much better than secondary data from many other developing countries. However, the ongoing armed conflict in the north and east of the country has made health information from this part of the country unreliable.

Chemoprophylaxis

The current policy in Sri Lanka is to provide chemoprophylaxis to selected groups living in malaria-endemic areas (Ministry of Health 1997). This is in line with the WHO recommendation that chemoprophylaxis should be restricted to:

- pregnant women, especially during first pregnancy
- migrant workers from non-endemic areas
- soldiers serving in highly endemic areas
- tourists

Little research has been done on the effects of malaria on anemia in pregnancy and on birth weight. This knowledge would be essential to determine whether chemoprophylaxis for pregnant women is a useful strategy under the transmission levels prevailing in Sri Lanka.

Chemoprophylaxis for Visitors to Sri Lanka: Can the Consumption of Antimalarial Drugs Be Reduced?

Wim van der Hoek

Visitors to a malaria-endemic country like Sri Lanka are advised to protect themselves against mosquito bites and to take malaria chemoprophylaxis. Most medical practitioners use the annual publications from the World Health Organization or the guidelines from the national health authority to instruct travelers from their countries. These documents do not contain very detailed information and it is common practice that travelers to countries where malaria is endemic are advised to take prophylactic antimalarial drugs irrespective of their style of travel and whether the area to be visited is free of transmission. It is likely that this causes a considerable overconsumption of antimalarial drugs in countries such as Sri Lanka, with only seasonal and localized transmission.

The majority of visitors to Sri Lanka are tourists from Western Europe (table 4). More than 80 percent of their nights are spent in resorts along the southwest coast (from Negombo, 35 km north of Colombo up to Galle, 110 km south of Colombo), and in Kandy. These areas are generally considered free from malaria transmission and cases reported by health facilities are imported from other parts of the country. Some of the important tourist destinations, such as the ancient cities of Anuradhapura, Polonnaruwa, and Sigiriya, and the Yala National Park are situated in the dry zone, but these are mainly popular for day trips. Most tourists will therefore not be exposed during the evening or nighttime, when Anopheles culicifacies, is most active.

Individual budget travelers often stay at guesthouses in malaria-endemic areas without the amenities, such as air conditioning of modern hotels, but even in these facilities mosquito nets are sometimes available.

It is likely that the consumption of antimalarial drugs by visitors to Sri Lanka can be reduced greatly if physicians, especially in Western Europe would give a more differentiated advice on chemoprophylaxis, tailored to the individual traveler, taking into account the travel itinerary and the time of travel. There is no justification in prescribing chemoprophylaxis to tourists who intend to remain at the resorts along the southwest coast and make only day trips to destinations in the malarial areas. Tourists who stay overnight in the dry zone and those individual travelers crossing the whole country do require antimalarial drugs starting when they leave the non-endemic zone until 4 weeks after their return to the Colombo area. The most appropriate regimen is still chloroquine plus proguanil as recommended by WHO. Carrying antimalarial drugs for self-administration ('standby treatment') should not be recommended for Sri Lanka. as facilities for diagnosis and treatment are available in all parts of the country. The possibility to reduce consumption of antimalarial drugs becomes even more attractive for travelers from countries such as the USA, that recommend mefloquine for chemoprophyiaxis (Centers for Disease Control and Prevention, Internet site http:liwww.cdc.govltravell indianrg.htm). All travelers to Sri Lanka, even the business traveler visiting the capital Colombo, should be told to protect themselves against mosquitoes. Although the risk of filariasis and Japanese encephalitis is very small for the occasional visitor, dengue fever is common in Colombo and in other urban centers along the southwest coast.

The epidemiological pattern, including resistance of the parasites against antimalarial drugs, and the proportion of infections due to *P falciparum*, is changing continuously and health authorities in travelers' home countries should ensure that the most recent information is made available to physicians, vaccination centers and others responsible for advice to travelers.

Table 4. Tourist arrivals in Sri Lanka by country of residence in 1998.

Country	Arrivals	
	n	%
Germany	74,058	19
United Kingdom	66,432	17
India	37,356	10
France	26,874	7
Netherlands	22.977	6
Italy	15,867	4
Japan	13,785	4
USA	9,987	3
Switzerland	9,048	2
Canada	7.542	2
Other countries	97.137	25
Total	381,063	100

Source: Ceylon Tourist Board (unpublished data).

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International Water Management *Institute.*

Control of Anopheline Vectors in the Riverbed Pools of a Malarial Area in Sri Lanka Using the Insect-Growth Regulator, Pyriproxyfen

A. M. G. M. Yapabandara and C. F. Curtis

Riverbed pools are the most important breeding sites of An. culicifacies, considered to be the main malaria vector in Sri Lanka. For a number of years the application of temephos has been widely used to control anopheline larvae in riverbed and streambed pools in the island.

A small-scale field trial was carried out in a gem-mining area of Sri Lankatotest the insect growth regulator, pyriproxyfen. as a vector-control measure. The test showed that two annual treatments with 0.01 mg/l of pyriproxyfen were more cost-effective than applying tempehos, using expanded polystyrene beads, spreading engine oil or filling the pits with soil. The result of a multi-village trial revealed a 60 percent reduction in adult An. culicifacies density and significant reduction in human malaria due to either *P.* falciparum or *P.* vivax. Further, twelve villages from the Dambulla area were selected to determine the long-term effect of pyriproxyfen on the adult-vector population and malaria incidence. A 2-km radius around each of the 12 villages was included in the study area.

The project was started in August 1998 and will be continued in the Dambulla area till October 2000. The study area is regarded as one of the highly malarial areas in Sri Lanka. A general survey of the population. houses and geographical distribution of mosquito-breeding sites in the twelve villages was made. Baseline data were collected in the first year in the selected villages. This included information on both mosquito populations and malaria positivity in the human population using mobile malaria clinics and hospital data. The mosquito population is monitored using partial night human-landing catches, light traps hung beside occupied bed nets, cattle-baited huts and pyrethrum spray-sheet collections. After completion of the baseline data collection the villages will be assigned as either control *or* treatment. Pyriproxyfen (0.5% granules) at the rate of 0.01 mg active ingredient per liter will be applied to the riverbed pools and other permanent breeding sites in six selected treatment villages. In these breeding sites efficacy of pyriproxyfen will be recorded monthly using larvae introduced into floating-screened buckets. The mosquito populations and malaria incidence in the human population will be monitored as during the 1-year baseline survey.

At the end of the intervention year, the long-term effect of pyriproxyfen on the adult-vector population and malaria incidence in treated villages will be compared with the control villages.

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Chemical-Based Vector Control

As already mentioned, the use of residual insecticides has been the mainstay of malaria control since DDT was first used in 1945. In late 1993, a strategy of selective spraying of insecticides was introduced, which has reduced the overall amount of chemicals used. At the same time, fenitrothion and lambda-cyhalothrin were included in the spray program to supplement malathion. The new approach stratifies areas according to their need for perennial spraying, seasonal spraying or focal spraying. The AMC is involved in some operational research assessing the impact of spray operations on the adult vector population, resistance development in the main vectors and changes in vector behavior in response to the insecticide (Wickramasinghe 1990). However, while this information is used for management purposes, there are no published studies that look at entomological and epidemiological impacts of the spray operations. To supplement the residual spraying operations the AMC has used chemical-based larvicides, e.g., temephos, in rivers and streams close to human habitation. This takes place in areas with a reported outbreak of malaria or when an entomological team identifies an area with unusually high Anopheles larvae abundance.

To improve the basis for implementing the new stratified spraying program it is necessary to have a good health-information system. Advances in the development of risk maps could improve the knowledge base for the new spraying operations. The effectiveness of the residual spraying operations needs to be documented under field conditions including both entomological and epidemiological studies.

Environment-Based Control

Environmental and biological interventions are important in an integrated control strategy. Unfortunately. this is receiving very little attention by the research community and control agencies. Early this century, environmental management for vector control was practiced but this was done away with when DDT was introduced. Rajendram and Jayewickreme (1951b) describe the case of Anuradhapura town, the first place in Sri Lanka where DDT was used as a residual spray:

> "On November 11. 1945, DDT in kerosene was first used in a 5 percent solution as a residual spray against the adult vector and all forms of larval control were abandoned."

Experiments with larvivorous fish are again taking place on a small scale in a few areas such as the Anuradhapura District. Here the AMC has constructed small tanks for the cultivation of fingerlings, which have been released into known breeding habitats on a regular basis. Experiments with the use of extract from the Neem plant *(Azadirachta indica)* for the control of anopheline larvae have also been tried on a small scale (Wijekoon and Ramasamy 1990). However, field-based quantitative evaluations of the effects of Neern products or larvivorous fish are not available in Sri Lanka.

Due to the breeding preference of *An. culicifacies* for streams and rivers, water management has long been considered an effective intervention. Between 1934 and 1936, experiments

Neem trees.

Larvivorous fish (Aplocheilus werneri, male*).*

were performed with engineering and manual measures to reduce the creation of pools in rivers close to the Badulla town. Clearing the stream from falling trees, creating drainage canals along the side of the stream, filling up permanent rock-pool formations and constructing special dikes made the stream less-conducive for the breeding of ***An. culicifacies*** (Worth 1937). Technical feasibility tests were carried out in a number of rivers and streams using automated siphons to flush waterways. However, automated siphons were found to be less-effective due to the high maintenance input needed and the difficulty of operation during low water flow. Hand-operated flushing devices were recommended instead of automated siphons (Worth and Subrahmanyam 1940). Much later, the Mahaweli Authority carried out flushing activities below the reservoirs close to Kandy town aimed at reducing the mosquito-breeding potential. However, due to the conflict with other water-management objectives, e.g., hydropower generation, this practice was stopped (Wijesundera 1988).

One of the salient features in the landscape of the dry zone of Sri Lanka is the large number of water reservoirs, locally known as tanks (figure 7). There are an estimated 18,000 of these tanks in Sri Lanka and many are interlinked through canals or natural streams to form cascades. In 1994, a 3.5-year entomological and hydraulic study was initiated in the Huruluwewa watershed assessing the options for control of malaria vectors through different water-management practices in a natural stream that formed part of such ***a*** tank cascade system. The interventions were based on the use **of** existing irrigation

structures and aimed at identifying the most feasible management strategy integrating agricultural and human-health considerations. The studies identified a critical water depth in the stream. The larvae abundance was reduced by 84 percent when the water level in the stream was increased from pooling level (close to 0 cm) to 50 cm. Different water-management scenarios were described, simulated and the impact on vector abundance estimated. Overall, the result demonstrated a high potential for effective vector control by feasible changes in irrigation and stream-water management resulting in periodic fortnightly releases from upstream reservoirs to eliminate mosquito breeding sites and rendering the habitat less-suitable for An. *culicifacies* oviposition for sometime after the water release (Konradsen et al. 1998; Matsuno et al. 1999).

At the moment, the use of environmental and engineering-based control interventions plays an insignificant role in the control strategy and only one recent substantial research

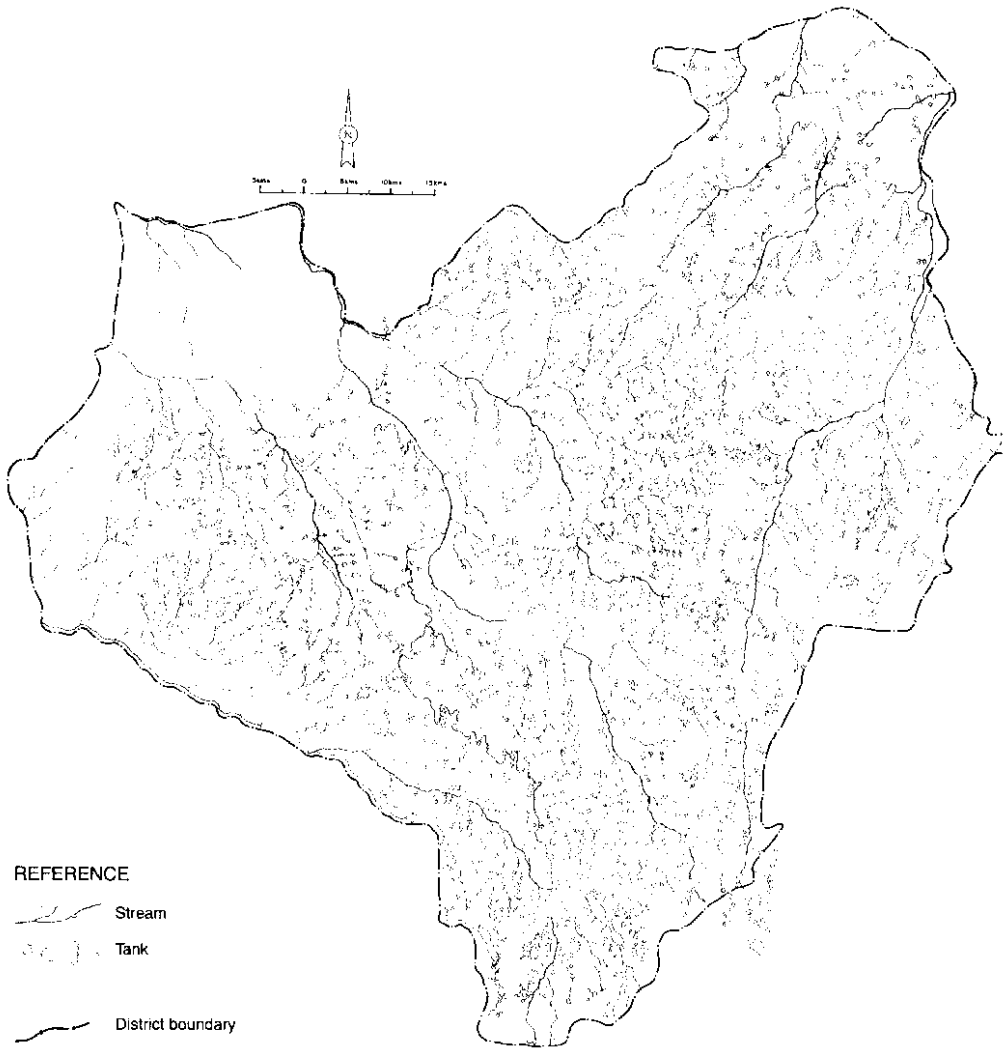
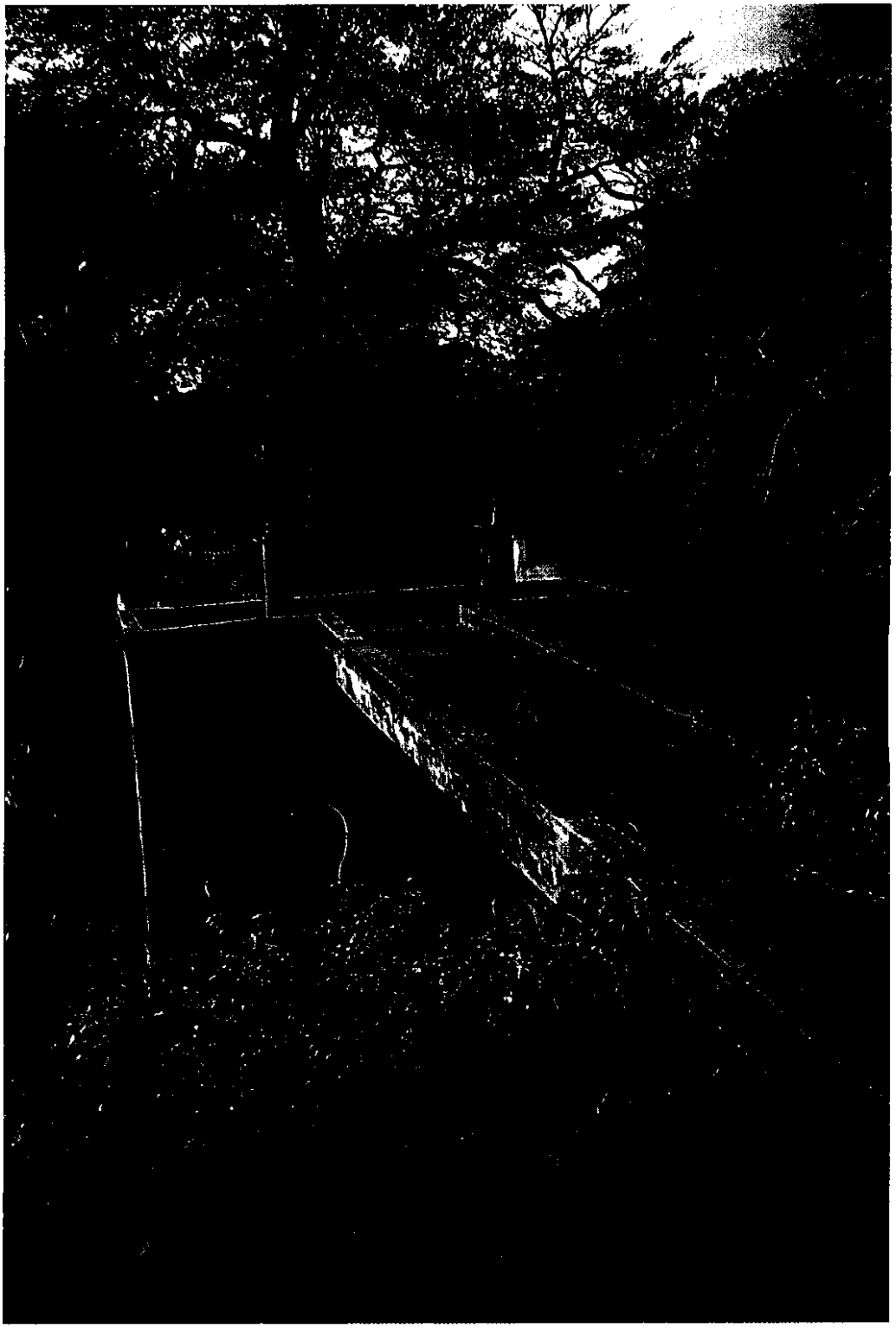


Figure 7. Irrigation reservoirs *(tanks)* and other water resources in *the Anuradhapura* District.



Sluice in the Habarana Tank, used to regulate the flow of water in the Yan Oya, Huruluwewa

project has been carried out in this field. This type of research calls for an interdisciplinary approach, which is likely to make it more difficult to design and implement. However, the situation in Sri Lanka calls for more research into the use of water management for vector control. It is important that the impact of the proposed interventions is quantitatively tested against both entomological and epidemiological parameters.

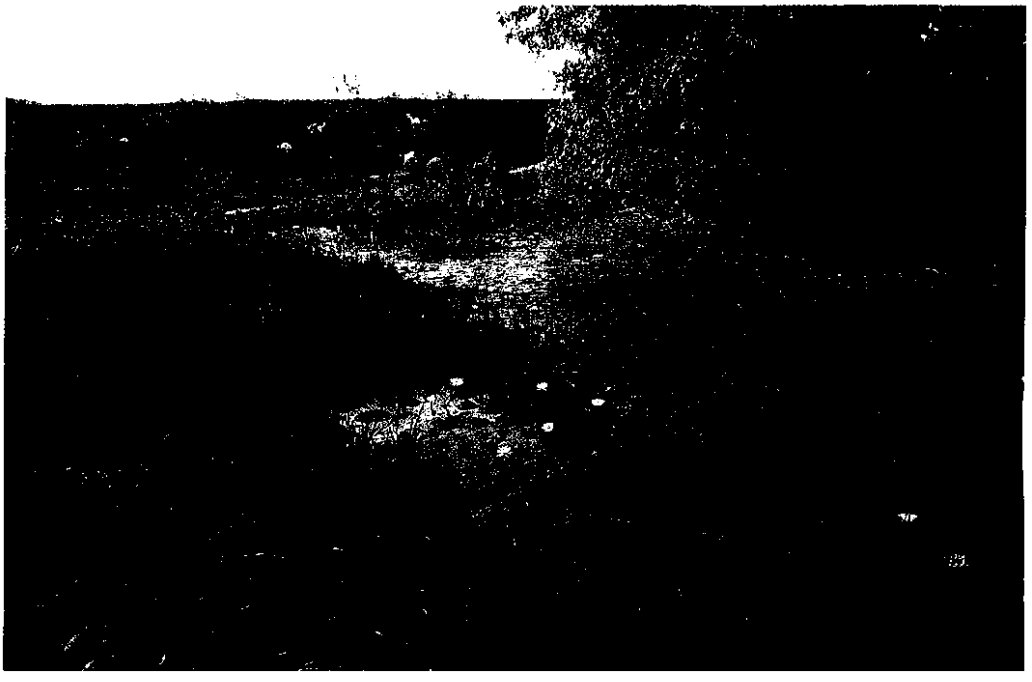
Malaria Control Policies

Silva (1997) discusses the malaria-control policies and programs as they have evolved in Sri Lanka historically and how they have been influenced by the ruling elites at the time. It is pointed out that some of the key problems of the control program today relate back to the colonial era such as the top-down approach, the technology bias, dependency on foreign aid and the bureaucratic setup.

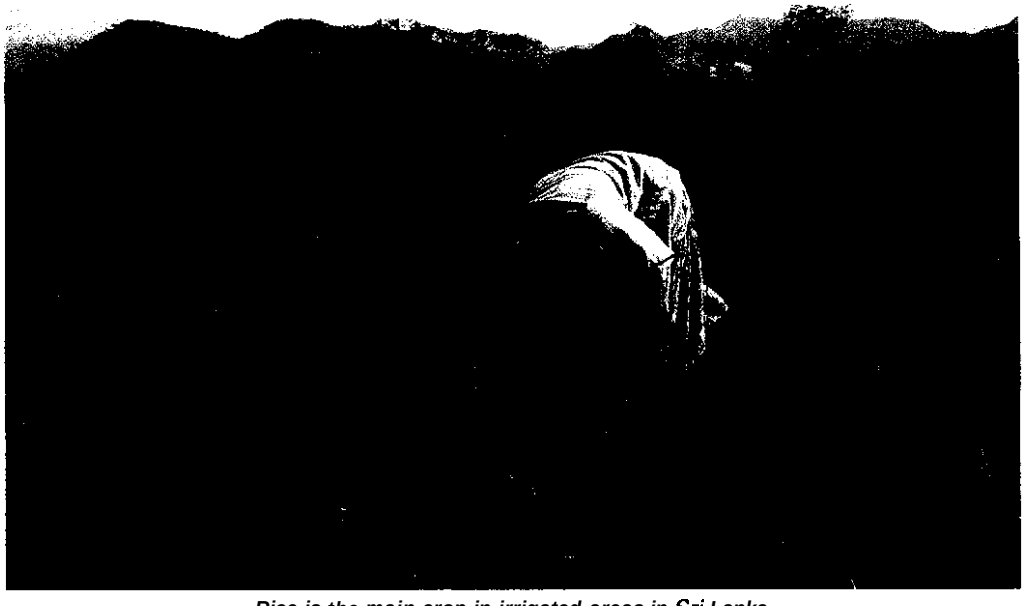
The Anti-Malaria Campaign (AMC) was established in Sri Lanka in 1910. Until 1991, all malaria-control activities were carried out by the AMC as a vertical program under the Ministry of Health, with Regional Malaria Officers (RMOs) being responsible for control activities in the 17 malarial regions identified throughout the country. Since then the activities have been decentralized and the RMOs now report on malaria-control and surveillance activities to the Provincial Directors of Health Services and the Deputy Provincial Directors of Health Services (responsible for a district). Primary responsibility for malaria control is now with the Divisional Director of Health Services, formerly designated Medical Officer of Health, who is responsible for all health-care activities in a Divisional Secretary Division. The average population size of the Divisional Secretary Divisions is 65,000. The main objective of the decentralization has been to integrate the malaria-control activities into the general health services. Today, the AMC is a directorate under the Department of Public Health Services of the national Ministry of Health & Indigenous Medicine with responsibilities for monitoring the countrywide malaria situation, formulating national policies and technical guidance and providing insecticides and drugs for control activities. Since 1993, the National Malaria Control Policy in Sri Lanka has adopted the "Global Malaria Control Strategy" (WHO 1993) including the four main principles:

- early detection and prompt treatment of malaria cases
- selective application of sustainable malaria-control measures including vector control
- development of mechanisms to forecast and prevent malaria epidemics and outbreaks
- regular assessment of the countries' malaria-control program

In Sri Lanka, the adoption of the new strategy has led to more emphasis on early diagnosis and prompt treatment and less reliance on chemical methods of vector control.



Seepage area from tank.



Rice is the main crop in irrigated areas in Sri Lanka

Chapter 6

Socioeconomic Aspects of the Malaria Problem

Economic and Social Impacts of Malaria

Gill (1940) reviewed existing information on malaria in Sri Lanka and reached a number of conclusions with respect to the impact of malaria on vital statistics. Two of the more significant conclusions were that endemic malaria does not exercise any appreciable effect on the birth rate of indigenous populations and that endemic malaria causes a change in the monthly distribution of births, the amplitude of which varies directly with its intensity. Barlow (1968) used Sri Lanka as an example in his work on the contribution of malaria control to economic growth. He concluded that in the short run, malaria eradication increased income per person, but that in the long run its associated growth in population outstripped the growth in per capita income. Barlow also looked at the economic implications of combined malaria-control and family-planning activities. These two activities in combination were shown to be highly favorable. With malaria eradication plus birth control, capital formation was projected to increase by 17 percent per year compared to 4 percent per year with malaria eradication alone (Gomes 1993). Brown (1986) reported somewhat similar findings. In an attempt to estimate the impact of the large-scale malaria-control operations in Sri Lanka, Brown concluded that the successful control efforts and the resulting marked decline in the general mortality had accelerated the population growth of the country. However, it was not possible to demonstrate that the control activities had resulted in significant economic development.

Few studies have been carried out in Sri Lanka to quantify the economic burden of disease on the households. One was a household survey linked to a cost-effectiveness study of antimalarial activities in the Matale District (Attanayake 1994). Jayawardene (1993) presented some findings on social impacts from a study among a newly settled population in an irrigation system in the east of the country. Information for this study was collected during 1986 when a number of households with a family member who had experienced an episode of malaria were visited to assess the coping-strategies and the cost implications. It was found that malaria imposed an additional stress on the community and resulted in a delay of implementing a range of development initiatives and the start of agricultural production. In the households where a male head had fallen ill it was estimated that for an average household approximately 14 working days were lost over the 10-month study period. However, the economic impact on the households was not estimated in this study.

Konradsen et al. (1997b) developed a methodology to assess the opportunity cost of labor days lost due to illness reflecting the demand for labor and the real wage rate in an area. The daily activity format was applied for the first time in a northern dry-zone rural community over a 1-year period in 1994–1995 covering all age groups. When including

Malaria Risk Map for Sri Lanka Using Environmental Data for Cost-Effective Control of Malaria

Risk maps for malaria are currently receiving much attention, especially on the African continent. New technologies such as geographical information systems (GIS), global positioning system (GPS), and remotely sensed satellite imagery make it possible to map the availability of surface water, vegetation, land use patterns, and other factors important for malaria transmission. Such a risk map makes it possible to target priority areas with control activities and can serve as a decision support tool in health impact assessments for future water resources development projects. One of the first international meetings on health applications of GIS took place in Colombo, in 1994 (de Savigny and Wijeyaratne, eds. 1995). The Malaria Research Unit (MRU), University of Colombo, in collaboration with the AMC, is currently developing en epidemiological monitoring and risk-assessment system for malaria in selected administrative districts. IWMI, in collaboration with the University of Peradeniya and the AMC, is developing a risk map for Sri Lanka using data from detailed studies on vector ecology, risk factors for malaria and socioeconomic aspects of the disease. In many countries, it is difficult to validate risk maps because of the lack of reliable data on malaria incidence or prevalence. This is caused by extensive self-treatment of patients with drugs bought at local shops or pharmacies, increasing use of private-health facilities that are not included in the regular health-information system, and high proportion of cases receiving presumptive treatment without laboratory diagnosis. In Sri Lanka, the situation is more favorable because government facilities are still the preferred diagnosis and treatment centers so that the AMC figures are a good indicator of the real malaria incidence. There is high acceptance of blood filming by the population and low self-treatment practices.

For the IWMI risk map, information will be obtained on vector occurrence and density, meteorological data, surface water, amount of irrigation, land use pattern, vegetation cover, and cattle densities. In a GIS, multiple layers will be created of mapped data in digital form. Inputs will also be from high resolution satellite images, agroclimatic databases, existing maps or databases of vector distribution, disease prevalence and density of human and animal populations. Selecting a random number of villages for a larval, adult and human malaria survey will validate predictive models. The model will then be modified if necessary. The data collection on the ground will be of a participatory nature. Workshops will be held where staff members from other divisions are encouraged to collect the necessary data from their own areas. Training will be provided to enable participants to process the data and make the resulting maps available for routine management. This exercise will be expanded to other divisions and districts in a stepwise fashion.

A researcher using a GPS device to find the exact coordinates of a tank in the Anuradhapura District.

only confirmed malaria cases in a year with an average incidence it was found that the economically active age group (14 to 60 years) lost 1.8 percent of working days due to malaria and 5.2 percent due to all other illnesses. Most of the labor days lost were concentrated in the important agricultural season. Children, not part of the economically active age group, lost 10 percent of school days due to malaria during the high transmission season. The annual economic loss per household amounted to US$15.5 for malaria and US$47.5 for all other illnesses. This corresponded to a loss of 6 percent and 18 percent of annual household net income, respectively. The cost of labor days lost due to malaria can be compared with the direct cost per episode of malaria calculated for the same community at approximately US$3.0 linked mainly to expenditures on special diets and transport to the treatment facility (Konradsen et al. 1997a).

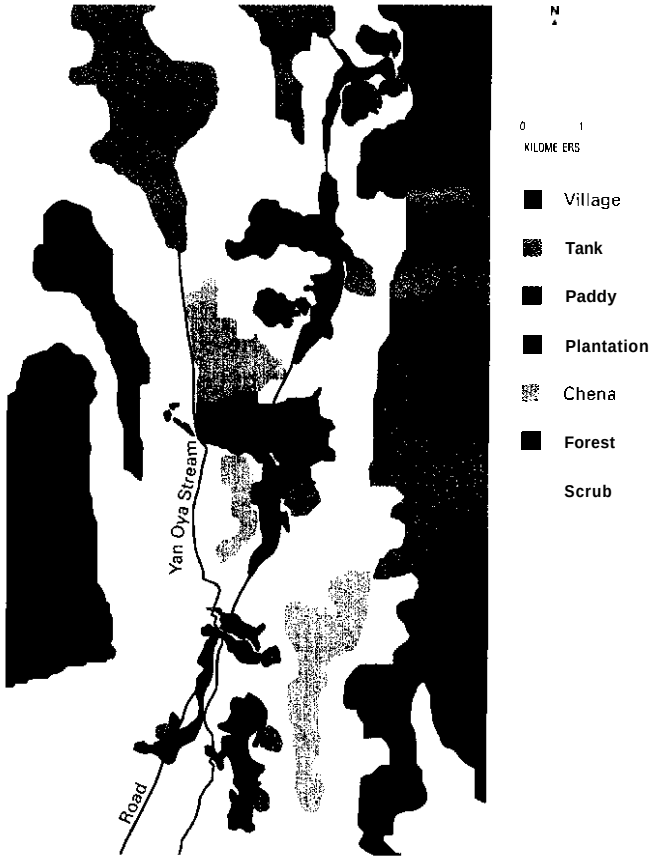


Figure 8. This GIS map shows the land use pattern in the IWMI-University of Peradeniya-AMC study area in the Horuluwewa watershed.

The Cost of Malaria Control

At present, the health services at provincial or central levels do not make use of cost-effectiveness estimates in the planning of different malaria-control interventions. Also, after the devolution of the malaria-control activities, no accounting system has been established that would make it possible to obtain specific cost estimates of individual control activities. Attanayake (1994) assessed the general cost-effectiveness of antimalaria activities and discussed the economic and policy implication of the different control approaches. The only other study conducted on the economics of malaria control included a wider range of preventive and curative measures for the north-central part of the country (Konradsen et al. 1999). It was found that from a government perspective, implementing a program of impregnating privately purchased mosquito nets provided protection to the households at less than half the cost compared with spraying residual insecticides in houses. Even when adding the household expense of purchasing the bed nets to the government cost of managing the impregnation program, the combined cost was still substantially cheaper than running the residual spraying activities. However, this is under the assumption that the population will make use of bed nets and can afford to buy them. For larvae control, the use of designated water management strategies should be explored since this option was far cheaper than the use of chemically based larvicides. For curative interventions, when including both operational and capital costs, the most cost-effective intervention for the government was a centrally located hospital with a relatively large catchment area (US$1.29 per malaria case treated). Mobile clinics (US$2.78 per malaria case treated) and village treatment centres (US$2.04 per malaria case treated) were a more expensive option for the government but incurred considerably lower expenditure for households than traditional hospital facilities.

Additional studies are needed under different epidemiological situations, including the analysis of alternative control strategies and new interventions. These studies should be supported by a cost-benefit analysis. Studies of the cost resulting from the increasing number of drug-resistant cases should be worked out supporting the development of an updated drug-distribution and administration policy.

Livestock are a preferred source of blood for many anopheline mosquitoes in Sri Lanka.

Slash-and-burn cultivation area. After burning, resting places ***for*** *mosquitoes are greatly reduced, pushing mosquitoes to rest in houses.*

Chapter 7

Concluding Remarks

Renewed Policy Focus

It is likely that the private sector will be increasingly involved in the diagnosis and treatment of malaria cases. The government will have to respond to this trend by establishing ways of maintaining the relatively good case-monitoring system in place in most parts of the country today. Also, the quality standards in diagnosis and case management should be strengthened through collaboration with private practitioners. The government health department will have to explore the opportunities for increased collaboration with community-based and nongovernmental organizations. This should be linked to both preventive and curative activities aimed at improving coverage and experiment with new control interventions. Due to the large fluctuations in incidence levels in both time and space, the government department will have to ensure a flexible organization capable of reallocating staff and resources to the areas of highest need within a short period of time. This, in turn, will require a good monitoring system identifying areas with increased transmission and an organization capable of quickly processing and responding to information from the field.

The formulation of a revised policy to reduce the spread of resistant *P. falciparum* cases is an urgent matter.

The communication and the number of joint research and training activities between the government health department and the various research institutions should be increased further. It is important that the research agenda and documentation needs are established in close communication between the different actors. The further testing of research findings by the control agencies could provide valuable feedback to the research community and establish an innovative environment.

Future Needs for Research

An impressive amount of research has been carried out in Sri Lanka and in-country investigators have headed the majority of studies, providing evidence for the large capacity for malaria research. However, a large proportion of the research papers has been generated from a relatively small number of sites and the findings should be verified in other parts of the country.

Generally speaking, health economics, health-systems management and socioeconomic impacts of the disease are the areas on which insufficient knowledge is available in Sri Lanka with only six reports identified. For example, it is essential that estimates be worked out for different combinations of curative services, including fixed government

facilities, mobile clinics, village centers and health volunteers, to identify the service approach that will provide flexibility, ensure prompt diagnosis and treatment and maintain a high cost-effectiveness under the highly fluctuating incidence levels in the country. This information should precede any new large-scale investments in the health services. The cost-effectiveness and cost-benefit estimations should be supported by further sociological studies to provide the rationale for treatment-seeking behavior of the community differentiated by gender, age and socioeconomic status. This information may provide an explanation for the frequent bypassing of peripheral health facilities, give the basis for establishing a service at village level and give an indication for the future role of private health-care providers. Additional studies on the social and economic impacts of malaria to both households and the government are needed to make a better-informed decision on priority setting within the health services and in relation to intersectoral allocations.

Innovative research is needed to identify new curative interventions that can supplement the government health service. This could include an increasing involvement of community-based organizations or the private sector. Also, action research is needed to identify the best means to increase the coverage of bed-net use among the general population.

A large amount of information is collected by the government AMC. However, this information should be documented and disseminated in a more useful manner. The infrastructure of the AMC allows for islandwide surveys that could provide very valuable input to generate an islandwide risk map. The risk map should be based on human-malaria-incidence data and site-specific entomological data. One of the top priorities of the AMC should be to quantify the impact of the residual spraying operations against both entomological and epidemiological parameters since this constitutes the largest part of the agency's activities. This should lead to operational research focusing on improving routines applicable to the different regions of Sri Lanka. It is likely that the information collected by the AMC would improve if part of the data was collected on a regular basis from a small number of fixed sites within each district that would serve as sentinel stations instead of the constant changing of collection points determined by local disease-incidence figures.

Further epidemiological studies are needed to assess the risk factors for malaria. For this purpose longitudinal studies should be supplemented with hospital-based case-control studies. Epidemiological studies should be supported by immunological surveys to provide further information on the role of immune status in the cyclical nature of transmission.

Very limited efforts have gone into researching environmental based vector-control interventions. Initial findings indicate that special emphasis should be given to water-management practices to control ***An. culicifacies*** breeding in streams and rivers.

Further studies combining entomological and epidemiological studies are needed to determine the relative importance of the secondary vectors. The primary and secondary vectors in Sri Lanka belonging to species complexes should be mapped out using advanced molecular techniques.

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