REVIEW

STATUS OF MALARIA IN THAILAND

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Abstract. Despite decades of control success and a competent network of country-wide health infrastructure, malaria remains an important health threat in rural Thailand. All 4 known human malaria parasites have been reported present, with *Plasmodium falciparum* and *Plasmodium vivax* predominant. The expansion and intensity of multi-drug resistant *Plasmodium falciparum* is the most serious development to occur the last several decades. Members of 3 anopheline species complexes, *Anopheles dirus*, *Anopheles minimus*, and *Anopheles maculatus*, are considered to be primary malaria vectors in the country. Representatives within all 3 taxa are difficult or impossible to separate morphologically from one another, and insufficient information exists about population genetics between sibling species and vector status. Vector control in Thailand has been the primary means of malaria control, mainly by the use of routine residual insecticide spray inside houses. The use of DDT in vector control has resulted in measurable successes to interrupt malaria transmission in many parts of the country. Since 1949, DDT has been the predominant compound used; however, its public health use has continued to decline as a result of perceived operational difficulties, political issues and environmental concerns. The increased use of pyrethroids to impregnate bednets and for intradomiciliary spraying are generally more accepted by rural populations and are rapidly replacing the use of DDT. Organized malaria control activities have reduced malaria morbidity from 286/1,000 population in 1947 to 1.5/1,000 population by 1996. Despite encouraging trends in dramatically reducing malaria, the rates of disease may be re-emerging in the country as evidence from an increased annual parasite index from 1.78/1,000 in 1997 to 2.21 in 1998. The possible reasons for the apparent increase in incidence are discussed in terms of the technical, operational and social obstacles in malaria control in Thailand.

INTRODUCTION

Malaria is still one of the important infectious diseases in Thailand, despite decades of successful control programs and dramatic reductions in morbidity and mortality. While deforestation has pushed malaria out of many regions in Thailand, malaria remains most prevalent along the undeveloped borders of eastern Myanmar, western Cambodia and northern Malaysia. The current distribution of malaria in Thailand is given in Fig 1. Based on the malaria surveillance activities in Thailand from 1985 to 1998 (Table 1), recorded malaria cases in Thailand totaled 275,443 in 1985, peaking to 349,291 cases in 1988, and declining thereafter to 85,625 cases in 1995. In general, from 1988 to 1996, detected malaria infections have dramatically declined. This continued improvement in reduced malaria has been, to a certain extent, the result of effective, well organized mosquito control program, concentrating activities on indoor residual insecticide spray and, more recently, distribution of pyrethroid-impregnated bed nets.

Recent surveillance data indicate malaria may be re-emerging in Thailand, as similarly witnessed in many other malaria endemic countries worldwide (Campbell, 1997; Roberts *et al*, 1997a). In spite of continued vigilance in control, malaria cases have shown a recent increase based on reports complied in 1997 and 1998 (Fig 1). The explanation for the increase is unclear, but it would appear to be a combination and consequence of the increased human and economic activities along forested, mountainous frontier international boundaries, and a recent reduction in vector control coverage, due to the Asean financial crisis 1997-1999. These areas are frequently associated with tribal populations that are highly migratory because of transient employment opportunities (logging, mining, road construction), hunting, gem mining

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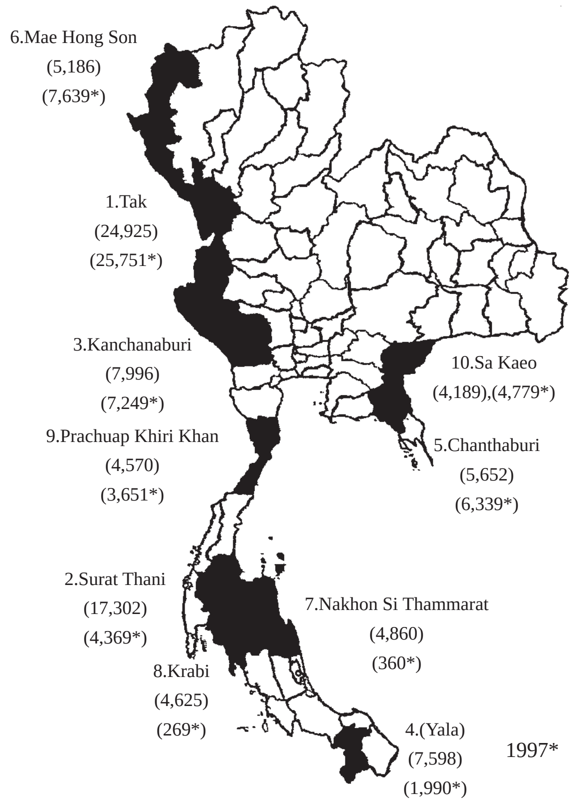

Fig 1–Map of Thailand depicting the general distribution of the 10 most malarious provinces in Thailand, 1997*-1998.

and other activities. The nomadic nature of these populations, with occupational movement and uncontrolled migration along the borders, confounds the problems associated with cross-border transmission and control. Furthermore, re-organization in 1996, as a consequence of a broader re-engineering policy by the government of Thailand, has resulted in drastic lack of manpower. In this re-organization five Regional Malaria Zones have been upgraded to Vector-Borne-Disease Centers (VBDC) and included dengue hemorrhagic fever and filariasis control within the framework.

In a time of decreasing health budgets and increasing population numbers, re-emphasis and support for increased systematic and careful surveillance of malaria in Thailand is imperative to define and direct anti-malaria activities. Thailand has had many years of success in its national control program, based primarily on vector control and the application of indoor residual DDT to control transmission (Prasittisuk, 1985). DDT, obtained from various donor agencies (*eg* United States Agency for International Development and UNICEF), was first used in Chiang Mai Province, northern Thailand from 1949 to 1951, beginning as a pilot project for mosquito control (Hongvivatana *et al*, 1982). Based on the highly successful field trials, DDT became the insecticide of choice for mosquito vector control in the country. In 1965, malaria eradication was adopted within the framework of the National Malaria Program. The aim was to completely interrupt malaria transmission using DDT by control of the *Anopheles* vectors in all malaria problem areas (Stein, 1970). However, malaria remained unexpectedly refractory during the period of eradication efforts. As is clear today, this initial optimism to eradicate malaria was not successful, although dramatic improvements in the reduction in malaria cases and mortality was achieved during years of organized countrywide activities.

Subsequent reassessment lead to a new malaria control strategy in 1971, as a consequence of a WHO revised global strategy of malaria control that was primarily directed at maintaining the significant gains already achieved and for the prevention of increases of disease in new or existing problem areas (Prasittisuk, 1985). The revised malaria national plan in Thailand was operationally carried out between 1971-1976. During this period, the malaria mortality rate remained constant (was not significantly reduced), suggesting little progress was made relative to the program's investment. In view of the apparent failure to control malaria, the Ministry of Public Health began to decrease or, in some cases, eliminate the use of DDT for residual house spraying. Malaria rates steadily increased during this period of decreased vector control activities. In 1979, a revised anti-malaria program was developed to provide a comprehensive control program to all at-risk populations of Thailand, and DDT was again reintroduced as the primary insecticide for indoor-residual spray in the national malaria control program. This organized program proved effective and malaria cases were reduced considerably. By 1981, nearly 80% of "eradicated" areas were no longer covered by routine vector control activities using DDT (Prasittisuk, 1985). Ironically, partly the result of the program's success in malaria reduction, DDT importation for public health use was stopped in 1995. Mounting pressure to reduce the reliance on DDT in public health, because of the perceived adverse environmental and human health issues and reports of poor community com-

Table 1
Malaria surveillance statistics in Thailand 1985-1998.

	1985	1986	1987	1988	1989	1990	1991[a]	1992	1993	1994[b]	1995[c]	1996	1997	1998
1	48,914,780	49,951,851	50,647,063	51,305,998	52,065,754	52,625,987	53,051,104	53,449,302	54,210,270	54,477,293	55,144,134	55,973,660	56,111,126	-
2	6,669,068	6,491,696	7,287,108	7,957,760	7,537,725	7,264,034	6,793,221	5,575,282	4,821,885	4,829,451	4,653,623	4,394,987	4,064,149	4,212,794
3	275,443	255,682	302,674	349,291	299,137	273,880	209,866	168,370	117,964	109,321	85,625	83,767	99,679	125,013
4	3.9	2.9	3.1	2.7	2.5	2.3	2.1	1.8	1.7	1.6	1.4	1.38	1.26	-
5	13.2	12.98	14.39	15.51	14.48	13.80	12.81	10.4	8.9	8.9	8.44	7.85	7.24	7.45
6	5.6	5.11	5.96	6.81	5.75	5.21	3.96	3.1	2.1	2.0	1.55	1.5	1.78	2.21
7	180,800	137,370	161,567	185,359	166,348	174,180	121,859	96,595	69,249	63,336	47,417	45,003	50,512	63,994
8	93,848	117,406	140,004	162,591	131,553	98,648	87,086	70,834	48,043	45,125	37,636	38,223	48,565	60,568
9	56	42	76	50	40	39	50	147	83	105	42	64	80	38
10	-	-	-	-	-	-	-	-	-	6	-	-	-	-
11	736	864	1,026	1,291	1,196	1,013	871	693	589	757	530	477	522	413
12	1,379,523	1,420,470	1,381,110	1,382,466	1,513,124	1,565,874	1,486,572	1,382,187	1,189,431	858,061	671,742	632,983	499,247	-
13	*	*	*	*	*	*	83,455	96,396	101,120	202,541	343,540	408,938	546,537	-
14			476	487	480	490	503	515	515	527	537	536	544	-

1. Total population
2. Blood smear examined
3. Positives slides
4. Death rate (per 100,000)
5. ABER (Annual Blood Examination Rate)
6 Annual Parasite Incidence (API)
7. *Plasmodium falciparum (Pf)*
8. *Plasmodium vivax (Pv)*
9. *Plasmodium malariae (Pm)*
10. *Plasmodium ovale (Pv)*
11. Mixed infection *(Pv/Pf)*
12. chemical spray (number of dwellings sprayed)
13. Bednet (number of impregnated net)
14. Malaria clinics

* non applicable - not available

[a]Beginning of inpregnated betnet with permethrin.
[b]Beginning of residual spray with deltamethrin.
[c]Beginning of residual spray with lambda-cyhalothrin.

pliance and acceptance contributed greatly to the decision to remove DDT (phase out period 1995-1999) from future procurement in malaria control. Nevertheless, the remaining stock of DDT is still being used in malaria problem areas of Thailand and it still serves as the primary chemical for mosqutio vector control compared to other compounds (*eg* pyrethroids). Over the span of 50 years, malaria rates have dramatically decreased in Thailand, strongly suggesting the significant reduction of malaria transmission has been partly due to the result of vector control and the efficacy of DDT (Annual Malaria Reports, 1985-1998).

OVERVIEW

Current operational strategy

The demise of the malaria eradication efforts was re-organized by the Malaria Division, Department of Communicable Disease Control (CDC), Ministry of Public Health, into a revised National Anti-Malaria Program in 1979. The program that is currently in place is stratified into 3 malaria control operational areas (commenced 1991) located in various areas throughout the country. The program structure forms the backbone for directing and focusing control and surveillance activities. In 1997, approximately 73% of the country's population (total country: 56,120,000) were covered with some form of surveillance and control. Nearly 550 malaria clinics, and over 15,000 malaria volunteers have been operational since 1998. So-called "self-reliant" villages in management of local malaria problems numbered near 2,000.

1. **Control areas** (CA): all areas receiving or needing *active* control and surveillance activities. These areas principally consist of hilly, forested areas, rubber plantations, mountainous areas, most borders areas and other endemic areas in the country, with a total coverage population of around 3.7 million (Fig 1). The active CA is divided into 2 epidemiological categories, designated transmission and non-transmission areas, which are further subcategorized based on degree of transmission. Additionally, 2 special categories exist for areas of intermediate/transition status.

1.1 **Transmission areas**: where active transmission is occurring, perennially or seasonally.

1.1.1 **Perennial transmission areas** (designated A1): transmission occurs year-round or at least 6 months of the year. Approximately 1.5 million people live within these important high-risk coverage areas.

1.1.2 **Periodic/seasonal transmission areas** (A2): transmission occurs 5 or less months per year. Approximately 2.3 million people reside in these localities.

1.2 **Non-transmission areas**: no transmission except when conditions (environmental, biological, social) change that may be conducive to outbreak transmission. The majority of the Thai population reside in this category, with a population of approximately 37.1 million people.

1.2.1 **High risk areas** (B1): no local transmission has been found for at least 3 consecutive years, although the environment can support primary or secondary vectors. Approximately 11.4 million people occupy these areas.

1.2.2 **Low risk areas** (B2): no transmission has been found for at least 3 consecutive years. Although no primary and secondary vectors are found, some suspected vectors may exist under favorable environmental conditions. Most large urban areas are considered B2. Approximately 25.7 million people live in these areas.

2. **Pre-integration areas** (PA): Areas defined as an entire administrative District. As transmission is no longer occurring, this area falls into a low risk category, without malaria transmission for a minimum period of 3 years. Approximately 4.4 million people reside in this area.

3. **Integration areas** (IA): Areas defined as an entire Province. Entry into the IA category requires a minimum of 3 years in a pre-integration status. Coverage includes 10.8 million people.

Most malaria cases in Thailand are currently restricted to the forested and hilly areas of the country along the border regions and southern peninsular. According to the 8th National Economic and Social Development Policy (1997-2001), health strategies for malaria control and prevention are focused mainly on these CA areas. The primary objective is to reduce malaria-related mortality to less than 1 per 1,000 population by the end of 2001. Additionally, prevention of the re-establishment of malaria transmission in the PA and IA areas is also given priority.

The actual control activities implemented depend upon the local epidemiological conditions and vector status. The main control measures in the CA zones still rely on countrywide intradomiciliary insecticide spraying once or twice a year with DDT or a synthetic pyrethroid, and if appropriate, the distribution of pyrethroid-impregnated bed nets. Limited biological control measures (*eg* larvivorous fish) applied to larval habitats, environmental management/modification where ecologically feasible, the provision of prompt diagnosis and treatment with appropriate antimalarial drugs in all government health clinics, and health education in schools and the general community are also structured into the general program. Supplemental activities, especially during outbreak response or increased transmission, have included space spray of insecticides against adult mosquito vectors, active case detection and treatment.

Malaria rates in Thailand

The Malaria Division is the primary government organization responsible for collecting and reporting malaria data in the country. The division has been recording malaria data since 1949. Epidemiological information has been used to present the current status of malaria, principally in the form of the Annual Parasite Incidence (API) and Annual Blood Examination Rate (ABER). The API is the number of positive cases per 1,000 population both from passive and active case detection. The API is the usual parameter used to compare malaria cases within geographically defined human populations. In contrast, the ABER is the number of blood slides examined per 1,000 population as a measure of general population coverage per given year. Malaria statistics are complied by the Epidemiology Section, Malaria Division, CDC, Ministry of Public Health (Table 1). It is acknowledged that the real annual incidence is higher, as data represents primarily passive case detection at government clinics and that many cases treated at private medical facilities and most asymptomatic infections remain undetected and/or unreported.

Morbidity

The number of malaria cases in Thailand has risen annually since 1996, after previous years of continual reduction (Table 1). A general and dramatic reduction in malaria incidence was observed from 1947 to 1979. Morbidity decreased from 286 cases per 1,000 population in 1947 to a low of 1.5 per 1,000 in 1996 (Annual Malaria Reports, 1985-1998). The decline in malaria rates is attributed to the development of a countrywide control program in 1951, and later to an organized, highly dedicated eradication program beginning in 1964. The interceding years saw control program objectives and strategies modified to fit changing needs. Malaria rates likewise fluctuated annually. Beginning in 1979-1980, malaria morbidity began to rise, reaching a peak in 1981 with 10.6 cases per 1,000 population. Massive outbreak in 1981 was due to influx of Cambodian regugees (parasite carriers) into the provinces along the Thai-Cambodia border where malaria transmission was intense, followed by the interval migration of Thai populations from other parts of the country into the same border areas. Furthermore, this increase has been blamed on the development of malaria parasite resistance to therapeutic drugs, especially sulfadoxine/pyrimethamine. Likewise, weaknesses and poor performance of DDT spray-team operations have also been cited for the breakdown in control effectiveness (Hongvivatana *et al*, 1982). By 1979, 174 malaria clinics located at regional malaria centers, unit and sector offices, including field and subfield sites, were established throughout the country.

Between 1981 and 1983 malaria morbidity declined significantly. The reason for this apparent improvement was due to 1) available funding sources from USAID and the Supreme Command Headquarters of Thailand, 2) strenghening existing program infrastructure including the vector control program, 3) promt diagnosis and treatment 4) decreasing of Cambodian refugees (parasite carriers). However, malaria cases slightly increased by the end of 1985 and reached a second peak in 1988 with 6.81 per 1,000 population. By the end of 1988, malaria cases began to decrease again, a trend that persisted through 1995 (Figs 2, 3). The numbers of malaria clinics and malaria village volunteers were dramatically increased resulting in greater population coverage, earlier case detection and appropriate treatment with the introduction of artemisinin derivatives in 1995. Furthermore, the introduction of bed-nets, often impregnated with permethrin, in addition to continued indoor house spraying with DDT, contributed to decreased transmission.

In 1997 the Malaria Division adopted a revised organization as the result of a broader "reengineering policy" by the Thailand government. As a result, by 1998, there were nearly 550 malaria clinics throughout the country and over 15,000 malaria community volunteers. However, beginning in 1997, malaria cases have actually increased (Table 1, Fig 4). The reason and causes for this increase remain unclear and somewhat controversial. Limited health budgets and increased population movement across malaria endemic borders has been considered a significant reason for the rise in cases. Most malaria cases appear associated with increasing large-scale ecological or sociological changes, especially in unregulated exploitation of rainforest areas (logging and gem-mining). Social and political unrest, often resulting in population displacement along the border areas, has also provided the opportunity for malaria to flourish.

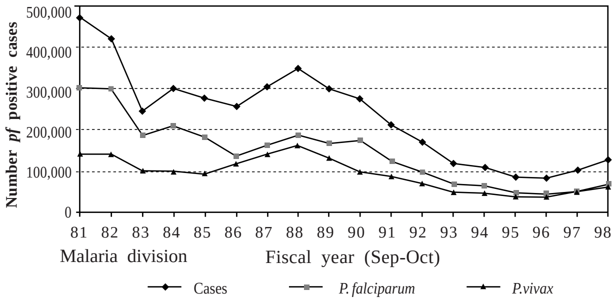

Fig 2–Total cases of malaria and cases by parasite species in Thailand, 1981-1998.

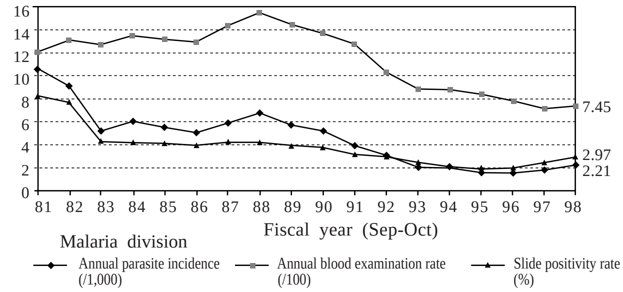

Fig 3–Total malaria cases (all species) measured by standard malariometric indices in Thailand, 1981-1998.

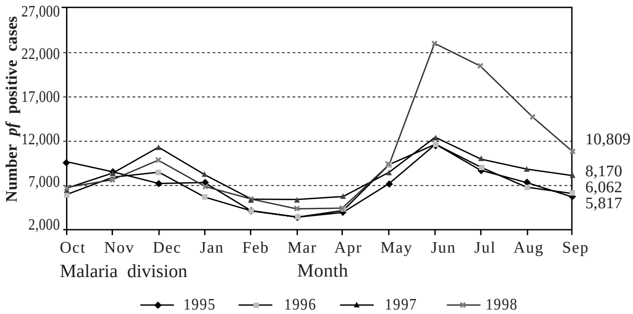

Fig 4–Total monthly malaria cases in Thailand, 1995-1998.

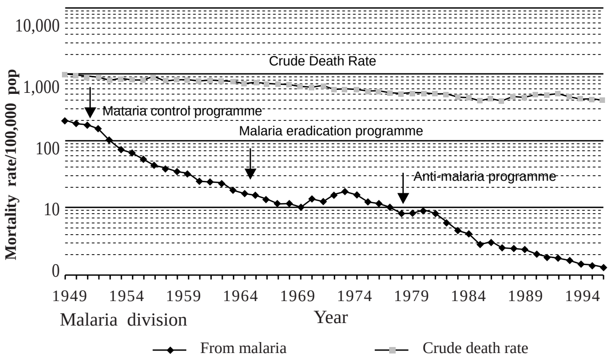

Fig 5–Annual malaria mortality rate in Thailand, 1949-1997.

Mortality

By 1930, malaria was recognized as one of the most severe diseases in Thailand, with mortality rates exceeding 400 cases per 100,000 population. In 1947, the mortality rate attributed to malaria was nearly 300 cases per 100,000 population, representing a major cause of premature death in rural populations. In the 1950s, intensified malaria control efforts using DDT significantly reduced malaria-related deaths over the ensuing years (Fig 5). By 1974, mortality was 16 per 100,000 population and in 1994, deaths decreased further to 1.6/100,000. In 1997, the mortality rate was 1.26/100,000 with 700 deaths. Mortality rates have been decreasing since 1987 in spite of fluctuation of malaria incidence over the past 15 years. The continued decrease in mortality since 1974 has been attributed to the expansion of peripheral health care delivery in more remote areas of the country and the establishment of malaria clinics providing rapid diagnosis and prompt treatment in the areas of high transmission (Prasittisuk, 1985). Despite these dramatic improvements, high rates of disease and death continue among people who resided in the forested hill areas, especially in economically depressed localities along the borders, most often associated with limited access to public health services.

Parasites

All 4 human malaria parasites have been reported in Thailand (Snounou *et al*, 1993; Zhou *et al*, 1998). *Plasmodium falciparum* and *Plasmodium vivax* are common whereas *Plasmodium malariae* and *Plasmodium ovale* are considered rare to very rare occurrences (Rattanarithikul and Panthusiri, 1994). Despite control efforts and the overall decrease of malaria during the last 20 years, *P. falciparum* remains more prevalent (commonly reported), relative to *P. vivax* (Annual Malaria Report, 1995). In 1998, the distribution of malaria parasites

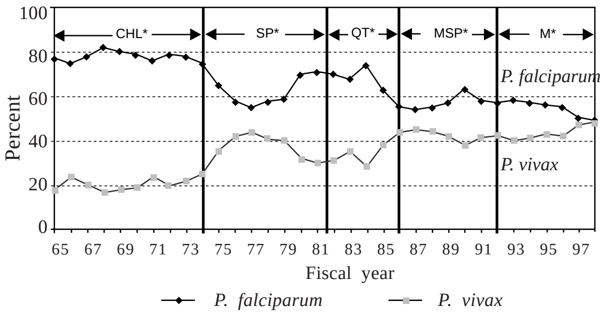

Fig 6–Proportion of malaria parasite species in Thailand, 1965-1998 during intervals of alternative antimalarial drug policy for the standard treatment of *P. falciparum.*

by species (from confirmed microscopy) for *P. falciparum*, *P. vivax* and *P. malariae* were 51.3 (63,994 cases), 48.6 (60,568), and 0.03 (38), respectively, with 413 mixed species infections.

Drug resistant malaria has been described as one of the most important problems in malaria control in recent decades (WHO, 1995; Fevre, *et al*, 1999). The existence of multi-drug resistance (MDR) is considered widespread in Thailand, and has been attributed mainly to strong selection pressures on *P. falciparum* because of the wide availability of drugs, poor compliance, indiscriminate or inappropriate therapy, and self treatment (Harinasuta *et al*, 1965). In Thailand, both humans and malaria vectors contribute to the spread the drug resistant parasites, compounding the problem. Drug resistant *P. falciparum* was first reported in Thailand in 1961 (Harinasuta *et al*, 1962, 1965; Kain *et al*, 1994) when strains of this parasite showed poor response to chloroquine (Ter Kuile *et al*, 1992). Around 1973, chloroquine was being replaced by the drug combination, sulfadoxine-pyrimethamine (S-P) and 4-aminoquinoline (Thaithong *et al*, 1988) (Fig 6). In 1985, these drugs too were found to become increasingly ineffective in treatment (Prasittisuk, 1985). Currently, more than 96% of falciparum malaria cases have shown some levels of resistance to S-P (Tanariya *et al*, 1995). In 1981, the decreasing effectiveness of S-P had been restricted to *P. falciparum* infections concentrated along the border areas near Cambodia, but has since been detected elsewhere in the country. As a result, a seven-day course of quinine-tetracycline was introduced to many problem areas where S-P resistance was reported (Pinichpongse *et al*, 1982). From 1985-1990, mefloquine, combined with S-P, was a commonly recommended treatment for falciparum malaria in Thailand. Because of the problems in administration and patient compliance with the protracted course of medication (1 week), intensive testing of new single-dose antimalarial drug, mefloquine, was initiated (Nosten *et al*, 1991). More recently, *P. falciparum* has demonstrated levels of resistance to mefloquine, and the cure rate using this drug has been reduced in some areas to less than 50%, particularly areas bordering Cambodia and Myanmar. By 1998, sensitivity to mefloquine was detected and found to be poor, with approximately a 10-fold decrease since 1984 (Suebsaeng *et al*, 1986; Fevre *et al*, 1999). Several other drugs are now being used in combination to combat MDR *P. falciparum* strains. Currently, anti-malarial drugs that are being used alone or in combination for the radical cure of falciparum malaria in Thailand include mefloquine, primaquine, quinine, tetracycline, and artemeter/artesunate compounds. In areas with a high degree of falciparum resistance to drugs, especially bordering Cambodia, artemeter/artesunate along with primaquine and mefloquine is recommended. Combination of quinine and tetracyeline is recommeded for severe cases in addition to some artemisinin derivatives (Looareesuwan, 1994). Chloroquine and primaquine remain the radical treatment of choice for *P. vivax*, despite more frequent reports of chloroquine resistance in the region. Infections with *P. malariae* are treated with chloroquine alone (Annual Malaria Report, 1997; Fevre *et al*, 1999).

Vectors

Of the approximately 74 *Anopheles* species recognized in Thailand, only 3 species (all complexes) are considered to be important malaria vectors, *Anopheles dirus*, *Anopheles minimus* and *Anopheles maculatus* (Pinichpongse and Bullner, 1967; Chareonviriyaphap *et al*, 1999). In Thailand, the primary vector is *An. dirus*, distantly followed by the other 2 species. All 3 taxa represent individual groups or complexes, of which the respective sibling species (senso lato) often are not possible to distinguish morphologically from one another (Rattanarithikul and Panthusiri, 1994) and have thus depended on techniques such as chromosomal analysis (Baimai *et al*, 1984a; Baimai, 1988) allozyme typing (Green *et al*, 1992) and more recently, an allele-specific polymerase chain reaction (AS-PCR) technique (Walton *et al*, 1999). The vectorial capacity of the sibling species often vary in behavior and geographic location, resulting in different abilities to transmit malaria in different areas of the country.

The *Anopheles dirus* complex contains at least 7 closely related species, *An. dirus* (species A), *An. dirus* B, C, D and E, *Anopheles nemophilous* (species F), and *Anopheles takasagoensis* (Walton *et al*, 1999). Among these, *An. dirus* E and *An. takasagoensis* have not been found in Thailand, while species A and D have been incriminated as a potential vectors for malaria (Xu *et al*, 1998). *Anopheles dirus* B, C, and F are suspected to be the major vectors in Thailand based on associated malaria transmission rates and geographic distribution of these vectors (Peyton and Ramalingam, 1988). However, little information exists about the taxonomic and vector status of *An. dirus* sensu lato from field studies. Identification of the 5 *An. dirus* sl present in Thailand is not possible for all members based on morphology. However, PCR-based techniques have been devised to clearly separate the complex members (Walton *et al*, 1999).

Generally, the *An. dirus* complex is a forest and forest-fringe inhabiting mosquito that demonstrates seasonal and geographic variation in biting cycles. Some members of this complex are considered highly anthropophilic and exophilic (Baimai *et al*, 1984b), contributing to the relatively high concentrations of malaria in areas associated with forests, orchards and tree plantations. Together with this complex's strong human-biting tendencies, it has been found to be refractory to contact with DDT and other chemicals (*eg* fenitrothion), and is generally long-lived, making it a particularly efficient vector even at low population densities (Ismail *et al*, 1974; 1975; Rosenberg *et al*, 1990). Larvae prefer shaded small, temporary groundwater collections or slow-moving perennial streams. These particular habitats are generally very abundant and hard to reach, making effective larval control impractical.

The *An. minimus* group consists of 3 related species (Sucharit *et al*, 1988; Green *et al*, 1990; Baimai, 1989) and all have been incriminated as vectors of malaria in Thailand. Species A is commonly found throughout the country; whereas, species C and D are found prevalent along the western Thai-Myanmar border, especially in Kanchanaburi and Tak Provinces (Baimai, 1989). *Anopheles minimus* complex is commonly found along the shaded, quiet edges of slow moving streams, associated with low hill zones. Vector contact with humans is usually greatest along the margin of villages. Generally, *An. minimus* sl have been reported as more zoophilic, exophilic, and exophagic in feeding and resting behavior (Nutsathapana *et al*, 1986), reducing their vector efficiency compared to *An. dirus* (Harrison, 1980).

The *An. maculatus* complex consists of at least 8 closely related sibling species (Kittayapong *et al*, 1993). Those formally described include *An. maculatus* (B), *An. swadiwongporni, An. dravidicus, An. nontanandai, An. willmori, An. psuedowillmori* (Green *et al*, 1985; Rattanarithikul and Green 1986; Rattanarithikul and Harbach 1990; Kittayapong *et al*, 1990; Green *et al*, 1992). *An. maculatus* is represented by 2 cytologically distinct forms; *ie* the widely distributed sensu stricto or B form, and the E form found in southern Thailand and northern Malaysia. Natural gene flow between northern (B) and southern (E) populations appears to be restricted, presumably because of geographic barriers (Rongnoparut *et al*, 1999). *An. maculatus* (B) also occurs in peninsular Thailand and Malaysia, where it plays a major role in transmission of human malaria (Baimai *et al*, 1988). *An. maculatus* (E) may serve as an important malaria vector in southern Thailand (Baimai, 1989), and *An. pseudowillmori* has been implicated as a vector along the northwestern border with Myanmar (Green *et al*, 1991). The complex is often present at the margin of hilly forest zones and in rubber-plantation areas. Preferred larval habitats are shaded puddles and other temporary collections of fresh water (*eg* drying streams).

Vectors of less importance include *An. sundaicus* (coastal, mangrove wetland zones), *An. aconitus*, and *An. philippinensis* (both associated with interior, rice field habitats) are considered to be a secondary (incidental) vectors in some areas (Prasittisuk, 1985).

Current problems in malaria control

Vector control remains on the forefront in the fight against malaria in Thailand, having relied principally on indoor chemical surface spray with DDT. For years, DDT has been used in national malaria control program; however, the true impact of DDT on mosquito vectors in terms of behavioral responses and disease transmission remains poorly known. Because of changing human response to spraying and the implied adverse long-term impact on environment, the use of DDT in vector control has been slowly replaced with various synthetic pyrethroids, such as deltamethrin, permethrin and lambda-cyhalothrin. Remaining stocks of DDT are still being used in some malaria problem areas of Thailand.

Recent reports indicate that chemical insecticides, including DDT, remain physiologically lethal to all malaria vectors in Thailand (Ismail *et al*, 1975; Ismail and Pinichpongse, 1980; Prasittisuk, 1985; Chareonviriyaphap *et al*, 1999). *An. minimus*, as well as most other malaria vectors, have shown greater outdoor biting abundance relative to indoor populations after indoor residual spraying (IRS) of DDT, indicating a general avoidance behavior of indoor sprayed surfaces (Prasittisuk, 1985; Suwanakerd *et al*, 1990).

Many public health authorities and vector control experts have assumed that the highly excito-repellent effect of DDT and some other insecticides on vectors, coupled with outdoor feeding and resting behavior, has resulted in the failure of IRS to interrupt malaria transmission in Thailand (Ismail *et al*, 1975, 1978; Bang, 1985; Prasittisuk, 1985). However, historical evidence of the successful and dramatic reductions in annual malaria incidence in Thailand during the years of routine DDT indoor spraying programs appear to contradict assessments that post-spraying would produce poor results. A recent review of the malaria situation in South America helps support this contention (Roberts *et al*, 1997a). Under most circumstances, the complete interruption of transmission by house spraying alone, although highly desirable, is not entirely possible and extends back to a bygone ideal when "eradication", not "control" was the objective. Unfortunately, few definitive studies have been made in Thailand, or elsewhere, to rightly conclude that increased malaria is the result of poor efficacy of DDT. Further observations on the vector responses to these chemicals, both physiological (toxicity) and behavioral (avoidance of sprayed surfaces) in relation to malaria transmission and control are needed to clarify the true role of DDT and IRS in malaria control strategies.

We believe the behavioral responses of mosquito vectors to insecticides are significant components of the insecticide-malaria control equation (Roberts and Andre, 1994). In the past, these responses have been generally overlooked in national control programs, with emphasis placed solely on toxicological responses to chemicals. The development of insecticide resistance in mosquitos in Thailand has been very limited despite long-term use of chemicals to control vectors. Evidence suggests that behavioral avoidance responses are significant and possibly of greater importance in effective reduction of human-vector contact than toxicity (Roberts *et al*, 1999, unpublished analysis). Understandably, more field research is needed on the behavioral responses of vector populations in Thailand from different geographical locations to confirm this. Excito-repellency (avoidance behavior) to insecticides by malaria vectors should be clearly defined using standardized methods (*eg* excito-repellency boxes and experimental huts) to measure the true impact of chemicals on transmission control (Roberts and Andre, 1994; Roberts *et al*, 1997b).

Along with chemical control measures (*ie* IRS, pyrethroid-impregnated bednets and focal space-spray fogging), biological control and environmental management are being selectively used today to control malaria vectors. Biological control, using larvivorous fish is being used when appropriate. Proper drainage or modification of larval habitats has been an activity receiving more attention by local populations as a means to control both disease vectors and pest mosquitos. In fact, biological control and environmental management has never been systematically assessed for its impact on the disease incidence. We doubt that it is cost-effective.

Conditions of population mobility in the forested foothill areas continue to hinder control operations, and conventional methods of control are found wanting or impractical (Singhanetra-Renard, 1993). Uncontrolled and increased occupational movement around the surrounding borders with other malaria endemic countries is of serious concern in Thailand. Labor movement, gem mining, and resource development and exploitation (*eg* logging) along the Cambodia and Myanmar borders have contributed to significant increases of *P. falciparum* malaria morbidity and dissemination of parasite strains highly resistant to many first-line anti-malarial drugs, including, chloroquine (and other 4-aminoquinolines), sulfadoxine/pyrimethamine, and mefloquine. The unstable political situations, recurring conflicts and racial tensions in the region, especially along the Thai-Myanmar border, have increased numbers of displaced persons, in areas of poor health infrastructure and malaria transmission. This particular situation continues to be addressed through increased community mobilization, health education, and expansion of malaria clinics into rural areas for greater access by populations.

CONCLUSION

This overview of the present malaria situation in Thailand reiterates the public health importance of malaria in many rural areas of the country, dampening the general quality of life and economic development in these affected populations. During the 1990s, malaria incidence and parasite resistance to antimalarials has been most serious along the borders shared with Cambodia and Myanmar. Although mortality continues to decrease, there has been a recent increase (1997-1998) in morbidity. In general, increases of malaria worldwide in the last decade, especially *P. falciparum*, have been linked to progressive changes in epidemiology, largely attributable to rapidly changing environmental conditions and intense economic development in malarious areas, as people claim new land, seek wealth or escape civil disturbances and war.

The last published review of the malaria situation in Thailand was in 1985 (Prasittisuk, 1985). The same year, Bang (1985) reviewed the insecticide resistance among known malaria vectors in Thailand, describing resistance to DDT and other chemicals as minimal. As far as known, the principal malaria vectors in Thailand have not developed any substantial levels of physiological (biochemical) resistance. Despite the past success achieved using DDT alone, owing to the "refractory behavior" (excito-repellancy) of mosquitos to DDT, most notably *An. dirus* and *An. minimus*, alternative and more costly compounds (organophosphates and synthetic pyrethroids) have systematically replaced or been temporarily used for vector control. Historically, the use of DDT (by far the most cost-effective insecticide ever used in malaria control) has had a dramatic impact on malaria incidence throughout Thailand (Stein, 1970; Hongvivatana *et al*, 1982). However, beginning in the 1980s, vector control programs have met with increased public resistance (resulting in poor house spray compliance), partly, because of inadequate training of spray teams, poorer supervision, and curtailed government support. Other control strategies, namely, emphasis on increased early diagnosis and adequate treatment campaigns at the community level have taken precedence over vector control activities (WHO Global Malaria Control Strategy, 1993-2000).

Since 1985, general malaria prevalence rates have dropped further; however, in the latter part of this decade (1997-98) case rates have either stabilized or there are signs of increased activity. Epidemic potential exists in Thailand, and it is recognized that complacency in control activities could quickly contribute to a disastrous and extensive increase in disease. Important concerns of widespread multi-drug resistance in *P. falciparum*, increased human population movements across malaria-endemic borders and within the country continuously places most areas of Thailand at risk for renewed transmission and potential outbreaks.

Over the past 15 years, a substantial body of vector research has emerged from Thailand. The increased number of *Anopheles* species and species complexes and their contribution to malaria has more clearly defined transmission risk by geographic location. However, most of this information has not, as yet, been translated into more focused operational strategies against vector species. More investigations on malaria field epidemiology, in particular vector ecological studies are needed (Service, 1989). More carefully designed and systematic research should be supported to clarify the vectors' response to insecticides and the impact on malaria incidence. A clearer understanding of specific and defined local conditions will allow for more appropriate and selective control measures. The historical importance of vector control in Thailand should serve as a clear lesson that vector control (*ie* use of residual spray) must remain as an important method of malaria suppression until more cost-effective alternative methods have been implemented and *proven* effective and sustainable.

It is important to consider that indoor residual spraying with DDT was the major reason for the overall success of malaria control in the 1950s and 1960s (WHO, 1995). Likewise, the subsequent reduction of vector control programs has been deemed the most important cause for increasing malaria in Africa, Asia and the Americas (Farid, 1991; Roberts *et al*, 1997a; Mouchet *et al*, 1998). The last several decades have seen a number of countries experience dramatic increases in malaria after having stopped routine spray programs. Likewise, there are examples of striking reductions in malaria incidence after resumption of spraying with DDT (Roberts *et al*, 1997a). Clearly, the general repercussion from stopping vector control activities has been an increase in disease incidence. It should be appreciated that the justification for the continued use of insecticides, under any circumstances, is simply the documented reduction in disease incidence and should not be deduced from studies of their effects on mosquito vectors alone.

Despite the impressive progress and reduction in prevalence over the previous 50 years, organized malaria control must remain vigilant by maintaining strong capabilities and training levels to effectively control transmission in high-risk transmission areas and during outbreak occurrences. Additionally, identification and promotion of research for improved control intervention should continue. The direction for malaria control in the future must be practical, integrated, cost-effective and, most importantly, sustainable. The Thailand Ministry of Public Health recognizes that effective malaria management must be able to respond to predicted and unexpected situations arising from rapid social, economic, or political changes. A move to strengthen and decentralize local capabilities has begun, addressing sustainable management capabilities down to the village level while improving communication at all levels. Social science initiatives, incorporating regional social and cultural aspects to local transmission, diagnosis, treatment, and prevention of disease are gaining greater acceptance as an integral adjunct to the more traditional approaches (Hongvivatana *et al*, 1986).

Efforts are being directed to strenghten malaria control along border areas. The problem of 'border' malaria is a vexing and complicated one. Collaborative efforts between neighboring countries with forest malaria have been difficult to implement. Control of forest malaria needs to incorporate a regional approach, first creating workable inter-country border area task forces, if programs hope to have any success. Lastly, the disturbing attrition in local expertise in malaria control, both technical and managerial, has been felt in Thailand and the Southeast Asian region in general. Capacity development, in the form of educational training technology and health education, training in vector control, drug policy development, control progam management, and data management, from the national to midlevel and community levels, has been supported by the combined efforts of EC-RMCP, SEAMEO-TROPMED, WHO, and ACTMalaria. More importantly, policies for retention and career promotion of professional staff will be essential if Thailand intends to continue to be successful in the fight against malaria.

ACKNOWLEDGEMENTS

The authors would like to thanks Dr Krongthong Thimasarn, Director of Malaria Division, CDC, for her critical review and suggestion. Special thanks to Dr Pornpimol Rongnoparat from the Faculty of Science, Mahidol University, Bangkok, Thailand for her valuable advice and encouragement. This work was supported by the Kasetsart University Research and Development Institute (KURDI) and the Thailand Research Fund (TRF), Bangkok, Thailand.

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