# EPIDEMIOLOGY OF MALARIA IN DISPLACED KHMERS ON THE THAI-KAMPUCHEAN BORDER

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## INTRODUCTION

Since 1979 large numbers of Khmers (Kampuchean people) have migrated from inside Kampuchea to the border of Kampuchea and Thailand as a result of political conflicts within their country. As malaria was the most serious disease problem for most of this period, information on malaria epidemiology from 1983 to 1985 was collected with the following objectives: to determine which sectors of the population were most at risk of malaria infection and mortality; to assess from the age and sex distribution of cases how much transmission occurred within the camps, where mosquito control was possible; to study the seasonal incidence of malaria for timing of control measures; and to evaluate the control measures used.

## MATERIALS AND METHODS

**Population:** Table 1 shows the population sizes of the camps and environmental factors relating to their potential as vector habitats. The total population, based on four-monthly headcounts, ranged from 218−246,000 from 1983 to 1985. On many occasions camps were evacuated temporarily into Thailand as a result of dry-season fighting on the border. In 1985, unlike previous years, the people remained just inside Thailand. Basic requirements for survival were provided by the World Food Programme/United Nations Border Relief Operation (WFP/UNBRO), which also coordinated voluntary agencies providing health services.

**Vectors:** The major vector of malaria in much of the border area was *Anopheles dirus*. *A. minimus* was often found in association with *A. dirus*, but its role in transmission was not clear; no specimens of *A. minimus* were positive for *Plasmodium falciparum* circumsporozoite antigens (Baker *et al*., 1987). In some northern camps *A. dirus* and *A. minimus* were not found despite frequent mosquito collections and high malaria transmission, but *A. maculatus*, *A. aconitus*, *A. nivipes* or *philippinensis* and the *A. barbirostris* group were present, and may have been involved in transmission (S.R. Meek, unpublished data). The latter are vectors in other parts of Southeast Asia, but their importance in malaria transmission in Thailand has not been proven (Prasittisuk, 1985).

**Control:** Control measures carried out by UNBRO included distribution of mosquito nets and mats, twice-yearly residual house spraying with DDT in most camps, night-time fogging with pyrethroids during the rainy season in camps with high transmission, malaria education and occasional use of mosquito repellents. The bamboo and thatch houses were very open, and after evacuations makeshift plastic tents were used, so that the value of residual spraying was questionable.

**Treatment:** Treatment of multi-drug resistant falciparum malaria was difficult. After failure of chloroquine and sulfadoxine-pyrimethamine to give an adequate cure rate (Hurwitz *et al.*. 1981; Reacher *et al.*. 1981), treatment was changed to quinine and tetracycline for 7 days with primaquine on day 7 in 1980 to 1981. Compliance with the 7 day course was very difficult to achieve, but a shorter course of 3 days quinine with 7 days tetracycline proved less effective (Meek *et al.*. 1986). In October 1984 the UNBRO protocol was changed to use of mefloquine-sulfadoxine-pyrimethamine (MSP) and primaquine in several camps. It was much easier to ensure compliance with the single-dose MSP treatment, but quinine was still required for severely ill or pregnant patients. Vivax malaria was treated with chloroquine; radical treatment with primaquine was not given, as the probability of reinfection was often high.

**Methods:** Data on malaria incidence were obtained from hospital laboratories, where Khmer technicians read malaria smears usually under supervision of an expatriate technician of the voluntary agency running the hospital. Giemsa-stained thick and thin smears were made on all patients attending hospital and outpatient facilities with a suspected diagnosis of malaria. Periodic cross-checking of smears showed a generally high level of accuracy. Morbidity and mortality data were reported by voluntary agencies.

## RESULTS

### Geographical variation

Four major zones could be distinguished clearly in 1983 and 1984 by location, environmental features (Table 1) and annual parasite incidence (API; Table 2), but the pattern began to break down in 1985, when several sites were evacuated from areas of intense transmission. For instance, Sok Sann showed a sharp decrease in incidence after moving (Fig. 1). The mountainous densely forested zones were more suitable habitats for *Anopheles* vectors than the central region (Zone LC). Increases in incidence in Zone LC sometimes occurred due to immigration of infected people from higher incidence zones (Fig. 2).

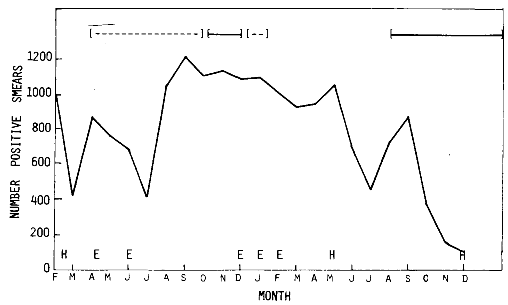


Fig. 1–Malaria incidence in Sok Sann (Zone HS) 1984–1985 (population 6–9,000). E = evacuation of camp to new site within 6 km. of previous site; H = house spraying with DDT; broken horizontal line = ultra low volume (ULV) spraying with battery-operated spinning disc sprayers; solid horizontal line = ULV spraying with petrol-driven sprayers.

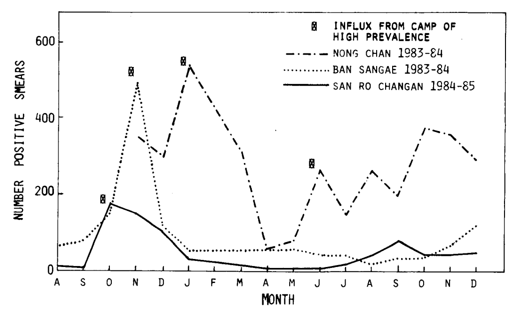


Fig. 2–Changes in malaria incidence following immigrations to San Ro Changan, Ban Sangae and Nong Chan (Zone LC) of people from areas of higher incidence.

Table 1

Population size and environmental characteristics of the camps.

| Zone* | Camp | Population range from 1983–1985 ('000) | Topography | Vegetation** In | Vegetation** Around | Streams | Rainfall in neighbouring Thai province |
|---|---|---|---|---|---|---|---|
| LC | Obok (85) | 1–3 | flat | – | – | – | low |
| | Ban Baranae | 3–4 | hilly | + | + | – | mod |
| | Dong Ruk | 16–20 | flat near hill | – | + | – | mod |
| | Site 2*** | 50–140 | flat | – | + | – | mod |
| | San Ro Changan | 6–11 | flat | – | + | – | mod |
| | Ban Sangae | 22–36 | flat | – | + | – | mod |
| | Site 7 | 48–63 | flat | – | + | – | mod |
| | Nong Samet | 45–63 | flat | – | + | – | mod |
| | Nong Chan | 16–22 | flat | – | + | – | mod |
| MN | Nam Yun | 1–3 | mountainous | + | ++ | + | low |
| | Greenhill | 28–35 | rolling | + | ++ | + | low |
| | Obok (83–84) | 1–3 | steep hillside | ++ | ++ | + | low |
| MS | Nong Pru area | 5–14 | rolling | + | ++ | river | mod-high |
| | Taprik area | 5–18 | rolling | + | ++ | river | mod-high |
| | Site 8**** | 30–37 | flat at foot of mountain | – | + | + | mod-high |
| HS | Sok Sann | 6–9 | mountainous | + | ++ | + | high |

* zones of similar location, environmental features and malaria incidence. LC = lowest transmission-central, MN = medium transmission-north, MS = medium transmission-south, HS = highest transmission-south.

** – sparse, + open secondary, ++ thick forest

*** Dong Ruk, San Ro Changan, Ban Sangae and Nong Chan were evacuated to Site 2 in early 1985; Site 7, the evacuation site for Nong Samet since early 1985 moved to Site 2 in September 1985

**** Nong Pru and Taprik areas were evacuated to Site 8 in February 1985

Except for one report of *P. malariae*, only *P. falciparum* and *P. vivax* were found. The ratio of *P. falciparum* to *P. vivax* was lower in camps with lower malaria transmission; in 1983, 1984 and 1985 the ratio in Zone LC was 1.0, 1.1 and 0.4 to 1 respectively, whilst in the other three zones it was 5.4, 7.9 and 5.4 to 1 respectively.

Morbidity due to *P. vivax* also appeared to be affected by stress in the human population. For instance, the population of Nong Samet was evacuated to a new site (Site 7) after the camp was attacked in late December 1984. Although Site 7 had little, if any, malaria transmission, the incidence of *P. vivax* in January 1985 rose to 2.34 per 1000 population compared to a monthly average of 0.97 in Nong Samet in 1984 and 0.64 in

Site 7 from March to August 1985, after the new camp had stabilized.

### Seasonal variation

The rainy season usually lasted from May to October, and, in 1983 and 1984, as expected, the malaria incidence began to increase in June to July to a peak in October to November, and to decline to its lowest in April (Fig. 3). In 1985 there was a decline in incidence throughout the year with no overall increase in the rainy season as a result of the relocation early in the year of many camps to less endemic sites.

The ratio of *P. falciparum* to *P. vivax* was higher in the rainy season in 1983 and 1984, but in 1985, when transmission actually decreased in the rainy season, the ratio was higher in the dry season. The difference between dry and rainy seasons was significant every year ($p < 0.001$).

### Age and sex ratios of patients

The population structure of the border camps was atypical with many under 5 years old (28% in 1985) and very few 5 to 9 years old (7%) (J. Borton, pers. commun.). Table 3 shows the age-sex breakdown of malaria incidence, mortality rate and case fatality rate in a camp from each zone over several months. In all camps there was some infection in all age groups showing that transmission occurred within the camps, as children rarely went outside. In Zones LC and MN, most transmission appeared to be outside the camps, as the risk of symptomatic infection was highest in adult males. In Zones HS and MS the highest proportion of cases was seen in young children suggesting that there was significant transmission within the camps and a high level of immunity in adults.

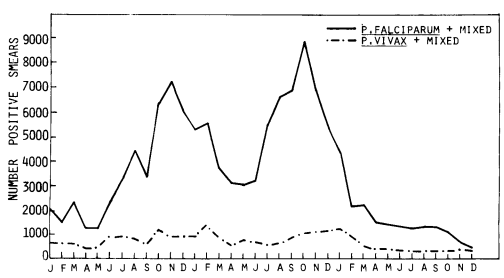


Fig. 3–Malaria incidence in all camps 1983–1985.

### Mortality rates

The overall malaria mortality rate fell from 77 to 28 per 100,000 from 1984 to 1985. In 1983 the mortality rate of 62 was underestimated, as deaths for several months were not reported. The rate varied considerably both by location and by age and sex of the population (Tables 3 and 4). The case fatality rate (CFR) was lower in 1984 (0.31%) than in 1983 (0.41%) and 1985 (0.42%) ($p < 0.05$). The mean CFR in camps with an API less than 180 per 1,000 was 1.95% in 1983, 0.92% in 1984 and 0.83% in 1985, whilst for camps with an API greater than 180 it was 0.34% in 1983, 0.27% in 1984 and 0.28% in 1985 ($p < 0.001$ each year).

### Malaria in pregnancy

In Kap Choeng hospital, a referral hospital for Greenhill (Zone MN), mortality rates per 100,000 were 68 for children less than 1 year, 158 for pregnant women and 7 for the rest of the population. Corresponding CFRs were 7, 10 and 1%. Criteria for admission of malaria patients were all third trimester pregnant women, all children under 2 years and others only if comatose or very anaemic, so the case fatality for the last group would be lower in the whole camp (approximately 0.20%). Of 193 pregnant women admitted to Kap Choeng with falciparum malaria from November 1983 to October 1984, 109 had

Table 2

Annual parasite incidence in camps on the Thai-Kampuchean border 1983 to 1985.

| Zone | 1983 | 1984 | 1985 |
|---|---|---|---|
| LC | 37 ( 30–49)* | 55 ( 19–173) | 28 ( 16–44) |
| MN | 562 (163–1,359) | 638 (421–1,132) | 210 (193–291) |
| MS | 970 (675–1,221) | 877 (331–1,219) | 129 ( 90–681) |
| HS | 2,073 | 1,276 | 1,036 |
| Mean | 359 | 350 | 116 |

* Mean and range of annual parasite incidence. API is the number of positive smears (both species) per 1,000 people per year. Data for 48 out of 372 camp-months were missing; in these cases API was estimated by dividing by the number of months with data and multiplying by 12. This does not allow for seasonal variation.

spontaneous abortions, 10 had stillbirths and 8 had premature babies who died, a pregnancy failure rate of 66% among women admitted with malaria and 13% of all pregnant women in the camp (S. Keller, per. commun.).

By contrast in Sok Sann (Zone HS) from 1983 to 1985 only two 15 to 44 years old women died of malaria, and yet a malaria survey in November 1985 of 135 pregnant women showed a prevalence of 11% *P. falciparum* and 19% *P. vivax;* 77% of the women were asymptomatic. Mortality risk in Sok Sann was higher in adult men because of frequent severe haemolysis in malaria-infected males (42 cases in 1985 and a larger unrecorded number in 1984), possibly related to frequent use of quinine. Several cases were later found not to be deficient in glucose-6-phosphate dehydrogenase.

Whereas the majority of the population of Sok Sann remained for about five years in an area of intense malaria transmission with *A. dirus* present, the Greenhill population had a somewhat lower, though still high, API (Sok Sann 1276 and Greenhill 627 in 1984), and before 1983, lived in an area of much lower transmission. Moreover, many of the female malaria patients from Greenhill were infected a few kilometres outside of the camp, and often returned very late for treatment.

**Cerebral malaria**

Cerebral malaria is defined here as *P. falciparum* infection accompanied by unrousable coma. However, as many different people were involved in diagnosis, it is not certain that all cases reported matched the definition exactly. In 1984 the percentage of cases of *P. falciparum* plus mixed infections developing into cerebral malaria was 2.5 in low incidence camps (API $<180$) and 1.0 in high incidence camps ($p < 0.001$); in 1985 the corresponding percentages were 1.7 and 1.0 ($p < 0.01$). However, there was no significant difference in cerebral malaria CFRs: in 1984 the CFR was 29.2% in low incidence camps and 18.8% in high incidence camps ($p < 0.1$), and in 1985 the rates were 33.9 and 19.7% respectively ($p < 0.5$). The CFRs of 21 and 26% in 1984 and 1985 were not significantly different.

## DISCUSSION

**The border ecosystem**

In Thailand the APIs in 1983, 1984 and

Table 3

Risks of malaria infection and mortality in different age groups and sexes in camps on the Thai-Kampuchean border.

| Zone/ camp/ dates/ population | Age (yrs) sex | % of population* | Rate *P. vivax* per 1000 per month** | Rate *P. falciparum* per 1000 per month** | Deaths | Mortality rate per 100,000 per month | Case fatality rate (%) |
|---|---|---|---|---|---|---|---|
| LC | <5 | 32 | 1 | 0 | 0 | – | – |
| Ban Sangae | 5–14 | 14 | 2 | 1 | 0 | – | – |
| 1–12/85 | 15–44M | 25 | 2 | 3 | 7 | 10 | 3.8 |
| 23,978 | 15–44F | 24 | 1 | 1 | 1 | 1 | 2.6 |
| | >44 | 5 | 1 | 1 | 1 | 7 | 8.3 |
| MN | <5 | 25 | 4 | 13 | 4 | 28 | 2.1 |
| Greenhill | 5–14 | 16 | 5 | 23 | 2 | 22 | 1.0 |
| OPD | 15–44M | 24 | 4 | 61 | 2 | 15 | 0.2 |
| 11–12/84 | 15–44F | 26 | 2 | 24 | 6 | 41 | 1.7 |
| 28,325 | >44 | 9 | 2 | 21 | 0 | – | – |
| Greenhill | <5 | 28 | 1 | 1 | 0 | – | – |
| OPD and | 5–14 | 15 | 2 | 2 | 1 | 10 | 4.3 |
| hospital | 15–44M | 23 | 1 | 10 | 0 | – | – |
| 11–12/85 | 15–44F | 25 | 1 | 3 | 0 | – | – |
| 35,043 | >44 | 9 | 1 | 4 | 0 | – | – |
| MS | <5 | 27 | 2 | 9 | 4 | 5 | 0.5 |
| Site 8 | 5–14 | 16 | 2 | 8 | 1 | 2 | 0.2 |
| 3–12/85 | 15–44M | 24 | 1 | 6 | 1 | 1 | 0.2 |
| 31,420 | 15–44F | 26 | 1 | 6 | 4 | 5 | 0.8 |
| | >44 | 7 | 1 | 5 | 2 | 9 | 2.0 |
| HS | <5 | 22 | 19 | 86 | 4 | 29 | 0.3 |
| Sok Sann | 5–14 | 13 | 15 | 72 | 1 | 12 | 0.2 |
| 5–12/85 | 15–44M | 29 | 9 | 54 | 3 | 16 | 0.3 |
| 7,982 | 15–44F | 26 | 7 | 38 | 0 | – | – |
| | >44 | 10 | 5 | 28 | 1 | 16 | 0.6 |

* Population figures for each age/sex group were obtained from surveys in 1985 (J. Borton, pers. commun.), and adjusted for 1984 to allow for increasing birth rate.

** including mixed infections

Table 4

Mortality rates in different age and sex groups along the Thai-Kampuchean border from 1983 to 1985.

| | | Mortality rate per 100,000 population | | | | | |
|---|---|---|---|---|---|---|---|
| Camps | Year | < 5y | 5–14y | 15–44y male | 15–44y female | > 44y | No. deaths with no age/sex record |
| Zone LC | 1983 | 28 (7)** | 17 (3) | 23 (6) | 15 (4) | 45 (4) | 4 |
| | 1984 | 9 (3) | 14 (3) | 41 (12) | 10 (3) | 40 (4) | 6 |
| | 1985 | 3 (1) | 25 (5) | 39 (11) | 3 (1) | 11 (1) | 1 |
| Zone MN | 1983 | 271 (20) | 91 (5) | 120 (10) | 189 (17) | 213 (7) | 7 |
| | 1984 | 222 (22) | 111 (7) | 127 (12) | 224 (23) | 216 (8) | 4 |
| | 1985 | 49 (5) | 89 (5) | 12 (1) | 11 (1) | 31 (1) | 1 |
| Zone MS* | 1983 | – (9) | – (0) | – (0) | – (2) | – (0) | 0 |
| | 1984 | – (0) | – (1) | – (0) | – (2) | – (0) | 23 |
| | 1985 | 45 (4) | 39 (2) | 13 (1) | 47 (4) | 87 (2) | 0 |
| Zone HS | 1983 | 258 (3) | – (0) | 91 (2) | – (0) | – (0) | 3 |
| | 1984 | 371 (6) | 180 (2) | 80 (2) | 90 (2) | – (0) | 4 |
| | 1985 | 276 (5) | 96 (1) | 213 (5) | – (0) | 125 (1) | 0 |
| Total | 1983 | 100 (39) | 28 (8) | 42 (18) | 51 (23) | 74 (11) | 14 |
| | 1984 | 57 (31) | 38 (13) | 51 (26) | 56 (30) | 69 (12) | 37 |
| | 1985 | 26 (15) | 41 (13) | 39 (18) | 12 (6) | 32 (5) | 2 |

* demographic information not available for 1983 and 1984

** Number of deaths shown in parenthesis:

1985 were 5, 6 and 6 per 1,000, and the mortality rates 8, 4 and 4 per 100,000 respectively. The corresponding APIs of 359, 350 and 116 and mortality rates of 62,77 and 28 on the border were thus much higher. There is little recent information from Kampuchea.

Malaria in Thailand and Kampuchea is a rural disease affecting sparse resident populations and mainly migrant workers temporarily visiting areas of transmission, which are limited by the restricted habitat requirements of the vectors. On the border, however, large populations settled in camps within the forested habitat of the vectors, especially *A. dirus*. Little of the forest was cleared for agriculture, and humans were the main source of blood, as livestock was scarce. The main vectors are thought to be anthropophilic, but if any were partially zoophilic, then both the human biting rate and the sporozoite rate would be higher than normal. Fighting resulted in frequent evacuation of large population groups to areas with different malaria transmission potential. Although later movements were usually to more sparsely vegetated areas of lower transmission potential, there were several movements to areas of much higher transmission potential in 1982 and 1983. After a few months in an area of low transmission the people may lose their protective immunity, resulting in more severe morbidity.

**Effects of and on drug use**

The effect of antimalarial drug use on the epidemiology of malaria is difficult to evaluate. No prophylaxis was used, as far as we know, and sulfadoxine-pyrimethamine ( Fansidar ) was not widely available, but there was widespread use of incomplete treatment coursès of quinine and tetracycline from outside sources, probably leading to frequent recrudescent infections of falciparum malaria with repeated production of gametocytes after a single infective mosquito bite. Because of the movement of the camps, it was not possible to determine if introduction of MSP resulted in a significant reduction in malaria transmission. In the main transmission areas no reduction in the ratio of falciparum to vivax malaria was noted after introduction of MSP.

Drug resistance may develop more rapidly where the parasites do not have to contend with a strong immune response as well as with the drug (Spencer, 1985; Verdrager, 1986). Since many of the people living in camps of high transmission were relatively non-immune, close monitoring of response to treatment was important.

**Practical implications**

Epidemiological data was used to determine priorities for control measures. For instance, night fogging was only used in camps found to have high transmission. The incidence in different age groups showed that it was clearly worthwhile to attempt vector control measures in Zone MN in 1984 and in Zones MS and HS every year, whereas they were less likely to have much impact in Zone MN in 1985 and in Zone LC, where most infections were probably acquired outside the camp.

Unfortunately, the information was not as useful as expected in evaluating the impact of control measures, because the instability of the populations rendered one season not comparable with the next. In Sok Sann (Zone HS) there was a dramatic decrease in malaria transmission in 1985 (Fig. 1), although the camp only moved about 6 kilometres from a site of high transmission in 1984, and *P. falciparum* incidence remained high for the first four months in the new site. Nightly fogging was carried out in 1985 with more powerful equipment than in 1984, more durable mats were distributed with the mosquito nets, and house spraying was done more frequently. All these factors could have contributed to reducing transmission, but the factors favouring transmission often appear so localised that even moving a few kilometres may have been important. For instance, it was noticed on one occasion that, when light traps were set in houses in Sok Sann, all but one trap caught no *Anopheles*, whilst the last trap, which was set in a newly-built, unsprayed house with no cooking fire on the edge of the camp caught several *Anopheles* including *A. dirus*.

Follow-up of monthly incidence of malaria after immigration of groups of infected people from more highly endemic areas to camps with low transmission showed that there was little risk of triggering a malaria epidemic in the resident population (Fig. 2), thus suggesting that it was availability of vectors rather than of parasites that limited the prevalence of malaria in such areas. There would therefore be little benefit from mass treatment of the immigrant groups with primaquine, to kill the gametocytes in an attempt to prevent an epidemic. The high numbers of infected Khmers on the border would also be unlikely to increase transmission in Thailand, as much of the Thai side of the border has sparse vegetation. There was, however, the possibility of exchange of parasites of different drug susceptibilities, when Thais and Khmers both entered areas of transmission, and later dispersed.

The collection of data on cerebral malaria and mortality allowed some assessment of malaria treatment in different parts of the border. Examination of the CFR of pregnant women alerted everybody to the necessity of special protection for this population. Only in pregnant women is it considered that chemoprophylaxis would be justified. Unfortunately, there is still no safe and effective prophylactic available, so it is necessary to rely on general vector control measures and special distributions of mosquito repellent. The higher CFR in areas of lower transmission may have resulted from lower immunity, a longer delay before treatment was sought or less experience in malaria treatment. However, mean CFRs were comparable to those found in other regions (Warrell *et al.*, 1982) despite the limited facilities available in the border hospitals.

The dramatic reduction in transmission resulting from relocation of the camps emphasises the potential for avoidance of malaria by appropriate siting of refugee camps, when a choice of sites is available. It is clear that detailed local epidemiological monitoring forms an essential basis for rational and economical use of control strategies.

## SUMMARY

Malaria epidemiology from 1983 to 1985 in displaced Khmers living in camps on the Thai-Kampuchean border was studied for planning and evaluation of control measures. The annual parasite incidence per 1000 people fell from 359 in 1983 and 350 in 1984 to 116 in 1985. Incidence varied by camp according to the suitability of the habitat for the vectors. Camps with high incidence had a higher ratio of *Plasmodium falciparum* to *P. vivax*, a higher mortality rate, especially in young children and sometimes pregnant women, but a lower case fatality rate than camps with low incidence. Transmission occurred year round, but peaked in the rainy season in 1983 and 1984. In 1985 there was a steady decline in incidence, largely owing to evacuation of many camps away from forested areas. Mortality rates per 100,000 people were 62, 77 and 28 and case fatality rates 0.41, 0.31 and 0.42% in 1983, 1984 and 1985 respectively. The case fatality rate for cerebral malaria was 21 to 26%. Epidemiological information has been more useful for planning than for evaluating control measures.

## ACKNOWLEDGEMENTS

Grateful thanks are extended to the Khmer and UNBRO staff and staff of the following Voluntary Agencies for their help in providing information on malaria incidence and demographics: Adventist Development and Relief Agency, American Refugee Committee, Avenirs (previously Monaco Aide et Presence), CAMA Services, Catholic Relief Services, Catholic Office for Emergency Relief and Refugees, International Committee for the Red Cross, Medecins sans Frontieres and Youth with a Mission. Special thanks to United Nations Volunteers for financial support in 1983 and 1984 and to Ms. Jean Schneller and Dr. Nicholas White for commenting on the manuscript.

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