

Advisory Group, United States Overseas Mission, are contacted for information and support. Through them the local civil authorities, medical and health officers and the regional officers of the Malaria Eradication Project, Royal Thai Ministry of Public Health, are contacted. It is the responsibility of the principal investigator to enlist the support of these officials. Where military populations are involved, the assistance of the Director of the US Component, SMRL, is requested to make the necessary contacts. Prior to commencement of the study, each site is visited by one or more investigators to inspect the local facilities and to make the necessary contacts.

Once an area is selected, sections of the population are screened for malaria. Those circulating one or more asexual parasites per 50 microscopic fields of stained thick blood film are singled out and interrogated. Children under the age of five years (weighing less than 26 pounds) are not incorporated in the study because they usually are unable to swallow capsules. Participants are each given an oral dose of chloroquine diphosphate, equivalent to approximately four milligrams (mgm) of the base per pound (lb) body-weight (600 mgm for a 150-lb man), by the principal investigator. Three days later they are screened for persisting asexual parasitemia. Those giving a history of vomiting within 24 hours of drug administration are dropped from the study. On completion of the investigation all participants are given sufficient chloroquine to complete the treatment at home.

Thick and thin blood films are prepared from finger punctures and rapidly stained with aqueous Romanowsky stains. Parasite densities are determined by counting the number of asexual malarial parasites per 500 white blood corpuscles (WBC) in a stained thick film. Species identification of parasites is based on the examination of stained blood films.

Chloroquine diphosphate in gelatin capsules is prepared commercially (Bayer Pharma (Thai)) in accordance with strict specifications. Dosage calculations are based on the medians of 13 weight groups. These groups range from 26 to 155 lb and each cover a ten-pound interval. A person belonging to a given weight group is administered an equivalent dose of base derived from the product of 4 mgm per pound and the median of that group. Therefore, individuals belonging to the 26-35 lb, 56-65 lb and the 136-145 lb groups are each given the respective equivalent doses of 120, 240 and 560 mgm of chloroquine base derived from the respective products of 4 mgm per pound and 30 lb, 4 mgm per pound and 60 lb, and 4 mgm per pound and 140 lb.

Progress:

a. Pilot Project in Kuankalong Self-Help Land Settlement: Since the aims of the study were somewhat new, a two-week pilot project was set up to evaluate field techniques. The original protocol required that dwellings in the study area be selected and the occupants screened for asexual malarial parasites in the peripheral circulation. Those having one or more parasites per ten microscopic fields of a thick blood film were to be assigned to one of three treatment groups

Table 1

PERSONS SCREENED FOR ASEQUAL MALARIAL PARASITES IN THE PERIPHERAL
CIRCULATION PRIOR TO CHLOROQUINE ADMINISTRATION

Self-Help Settlement	Group Examined	Number Examined	Falciparum		Vivax Infections		Mixed Infections*		Total Infected
			Number	Percent	Number	Percent	Number	Percent	
Kuankalong	School children	187	83	44.1	2	1.1	1	0.5	86
	Occupants of dwellings	200	78	39.0	3	1.5	0	0.0	81
	Total	387	161	41.6	5	1.3	1	0.3	167
Tantoe (Yala Province)	School children	172	52	30.2	0	0.0	2	1.2	54
	Construction personnel	47	23	48.9	0	0.0	0	0.0	23
	Total	219	75	34.2	0	0.0	2	0.9	77
Waeng (Narathivas Province)	School children	153	100	65.4	0	0.0	0	0.0	100
	Residents On Soi 2	71	30	42.3	0	0.0	0	0.0	30
	Total	244	130	58.0	0	0.0	0	0.0	130
GRAND TOTAL:		850	366	43.1	5	0.6	3	0.4	374

* *P. falciparum* and *P. vivax*.

Table 2

PERSONS LOST TO THE STUDY THREE DAYS FOLLOWING A DOSE OF FOUR MILLIGRAMS
OF CHLOROQUINE BASE PER POUND BODY-WEIGHT

Self-Help Settlement	Group studied	Number of Falciparum Infections			Number of Vivax Infections			Number of Mixed Infections *		
		Treated	Lost	Followed	Treated	Lost	Followed	Treated	Lost	Followed
Kuankalong (Satul Province)	School children	81	5	76	2	0	2	1	0	1
	Occupants of dwellings	73	5	68	3	1	2	0	-	-
	Total	154	10	144	5	1	4	1	0	1
Tantoe (Yala Province)	School children	42	3	39	0	-	-	2	0	2
	Construction personnel	23	5	18	0	-	-	0	-	-
	Total	65	8	57	0	-	-	2	0	2
Waeng (Narathivas Province)	School children	90	7	83	0	-	-	0	-	-
	Residents On Soi 2	25	2	23	0	-	-	0	-	-
	Total	115	9	106	0	-	-	0	-	-
GRAND TOTAL:		334	27	307	5	1	4	3	0	3

* *P. falciparum* and *P. vivax*.

and given one of the following three doses of chloroquine base: one milligram per pound body-weight, two milligrams per pound and four milligrams per pound. Thick and thin blood films were then to be prepared daily for five days from all members of the dosage groups to determine the rate of disappearance of asexual parasites from the peripheral circulation. On completion of the observation period the participants were to be given chloroquine to complete the treatment.

On 2 November 1964 the principal and associate investigators visited Southern Thailand. Following discussions with officials and a general tour of the area, Kuankalong Self-Help Land Settlement in Satul Province was selected. On 16 November 1964 the team proceeded to the settlement and initiated the pilot project. Using available maps, houses were randomly selected and visited. Only ten out of 78 occupants were found to have frank parasitemia (Plasmodium falciparum). Of these only eight could be located for one-dose treatment. Three individuals received one milligram per pound body-weight of chloroquine base, three 2 milligrams per pound and two 4 milligrams per pound. During the five-day observation period two persons were lost to the study; one had received one milligram per pound of the drug and the other two milligrams per pound. The six individuals observed continued to circulate asexual parasites over a five-day period without significant reduction in density.

On reviewing the pilot project it was decided: 1. to reduce the crude criterion for selecting infected subjects to one or more asexual parasites per 50 microscopic fields of a stained thick blood film, 2. to administer only four milligrams of chloroquine base per pound body-weight to all participants, and 3. to screen participants for persisting asexual parasitemia three days after drug administration. It was felt that these modifications would yield significant data and reduce the number of anticipated drop-outs during the observation period.

b. Survey in Kuankalong Self-Help Land Settlement, Satul Province, Southern Thailand: On 1 December 1964 the team returned to Kuankalong Self-Help Land Settlement. Two days were devoted to visiting homes and collecting blood films. It soon became apparent that, owing to the size of the team, the settlement could not be adequately covered. Because the local primary school draws students from all parts of the area, the investigators decided to screen the school children. This proved to be so successful that plans have been drawn up to utilize primary schools in the Self-Help Land Settlements of Thailand.

The age range of persons screened during house visits was 5-66 years and during school visits 5-14 years. Asexual parasite densities in falciparum and vivax infections ranged from 25 to 375/500 WBC, and from 100 to 410/500 WBC respectively. Table 1 gives a breakdown of the numbers screened for asexual malarial parasites. A high prevalence of falciparum malaria was noted in both groups. Only five cases of vivax malaria were detected. One case was infected with both falciparum and vivax malaria. Table 2 shows the number of infected persons treated with the standard dose of chloroquine base, and the number followed for persisting infection. Drop-outs during the observation period did not inter-

Table 3

PERSONS CIRCULATING ASEQUAL MALARIAL PARASITES PRIOR TO, AND THREE DAYS FOLLOWING A DOSE OF FOUR MILLIGRAMS OF CHLOROQUINE BASE PER POUND BODY-WEIGHT.

Self-Help Settlement	Group studied	Falciparum Infections			Vivax Infections			Mixed Infections *		
		Pre-treatment	Post-treatment	Per cent persisting	Pre-treatment	Post-treatment	Per cent persisting	Pre-treatment	Post-treatment	Per cent persisting
Kuankalong (Satul Province)	School children	76	59	77.6	2	0	0.0	1**	0	0.0
	Occupants of dwellings	68	57	83.8	2	0	0.0	0	-	-
	Total	144	116	80.6	4	0	0.0	1	0	0.0
Tantoe (Yala Province)	School children	39	30	76.9	0	-	-	2**	0	0.0
	Construction personnel	18	16	88.9	0	-	-	0	-	-
	Total	57	46	80.7	0	-	-	2	0	0.0
Waeng (Narathivas Province)	School children	83	61	73.5	0	-	-	0	-	-
	Residents On Soi 2	23	21	91.3	0	-	-	0	-	-
	Total	106	82	77.4	0	-	-	0	-	-
GRAND TOTAL:		307	244	79.5	4	0	0.0	3	0	0.0

* *P. falciparum* and *P. vivax*
 **Asexual forms of *P. falciparum* persisted.

ferred with the outcome of the study. Table 3 gives the numbers and percentages of persons circulating asexual parasites three days after chloroquine administration. These data indicate that the majority of strains of *P. falciparum* circulating in the population of Kuankalong exhibited some degree of insensitivity to chloroquine. All vivax infections cleared. Only the asexual forms of *P. falciparum* persisted in the peripheral circulation of the one case with mixed infection.

c. Survey in Tantoe Self-Help Land Settlement, Yala Province, Southern Thailand: During February 1965 a screening dose of four milligrams of chloroquine base per pound body-weight was administered to each of the following: a. infected school children and b. infected construction personnel. Each infected school child was further screened with a full therapeutic course of ten milligrams of chloroquine base per pound body-weight six days following the administration of the screening dose. Additional activities unrelated to the survey included the screening of inhabitants on Soi 3 for malaria, and an abortive attempt to survey a Sakhai village.

The age range of the school children was 5-16 years, and that of the construction personnel 19-49 years. Asexual parasite densities of falciparum infections ranged from 37 to 388/500 WBC. Table 1 gives a breakdown of the numbers screened for asexual parasites. The prevalence in school children is lower than that observed in Kuankalong. Although the numbers are small, a high infection rate was noted in the construction personnel. Apart from two cases infected with

Table 4

SCHOOL CHILDREN CIRCULATING ASEQUAL FORMS OF *P. FALCIPARUM* PRIOR TO, AND 3 AND 6 DAYS AFTER A DOSE OF FOUR MILLIGRAMS OF CHLOROQUINE BASE PER POUND BODY-WEIGHT FOLLOWED 5 DAYS LATER BY TREATMENT WITH TEN MILLIGRAMS OF BASE PER POUND BODY-WEIGHT.

Self-Help Settlement	Number Infected Prior to treatment	3 Days After 4 mgm of base/pound		6 Days After 4 mgm of base/pound		5 Days After 10 mgm of base/pound		Per cent
		Number	Per cent	Number	Per cent	Number	Per cent	
Tantoe (Yala Province)	39	30	76.9	32	82.1	20	51.3	
Waeng (Narathivas Province)	72	52	72.2	51	70.8	39	54.0	
TOTAL:	111	82	73.9	83	74.8	59	53.2	

Table 5

ADDITIONAL ACTIVITIES UNRELATED TO THE SURVEY; PREVALENCE OF MALARIA IN SELECTED GROUPS.

Self-Help Land Settlement	Group studied	Number examined	Falciparum Infections		Vivax Infections		Mixed Infections*		Total	
			Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Tantoe (Yala Province)	Residents On Soi 3	95	51	53.7	4	4.2	1	1.1	56	
	Residents of Sakhai village	5	4	-	1	-	0	-	5	
	Total	100	55	-	5	-	1	-	61	
Waeng (Narathivas Province)	Construction personnel	45	27	60.0	2	4.4	1	2.2	30	
	Recent arrivals	38	33	86.8	2	5.3	0	0.0	35	
	Total	83	60	72.3	4	4.8	1	1.2	65	

* *P. falciparum* and *P. vivax*.

falciparum and vivax malaria, P. falciparum was responsible for all the infections. The number of drop-outs (Table 2) did not interfere with the overall result. The percentage of infected persons circulating asexual parasites three days after a single dose of four milligrams of chloroquine base per pound (Table 3) is comparable with that of Kuankalong. Once again, only the asexual forms of P. falciparum persisted in the peripheral circulations of the two cases of mixed infection. These data indicate that the majority of strains of P. falciparum circulating in the population of Tantoe exhibited some degree of insensitivity to chloroquine.

A further study was conducted in the school children. All falciparum infections previously screened with four milligrams of chloroquine base per pound were each treated six days later with ten milligrams per pound of the base by administering four and two milligrams per pound on the first day, and two milligrams per pound on the second and third days. A total of 39 infected children were examined for circulating asexual malarial parasites three and six days following the screening dose, and five days following the completion of treatment (Table 4). Approximately eighty per cent continued to circulate parasites three and six days after the screening dose. Fifty-one per cent continued to circulate parasites five days after treatment, thus representing the proportion of infections insensitive to standard therapy. It therefore seems reasonable to suppose that strains of P. falciparum exhibiting varying degrees of sensitivity to chloroquine were present in the settlement during the study period, because a greater proportion responded to ten milligrams per pound of the base than to four milligrams per pound.

Ninety-five residents on Soi 3 were screened for malaria. Approximately 54 percent were infected with falciparum malaria and four percent with vivax malaria (Table 5). One person was infected with both falciparum and vivax malaria. Only five of the 50 or so residents of the Sakhai village were willing to give blood; four were infected with P. falciparum and one with P. vivax.

d. Survey in Waeng Self-Help Land Settlement, Narathivas Province, Southern Thailand: During February 1965 the following were each screened with four milligrams of chloroquine base per pound body-weight; a. infected school children and b. infected residents on Soi 2. The children were further screened with a therapeutic course of ten milligrams of base per pound. Additional activities unrelated to the survey were the screening for malaria of construction personnel and recent arrivals from Rayong Province.

The age range of the school children was 6-13 years and that of the Soi 2 residents 5-73 years. Asexual parasite densities of falciparum infections ranged from 45 to 382/500 WBC. The prevalence of infections in school children (Table 1) exceeds those of Kuankalong and Tantoe; it also exceeds that observed in the residents of Soi 2. P. falciparum was responsible for all infections. As before, the drop-out rates (Table 2) were low and did not interfere with the overall results. The percentage of infected school children circulating parasites three days after a single dose of four milligrams of chloroquine base per pound (Table 3) is slightly less than those recorded in the other two settlements. Although the infected

residents on Soi 2 had a high persisting infection rate, the small numbers tested negate the significance of the observation. These data indicate that the majority of strains of P. falciparum circulating in the population of Waeng exhibited some degree of insensitivity to chloroquine.

A further study was conducted in the school children utilizing the protocol described under the Tantoe survey. A total of 72 infected school children were examined for circulating asexual parasites three and six days following the screening dose of four milligrams of chloroquine base per pound body-weight, and five days following ten milligrams of base per pound (Table 4). Approximately seventy-one per cent continued to circulate parasites three and six days after the one screening dose. Fifty-four per cent continued to circulate parasites five days after treatment, thus representing the proportion of infections insensitive to standard therapy. It also seems reasonable to suppose that, as in Tantoe, strains of falciparum malaria exhibiting varying degrees of sensitivity were present in the settlement during the study period, because a greater proportion responded to ten milligrams per pound of the base than to four milligrams per pound.

Forty-five construction personnel and 38 recent arrivals from Rayong Province were screened for malaria (Table 5). Sixty and eighty-seven per cent respectively were infected with P. falciparum. Two vivax infections were picked up in both groups and one mixed (falciparum and vivax) infection in the construction personnel.

Conclusion: A review of previous reports in the literature indicates that infected persons receiving approximately 600 milligrams of chloroquine base per 150 pounds body-weight are generally free from asexual forms of P. falciparum within three days. Since this was not observed in over seventy per cent of the 307 infections treated with four milligrams of chloroquine base per pound, and in approximately fifty per cent of the 111 infections given a further treatment of ten milligrams of base per pound, the data suggest that strains of falciparum malaria exhibiting varying degrees of insensitivity to the drug were circulating among the inhabitants of Kuankalong, Tantoe and Waeng during the study periods. All vivax infections, however, were sensitive to four milligrams per pound of the drug.

Summary: A study to determine the approximate prevalence of malaria exhibiting reduced sensitivity to four milligrams of chloroquine base per pound body-weight was undertaken in the Self-Help Land Settlements of Satul, Yala and Narathivas Provinces, Southern Thailand. A further study to determine the approximate prevalence of malaria unresponsive to a therapeutic course of ten milligrams of base per pound was conducted in the Self-Help Land Settlements of Yala and Narathivas Provinces. The data indicate that at least seventy per cent of the falciparum infections were insensitive to four milligrams per pound of the drug, and approximately fifty per cent were unresponsive to ten milligrams per pound. The four vivax infections appeared to be highly sensitive to chloroquine. The three mixed (vivax and falciparum) infections reverted to simple falciparum infections.