

## Quinine Treatment of Acute Falciparum Malaria in Central Thailand

Principal Investigator: Edward J. Colwell, LTC, MC

Associate Investigators: Suphat Neoypatlmanondh, MD  
Robert L. Hickman, MAJ, VC

**OBJECTIVE:** Chloroquine resistant falciparum malaria is distributed throughout all of Thailand and, in areas of intensive study, the majority of strains are resistant to conventional doses of chloroquine. Consequently, the treatment of choice for many hospitalized patients with moderate to severe degrees of Plasmodium falciparum infections is a 7 to 10 day course of quinine. In 1965, Pinswasdi and Charoenkwan observed an adult Thai male infected with P. falciparum who was unresponsive to chloroquine therapy and who exhibited a poor response to multiple courses of quinine administration. During the 12 months prior to our study, there have been several isolated, unconfirmed reports of patients who showed a poor or no response to quinine administration. Because quinine is the treatment of choice for moderate to severe P. falciparum infections at most provincial hospitals in Thailand, it was considered highly desirable to examine the quinine sensitivity of this parasite and attempt to confirm resistant strains.

**DESCRIPTION:** The investigation was conducted at Phrabuddhabat Hospital, Saraburi Province in Central Thailand, which was one of the locations for unconfirmed reports of quinine resistance. This area has been shown to be highly endemic for chloroquine resistant falciparum malaria. Patients considered for admission to the study were acutely ill males and females, aged 14 to 60 years, exhibiting moderate to severe degrees of illness. Those patients with a history of antimalarial drug intake during the preceding 3 days were excluded.

Subjects so selected were hospitalized and given oral quinine, 540 mg base, thrice daily for 7 to 10 days. One patient presented with protracted emesis and was administered intravenous quinine (1.62 gm base a day) for the first 4 days. Blood smear examinations for quantification of asexual parasites were obtained daily during the treatment period and, subsequently, on the 17th, 24th and 31st days of observation.

**PROGRESS:** Thirty-three patients were selected for study. There were 28 males and 5 females, ranging in age from 14 to 57 years of age (mean was 26.5 years). The pretreatment levels of asexual parasitemias and the intervals for asexual parasite clearance for these patients are shown in Table 1. The mean parasite clearance time for 31 subjects who showed initial clearing was 3.3 days (range 1 to 6 days). Parasite clearances for the other 2 patients were excluded from the mean computation because they expired during the early treatment period while still demonstrating patent parasitemia.

Twelve of 30 patients remained available for prolonged follow-up examinations. None showed a recrudescence.

Three of the 33 subjects originally selected for study expired during the treatment period. Two were males, aged 14 years (# 32 in Table 1) and 57 years (# 31), who died on the 3rd and 4th day, respectively. These two deaths were noted on early morning nursing rounds. The exact time and manner of demise was unknown. Postmortem examinations were not accomplished. Because these expirations occurred during the early treatment period, it is impossible to determine the major precipitating event; complication of the infection, intercurrent illness or drug toxicity. The extremely high degrees of erythrocytic parasitization in these two subjects would appear to indicate that the more probable event was a complication of the infection.

The remaining patient who expired was a 57 year old woman who was admitted with an asexual parasite count of 231,000 per cmm and no evidence of renal, hepatic or cerebral complications. On the 9th

treatment day at which time fever and patent parasitemia were absent, she experienced sudden death in the early evening hours. Gross findings at autopsy revealed only pulmonary congestion. It is our opinion that the most probable cause of death in this patient was a cardiotoxic event precipitated by quinine.

SUMMARY: Thirty-three Thai subjects acutely ill with falciparum malaria were given quinine treatment at a daily dose of 1.62 gm base for 7-10 day periods. The mean parasite clearance time in 31 of 33 patients, who exhibited initial clearing of asexual parasites, was 3.3 days. Prolonged follow-up examinations were accomplished in 12 patients and none showed a recrudescence. Three patients expired during the treatment period. Quinine cardiotoxicity was believed to be the cause of death in 1 of the 3 mortalities.

Table 1.  
Results of Quinine Treatment of Acute Falciparum Malaria in Central Thailand

Patient #	Age (years)	Sex	Pretreatment asexual parasitemia*	Duration of asexual parasitemia (Days)	Comment
1	17	M	397,360	5	Cure**
2	18	M	373,120	4	NF***
3	53	M	231,740	4	Hepatitis, NF
4	21	M	140,140	4	NF
5	25	M	136,400	4	NF
6	43	M	127,770	4	NF
7	18	M	104,470	3	Hepatitis, NF
8	27	M	96,230	4	Hepatitis, NF
9	42	F	52,980	2	Cure
10	15	M	44,880	3	NF
11	20	M	44,040	3	Cure
12	17	M	36,260	3	Cure
13	40	F	33,000	3	NF
14	20	M	32,040	3	Cure
15	16	M	30,840	4	NF
16	15	M	25,280	4	Hepatitis, NF
17	18	M	24,120	3	Cure
18	16	M	23,320	3	Cure
19	18	M	23,000	4	NF
20	18	M	21,929	4	Cure
21	19	M	20,800	3	NF
22	16	M	17,850	4	NF
23	37	M	11,240	3	NF
24	40	M	11,000	3	Cure
25	49	M	7,360	2	NF
26	25	M	5,360	4	Cure
27	24	M	5,240	3	Cure
28	16	F	2,120	2	Cure
29	46	F	200	2	NF
30	19	M	20	1	NF
31	37	M	495,000	—	Expired
32	14	M	353,320	—	Expired
33	57	F	231,140	4	Expired

\* Per cmm

\*\* Cure indicates no recrudescence within 31 days of followup

\*\*\* No followup after treatment