

Pyrimethamine Resistant Falciparum Malaria in Thailand

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OBJECTIVE: The pyrimethamine response of naturally acquired falciparum malaria in Thailand has not been studied. Because it is a widely used antimalarial drug either alone or in combination, its therapeutic efficacy was tested.

DESCRIPTION: The studies were conducted at the Trad Provincial Hospital in February 1973. The patients were first seen at the SMRL Malaria Clinic and quantitative parasite counts performed. Mild cases of falciparum malaria were selected for study. Informed consent was obtained in all patients.

PROGRESS: Three patients were treated.

1. The first patient was seen on 6 February 1973. He was a 40 year old farmer with fever, headache and weakness for a few days. The only therapy was two unidentified tablets 2 days previously. He said that he had had an attack of malaria 1 month earlier. His temperature was 98.6°F on admission. Splenomegaly was present throughout the 6 days in the hospital. His asexual count of *P. falciparum* was 810/cmm (Table 1). 50 mg pyrimethamine was given daily for 3 days (total dose 150 mg). The parasitemia decreased but rose again on the 6th day at which time quinine was administered on an outpatient basis for 6 days. Parasitemia was absent at follow-up examinations on days 14, 21 and 28.

2. This 32 year old man gave a history of fever and headache for one month. He had taken no antimalarials for 6 days. His asexual count was 8580/cmm and there was a partial response to the standard 150 mg course of pyrimethamine (Table 2); however, on day 4 his count rose sharply to 1377/cmm and quinine was administered. The patient did not attend follow-up.

3. This 19 year old man gave a 3 day history of fever, weakness and myalgia. His parasite count of 940/cmm was decreased by pyrimethamine therapy but a resurgence of parasitemia on day 6 responded to quinine therapy (Table 3).

COMMENT: In all three patients, the falciparum parasitemia made only a temporary response to pyrimethamine. This is an RII response under WHO criteria. Pyrimethamine resistance has been previously shown in artificially induced infections in the USA using a strain isolated from a white man in Thailand (see references). This report confirms that pyrimethamine resistance is found in natural infections in Thailand.

REFERENCES:

1. Jeffery, G.M., Collins, W.E., and Skinner, J.C. 1963. Antimalarial drug trials on a multiresistant strain of *Plasmodium falciparum*. *Am. J. Trop. Med. Hyg.* 12; 844-850.
2. Powell, R.D., Brewer, G.J., Alving, A.S., and Miller, J.W. 1964. Studies on a strain of chloroquine-resistant *Plasmodium falciparum* from Thailand. *Bull. W.H.O.* 30; 29-44.
3. Young, M.D., Contacos, P.G., Sticher, J.E., and Miller, J.W. 1963. Drug resistance in *Plasmodium falciparum* from Thailand. *Am. J. Trop. Med. Hyg.* 12; 305-314.

Table 1.
 The Parasitemia of *P. falciparum* in Case 1
 Only Partially Responded to Pyrimethamine (R11 Response)

Date	Day	Time	Asexual Count	Gams	Therapy	Comment
6 Feb 1973	0	1000 1400	810 3812	72	Pyrimethamine 50 mg	R11 Response
	1	0800 1400	200 20	Rare 20	Pyrimethamine 50 mg	
	2	0800 1400	40 100	20 20	Pyrimethamine 50 mg	
	3	0800 1400	Rare Rare	20 20		
	4	0800 1400	Rare Rare	20 20		
	5	0800 1400	Rare Rare	20 20		
	6	0800	40	20	Quinine (6 Days)	S Response
	14		0	48		
	21		0	Rare		
	28		0	0		

Table 2.
Case 2. Pyrimethamine Therapy of Falciparum Malaria
Followed by RII Response

Date	Day	Asexual Count	Gams	Therapy	Comment
7 Feb 1973	0	8580 7007	0 0	Pyrimethamine 50 mg	RII Response
	1	3160 1720	0 0	Pyrimethamine 50 mg	
	2	1140 660	0 0	Pyrimethamine 50 mg	
	3	960 580	0 0		
	4	80 1377	0 81		
	5	3185		Quinine (6 Days)	

Table 3.
Case 3. RII Response of Falciparum Malaria to Pyrimethamine

Date	Day	Asexual Count/cmm	Gams	Therapy	Comment
19 Feb 1973	0	940	40	Pyrimethamine 50 mg	RII Response
	1	1296 20	162 20	Pyrimethamine 50 mg	
	2	20 Rare	20 20	Pyrimethamine 50 mg	
	3	Rare Rare	72 48		
	4	Rare 192	20 24		
	5	40 40	20 40		
	6	1512 1080	0 40	Quinine (6 Days)	
	7	360	20		
	14	0	0		