

TREATMENT OF THE ACUTE ATTACK OF MALARIA CAUSED BY
Plasmodium falciparum : RESPONSE OF FANSIDAR
RESISTANT MALARIA TO OTHER
THERAPEUTIC REGIMENS

Principal Investigators : David E. Johnson, MAJ, MC
Preecha Roendej, LTC, MC, RTA
Ronald G. Williams, LTC, MC

OBJECTIVES :

1. To assess the efficacy of various treatment regimens in an area of documented Fansidar resistance.
2. To document the optimal therapy for malaria in a military unit without severely disabling that unit.

BACKGROUND : In mid-January 1980, The Armed Forces Research Institute of Medical Sciences was asked to help evaluate the efficacy of anti-malarial regimens currently being used at the 1st Medical Battalion. It was the impression of local medical officers that 1) malaria, particularly *P. falciparum* infection, was having a severely detrimental effect on the military posture of units deployed along the Thai-Khmer border, 2) response of these infections to the usual anti-malarial regimens was inadequate and 3) there may be a place for chloroquine in the treatment of *P. falciparum* infections, presumably introduced from Kampuchea. Having documented that between 90-100% of all cases of falciparum malaria in this area were resistant to single drug therapy with either chloroquine or Fansidar, random patients were treated with combinations of Fansidar and quinine or Fansidar and chloroquine and their efficacy was assessed versus a 7 day quinine therapy response. Hall et al.¹ found that, with four or fewer doses of quinine plus Fansidar, they cured 87 of 89 patients (over 95%), but concluded that at least four doses of quinine should be given. (They also reported 85% efficacy of Fansidar alone², a rate which is no longer tenable in the area of the Thai-Khmer border). Chloroquine, pyrimethamine and sulfa, in very high doses, was used in Vietnam as an alternative to quinine therapy with satisfactory results³. With a 28 day follow-up, cure rates of 85% have been reported with a six day course of quinine therapy alone⁴.

METHODS : The results of therapy were as presented in Table 1. Neither combinations 1 nor 2 is ideal therapy. However, they do offer the advantages of relatively low cost and short duration of therapy (and consequent length of hospital stay). There does not appear to be a real difference in either the rate of parasitemia clearance or the presumptive cure rate between therapies 3 and 4. All therapy combinations that included some quinine with Fansidar resulted in parasitemia clearance in excess of 90%, but none of these anti-malarial regimens resulted in satisfactory cure rates. Bothersome, also, is the depressed cure rates seen for quinine therapy alone.

Since, logically, soldiers who are clinically ill at day 14 are more likely to reappear for follow-up than those who are healthy, the number of therapy failures may be unduly exaggerated. Conversely, 14 days is a very short follow-up period compared to the more traditional 28 day follow-up⁵, thus allowing a case to be called a "cure" although recrudescence may occur later.

Under some military situations efficacy may have to be judged on the basis of "percentage of soldiers returned to combat (and, possibly, to re-infection) in the shortest period of time" rather than "percentage radical cure after one month outside of a malaria transmission area"¹. Prolonged quinine therapy, with or without Fansidar, may be more responsive to the latter rather than the former.

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4. Hall, A.P. H.E. Segal, E.J. Pearlman, P. Phintuyothin and S. Kosakal : Comparison of a 9-Phenanthrene Methanol (WR33063), A 4-Quinoline Methanol (WR30090), and Quinine for Falciparum Malaria in Thailand. Trans. Roy. Soc. Trop. Med. & Hyg. 69: 342-349, 1975.
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Table 1. Results of Therapy with Various Antimalarial Regimens, 1st Medical Battalion,
1st Infantry Division, Thailand

	Therapy response					%	Parasitemia clearance	Presumptive cure*
	R3	R2	R1	S*	Cleared parasitemia without follow-up			
1. Chloroquine (1500 mg po over 3 days) plus Fansidar (3 tablets)	3	7	10	5	2	63	20	
2. Quinine-4 doses (750 mg po q8h per dose) plus Fansidar	1	-	10	5	6	95	31	
3. Quinine - 9 doses plus Fansidar	-	1	10	10	17	97	48	
4. Quinine - 21 doses plus Fansidar	-	4	9	10	20	91	43	
5. Quinine - 21 doses	-	3	2	10	-	80	67	

* Sensitivity and presumptive cure based on follow-up 14 days following initiation of therapy.