

## Treatment of Falciparum Malaria with Pyrimethamine and DFD

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**OBJECTIVE:** Pyrimethamine in combination with DFD has been developed and tested for the prophylaxis of malaria. We have tested a single dose for therapy.

**BACKGROUND:** DDS (Dapsone) is a sulfone with antimalarial activity, but its short half-life (17 hours) dictates daily administration for prophylaxis. DFD, a diformyl derivative of DDS, was developed as a longer acting compound (half-life 30 hours) suitable for weekly dosage. Clyde found that DFD with pyrimethamine, given weekly, was effective in the prophylactic suppression of both falciparum and vivax malaria.

**DESCRIPTION:** Patients with clinically mild or moderate falciparum malaria were treated with pyrimethamine 50 mg and DFD 800 mg (4 tablets). Initially a few patients received a 2 tablet dose.

**PROGRESS:** Three patients received a 2 tablet dose (Table 1). One patient was cured (S response) but in two others the parasitemia was not cleared in hospital (RII response).

Thirty patients were given a single dose of 4 tablets (Table 2). The results are given in Table 3. The over-all cure rate was 43% (10/23).

The cured cases included many mild infections. Generally the initial clinical response was slow. In cases No. 2 and 4 the patients remained ill from their malaria on day 2 with a high fever. In both patients the total parasite count was low, although schizonts were seen on the blood films. It is probable that DFD has the unusual effect of clearing the parasites out of the blood into the deeper tissues.

**SUMMARY:** Single dose therapy with pyrimethamine 50 mg and DFD 800 mg was insufficient to cure a majority of patients infected with falciparum malaria.

Table 1. Falciparum Malaria Treated with 25 mg Pyrimethamine and 400 mg DFD.

Case No.	Parasite Count (per cmm)	Parasite Clearance (Hours)	Initial Fever (°C)	Fever Clearance (Hours)	Result*
1	57785	NC	39.0	NC	RII
2	3360	—	40.4	NC	RII
3	1539	41	37.8	—	S

- \* RIII = parasitemia did not respond to treatment.
- RII = partial response of parasitemia.
- RI = clearance of parasitemia followed by recrudescence.
- S = cure
- NC = not cleared.

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Table 2. Falciparum Malaria Treated with 50 mg Pyrimethamine and 800 mg DFD.

Case No.	Parasite Count (per cmm)	Parasite Clearance (Hours)	Initial Fever (°C)	Fever Clearance (Hours)	Result*
4	41040	NC	38.4	NC	RII
5	1560	45	38.7	37	RI
6	7209	44	37.1	—	S
7	20200	44	39.0	50	S
8	1820	61	39.6	12	RS
9	1420	61	38.8	36	S
10	5400	92	39.2	67	RI
11	12393	45	37.3	—	S
12	11220	NC	40.5	—	RIII
13	7290	66	37.7	—	RS
14	6885	43	37.8	—	S
15	12150	67	36.9	—	S
16	5670	40	37.0	—	S
17	13013	52	40.5	92	RS
18	2568	41	38.6	NC	RI
19	12312	70	40.4	93	RI
20	18382	117	37.8	NC	RI
21	4920	72	40.3	40	RI
22	11664	84	39.8	N/A	S
23	1040	61	38.7	—	RI
24	30294	69	39.1	69	S
25	1220	14	39.8	—	S
26	1120	—	40.0	—	unknown
27	9963	—	40.4	—	RIII
28	7220	60	39.3	59	RI
29	40708	—	40.0	—	RII
30	12960	62	38.3	12	RS
31	95580	93	39.0	84	RI
32	46137	43	39.2	42	unknown
33	63700	—	39.2	—	unknown
Average	16900	60	38.9	53	