

Evaluation of the Sporonticidal Activity of Pyrimethamine-sulfadoxine  
(Fansidar) Against *P. falciparum* in Thailand

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**OBJECTIVE:** To determine the effect of single dose Fansidar therapy upon the subsequent development of oocysts and sporozoites of *P. falciparum* in vector mosquitoes and to correlate this information with plasma levels of pyrimethamine and sulfadoxine at the time of mosquito feeding. The activity of pyrimethamine alone will also be evaluated.

**BACKGROUND:** Fansidar, the fixed combination of pyrimethamine and sulfadoxine, has been shown to be very effective against chloroquine resistant and chloroquine sensitive strains of *P. falciparum* as well as *P. vivax* malaria in many parts of the world. It is currently recommended in Thailand as an alternative therapeutic regimen in the guidelines of the National Malaria Eradication Project. A number of studies (1, 2) have proven its effectiveness as a schizonticide, but it has not heretofore been adequately investigated as a gametocytocide and sporonticide. Chin, et al. (1) fed *Anopheles b. balabacensis* mosquitoes on patients following single-dose therapy; however, plasma levels of the constituent drugs were not determined at any time. In their series, 47% of mosquitoes fed on patients with gametocytemia showed development of the parasite up to the sporozoite stage, after feeding on days 7-9 and 13-14 following therapy.

In view of the already widespread use of Fansidar in the therapy of malaria in Southeast Asia, and its emergence as the drug of choice for chloroquine-resistant malaria in many parts of the world, the effect of this drug upon the infectivity of gametocytes needs to be conclusively determined. Epidemiologically, it is essential to be aware of the need for the additional use of a sporonticidal such as primaquine, in combination therapy.

**DESCRIPTION:** Patients presenting to the Malaria Eradication Service and district hospital outpatient clinics in Phrabuddhabat, Central Thailand, who are at least 15 years old and are found to have infections with *P. falciparum* are considered eligible for admission to the study.

Eligible patients are then randomly assigned to one of three groups: Group A: patients are treated with a single dose of Fansidar, two tablets (total 50 mg pyrimethamine, 1000 mg sulfadoxine). Group B: patients are treated with quinine, 10 grains every eight hours for six days. Group C: patients receive quinine as in Group B, plus pyrimethamine 50 mg daily for three days.

Fansidar, either alone or in combination with quinine, is the standard therapy for *P. falciparum* used in the outpatient clinic and on the wards in Prabuddhabat Hospital, and in the clinic operated by the National Malaria Eradication Project.

Medications are administered by the nursing staff, under the supervision of the study physicians. At the conclusion of the 21-day study period, patients from Group B and C are given two tablets of Fansidar. Recrudescences, if they occur, are re-treated with Quinine-Fansidar on an individualized basis.

Parasite counts are performed and blood is drawn for pyrimethamine and sulfadoxine levels before treatment is begun, daily in hospital and on days 5, 10, 15 and 20. Mosquito feeds are performed on days 0, 5, 10, 15 and 20 using colonized *A. b. balabacensis* from the SEATO Medical Research Laboratory

Phrabuddhabat insectary. Patients are asked to return to the SEATO Medical Research Laboratory insectary for follow-up. If necessary, they are followed at home.

Ten percent of the mosquitoes fed on the patients are dissected ten days after feeding, and all mosquitoes are dissected on day 15, regardless of the results of the day 10 dissection.

Plasma pyrimethamine and sulfadoxine levels are performed at the SEATO Medical Research Laboratory Biochemistry Laboratory.

Numbers of mosquitoes developing oocysts and sporozoites will be evaluated as a function of plasma levels of drug at the time of feeding. Patients treated with quinine, which is known to have no effect on gametocytogeny or the development of mosquito forms, will provide the control population.

**PROGRESS:** Data collection is incomplete, and biochemical analyses are still pending, but it is becoming apparent that gametocytes from patients with detectable pyrimethamine and sulfa are infective to mosquitoes in some cases. To date, four of eight patients treated with the pyrimethamine-sulfadoxine combination developed gametocytes infective to the vector mosquitoes. All patients had detectable serum levels of pyrimethamine and sulfadoxine at the time of mosquito feeding.

**REFERENCES:**

1. Chin, W., and Rattanarithikul, M.: The Evaluation of the Presumptive and Radical Treatments against *Falciparum* Malaria in Thailand. *Southeast Asian J. Trop. Med. Pub. Health*, 4; 400, 1972.
2. Chin, W., Bear, D.M., Colwell, E.J., and Kosakal, S.: A Comparative Evaluation of Sulfalene-trime-thoprim and Sulphormethoxine-pyrimethamine against *Falciparum* Malaria in Thailand. *Am. J. Trop. Med. Hyg.* 22:308, 1973.