

## Mefloquine Pharmacokinetics Following Oral Administration

Investigators :

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**OBJECTIVE :** To determine the pattern of absorption and elimination of orally administered doses of mefloquine.

**BACKGROUND :** A technique for accurate chemical analysis for mefloquine in blood specimens is now available in the laboratories of the Department of Pharmacology at the Walter Reed Army Institute of Research. This provides an opportunity to develop detailed pharmacokinetic information from use of the drug in humans. Data has been collected in the United States from normal, uninfected volunteer subjects, who were given several different oral dosages of mefloquine. However, no data on the absorption and the elimination patterns of this antimalarial in human subjects infected with *P. falciparum* malaria have hitherto been collected. Information currently available indicates that the drug does have a prolonged biologic half-life in man (15-25 days) which probably accounts for its efficacy as a single-dose therapeutic, and also its success as a chemosuppressant.

Data collected both in the United States and in Thailand have already shown that mefloquine is a safe and effective antimalarial.

**METHODS :** Fifteen subjects were admitted to the study, selected from those presenting to the hospital out-patient department in Phrabuddhabat, Saraburi Province, Central Thailand, as well as the Passive Detection Center of the National Malaria Eradication Project in Phrabuddhabat. The patients were presumably infected with a chloroquine-resistant strain of *P. falciparum* since current *in vitro* data suggests that chloroquine-sensitive strains are no longer seen in the Phrabuddhabat area. Patient selection criteria were identical to those used in previous mefloquine studies; i.e.,

1. Males at least 18 years of age.
2. Moderate parasitemia (greater than 1,000, less than 100,000/cu.mm.).
3. Uncomplicated disease.
4. Willingness to sign a consent form for the use of a new drug.

Patients considered eligible were admitted to the medical ward of Phrabuddhabat Hospital and were followed by one of the investigators with clinical rounds conducted at least twice daily. Parasite counts were performed three times daily and a detailed record was kept of signs and symptoms. Patients were kept in the hospital an average of four days, and then followed as

out-patients for up to 84 days following therapy. A total of 32 blood specimens per subject was obtained over this period of twelve weeks. Sampling times were selected to minimize the variance estimate of the slope of each of the three kinetic phases anticipated. The long duration of this study was required to provide specimens for analysis at three to four times the elimination half-life of the drug.

**RESULTS :** Fifteen patients were studied according to the protocol and all were clinically and parasitologically cured. Specimens of heparinized whole venous blood were collected and have been sent to the Division of Medicinal Chemistry, Walter Reed Army Institute of Research in Washington. Analysis of the samples is currently underway and results are pending.