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Reprinted from THE AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE
Vol. 24, No. 2, March 1975
p. 168-173

Printed in United States of America

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CHEMOTHERAPY OF *PLASMODIUM VIVAX* IN *SAIMIRI* AND *AOTUS* MODELS*

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Abstract. Three standard antimalarial compounds were tested against trophozoite or sporozoite induced infections of the Panamanian Achiote strain of *Plasmodium vivax* in two species of monkeys. In *Saimiri sciureus* (24 subjects) and *Aotus trivirgatus* (11 subjects), parasite clearance from the peripheral blood averaged 3 days after initiating chloroquine therapy (total dose of 25 mg base/kg body weight over 3 days or single dose of 10 mg base/kg). Trophozoite induced infections were cured in all of 10 *Saimiri* and all of 6 *Aotus*, as indicated by the absence of relapses. Relapses did occur in 3 of 11 tests with *Saimiri* and 3 of 5 tests with *Aotus* against sporozoite induced infections. Subpatent periods ranged from 38 to 111 days among intact and splenectomized hosts. This is the first chemotherapeutic evidence for the persistence of exoerythrocytic stages of *P. vivax* in New World monkeys. Pyrimethamine (single dose of 1 mg/kg) cured trophozoite induced infections in all of five *Saimiri* hosts. Radical cure of sporozoite induced infections was accomplished in each of six trials with chloroquine (25 mg base/kg) plus primaquine (1 mg base/kg for 14 days). The primary attack or relapse was treated. These models warrant further investigation in chemotherapy.

With the advent of the adaptation and transmission of *Plasmodium vivax* to *Aotus trivirgatus* (the night monkey),^{1,2} this new model and others became available for diverse investigations in malaria. Of particular importance is that the evolution of these systems has offered the opportunity to study the chemotherapeutic response of human malarial parasites to standard, as well as experimental, antimalarial compounds in a small easily manipulable host, rather than directly in man.

Panamanian squirrel monkeys, *Saimiri sciureus* (= *oerstedii*), recently shown to be susceptible to infections induced by trophozoites or sporozoites of *P. vivax*,^{3,4} served as the primary host in the current investigations. *Aotus* monkeys were utilized in limited companion trials.

The objectives of these studies, incorporating the new models, were to establish the following: 1) curative activity of the blood schizontocides, chloroquine or pyrimethamine, against trophozoite induced infections; 2) response of sporozoite

induced infections to chloroquine alone; and 3) radical curative properties of chloroquine plus a tissue schizontocide, primaquine, against sporozoite induced infections.

MATERIALS AND METHODS

All data were acquired with the Achiote strain of *P. vivax*, passaged in New World monkeys since 1966.⁵ Citrated blood, containing 10⁷ parasites from the homologous donor species, was inoculated intraperitoneally for each trophozoite induced infection.

Sporozoites were obtained via infected *Anopheles albimanus* subsequent to feeding only on *Aotus*, as *Saimiri* are poor hosts for infecting mosquitoes.⁴ Sporozoites were introduced by the interrupted bite technique (*Saimiri*) or by intravascular inoculation (*Aotus*). No attempts were made to standardize the sporozoite inoculum, as all those available were used; the number of positive mosquitoes per recipient ranged from 5 to 142 (\bar{x} = 45), with average gland sporozoite densities between 100 and 1,000.

Routinely, blood films were obtained daily throughout the test periods. Parasites were stained with Giemsa and enumerated by the Earle-Perez method. Trophozoite induced infections were treated when the parasitemia first

Accepted 13 July 1974.

* This work was sponsored by the U.S. Army Medical Research and Development Command under Grant No. DADA 17-71C-9126. This is Contribution Number 1272 to the Army Research Program on Malaria.

