

Evaluation of Experimental Antimalarial Drugs in
Rhesus Monkeys Infected with *Plasmodium*
cynomolgi (Blood Schizonticidal Tests)

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OBJECTIVE : To evaluate the blood schizonticidal activity of selected experimental drugs against *P. cynomolgi* in rhesus monkeys (*Macaca mulatta*).

BACKGROUND : This is a continuation of studies initiated in 1971. A chronological report of methodology and results are available in SEATO/AFRIMS Medical Research Laboratory Annual Reports, 1971 through 1977. These studies are conducted in association with the Division of Experimental Therapeutics, Walter Reed Army Institute of Research.

METHODS : Experimental drugs were evaluated in rhesus monkeys utilizing various dosage levels. Rhesus monkeys, negative for malaria parasites on prestudy examination, were infected by intravenous inoculation of 5×10^8 parasitized erythrocytes obtained from donor monkeys infected with *P. cynomolgi* Strain B.

Beginning on post-inoculation day 4, test drugs were administered orally, via gastric intubation, for seven days. Malaria parasitemia was monitored in each monkey by daily bleedings for the first fifteen days following inoculation and then every other day for the remainder of the study. Post-treatment day 20, monkeys positive for malaria parasites were terminated and those negative for malaria parasites were splenectomized. Splenectomized monkeys continuously negative for malaria parasites through post-treatment day 50 were considered cured.

RESULTS : Suppression of parasitemia was indicative of blood schizonticidal activity. Ten experimental drugs were evaluated, with results summarized in Table 1.

Each infected donor monkey was utilized as the vehicle control for the previous drug study. This passage system for the malaria parasite has resulted in 125 monkey to monkey passages of the original *P. cynomolgi* Strain B parasite used in these studies.

Due to the ban of the exportation of rhesus monkeys by the Indian government, the blood schizonticidal testing was suspended in March 1978. Testing will be continued when additional monkeys become available.

Table 1. Summary of Blood Schizonticidal Tests in Rhesus Monkeys.

| Type of Compound | WRAIR Drug Number | Minimum Curative Dose (mg/kg/day) |
|---------------------|-------------------|--------------------------------------|
| 4-Aminoquinoline | 228258 | *TNC |
| | 228979 | 0.316 |
| 8-Aminoquinoline | 232584 | 3.16 |
| | 232956 | TNC |
| | 233078 | 3.16 |
| | 233195 | TNC |
| | 234578 | 1.0 |
| Quinoline methanols | 215440 | 3.16 |
| Miscellaneous | 229049 | **NC(100.0) |
| | 231135 | 10.0 |

* - TNC - Testing Not Completed - Testing on these drugs had not been completed when the program was suspended.

** - NC - Not Curative - The compound had suppressive activity but did not cure at the maximum dose tested. Maximum dose tested is indicated in parentheses.