

Evaluation of the Effectiveness of Experimental Antimalarial Drugs in Rhesus Monkeys
Infected with *Plasmodium cynomolgi*

Principal Investigators : David E. Davidson, Jr., LTC, VC
Prayot Tanticharoenyos, DVM

Associate Investigators : Harry Rozmiarek, MAJ, VC
Dennis O. Johnsen, MAJ, VC
John W. Sagartz, CPT, VC
Markpol Tingpalapong, DVM

OBJECTIVE: To determine the efficacy of experimental antimalarial drugs in rhesus monkeys infected with blood-induced *Plasmodium cynomolgi*. The experimental drugs are furnished by the Division of Medicinal Chemistry, Walter Reed Army Institute of Research.

DESCRIPTION: Rhesus monkeys (*Macaca mulatta*) of either sex, weighing 2–4 kg, are infected by the intravenous administration of 5×10^8 parasitized cells from a donor monkey infected with *Plasmodium cynomolgi* strain—B. Four days later, when the parasitemia is well-established, a 7 day course of daily drug administration is initiated. Drugs are routinely prepared in a suspension and given orally by stomach tube, but other methods of treatment are used on occasion. The effectiveness of the drug is determined by following the parasitemia over a thirty day period. At the end of thirty days, monkeys with negative blood smears are splenectomized. Only those monkeys which remain negative for 30 days after splenectomy are classified as CURED. In addition to parasite counts, each monkey is observed daily for clinical signs of drug toxicity or intercurrent disease. Necropsy examinations are performed terminally.

Each experimental drug is evaluated over a series of doses to determine a minimum curative dose, a minimum effective dose and a maximum tolerated dose. Normally two monkeys are treated at each dose level, with doses spaced 0.5 Log 10 apart (316, 100, 31.6, 10.0, 3.16, 1.0 mg/kg, etc).

PROGRESS: During the 15 month period terminating 1 April 1973, 47 drugs were evaluated for antimalarial efficacy in *P. cynomolgi*-infected rhesus monkeys. A tabulation of the drugs studied and their minimum curative doses is presented in Table 1.

Table 1.
Minimum Curative Doses of Experimental Antimalarial Drugs
In Rhesus Monkeys Infected with *Plasmodium Cynomolgi*

TYPE OF DRUG	WRAIR DRUG IDENTIFICATION NO.	MINIMUM CURATIVE DOSE (mg/kg)	TYPE OF DRUG	WRAIR DRUG IDENTIFICATION NO.	MINIMUM CURATIVE DOSE (mg/kg)
4-Aminoquinolines	WR 1544 (Chloroquine)	5.0	Pyridinemethanols	WR 148946	100.0
				WR 154904	3.16
8-Aminoquinolines	WR 2975 (Primaquine)	Not curative		WR 172435	10.0
	WR 161085	100.0		WR 175039	3.16
	WR 180411	31.6		WR 178919	10.0
				WR 182123	3.16
Quinolinemethanols	WR 30090	100.0	2,4-Diamino- quinazolines	WR 141871	10.0
	WR 166391	Not curative		WR 154928	1.0
	WR 171668	31.6		WR 158122	1.0
2,8-Trifluoromethyl Quinolinemethanols	WR 142490	10.0		WR 159412	0.1
	WR 177504	10.0		WR 162878	0.1
	WR 177602	10.0		WR 164104	0.1
	WR 183544	31.6		WR 180153	0.316
	WR 183545	100.0		WR 181953	1.0
	WR 183546	31.6			
	WR 183606	31.6	Miscellaneous	WR 448 (Dapsone)	10.0
	WR 184806	10.0		WR 25187 (Prodigiosin)	Ineffective
				WR 49808 (Menoctone)	Ineffective orally
Phenanthrenemethanols	WR 122455	7.0		WR 150008	31.6
	WR 143803	100.0		WR 178340	Ineffective
	WR 146459	31.6		WR 178448	10.0
	WR 150726	31.6		WR 179305	31.6
	WR 165355	10.0			
	WR 165533	31.6			
	WR 171669	3.16			
	WR 175412	3.16			
	WR 178979	10.0			
	WR 185020	31.6			
	WR 190420	31.6			