

Reprinted from AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE

Vol. 3, No. 2, March, 1954

*Printed in U.S.A.*

THE SUPPRESSIVE TREATMENT OF MALARIA IN A RURAL  
VILLAGE WITH PRIMAQUINE AND PLAQUENIL

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# THE SUPPRESSIVE TREATMENT OF MALARIA IN A RURAL VILLAGE WITH PRIMAQUINE AND PLAQUENIL

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For many years we have been trying several of the new antimalarial drugs. Our object in treating rural malaria is the saving of labor days and the improvement of school attendance rather than a full course of treatment directed at complete eradication of the parasites. We have had such good results in the mass treatment of rural villages with chloroquine (Aralen) that we have hesitated to change to primaquine or any of the newer drugs. Some writers say that the suppressive effect of chloroquine is superior to that of primaquine and that toxicity is less apparent. During the past two years Col. John R. Wood, M.C., Chairman, Medical Research and Development Board, Office of the Surgeon General, has suggested to our home office in Washington, D. C. that we try out primaquine in the dark and black skinned races. Some evidence had accumulated that these races are more sensitive to the toxic effect of the drug than others. Experience with other 8-aminoquinolines suggested that hemolytic anemia might occur if the drug were given over a long period of time.

We employed a tablet containing 30 mg. of primaquine and 300 mg. of Plaquenil, kindly furnished by Winthrop-Stearns, Inc. Plaquenil is similar to chloroquine but may be less toxic. The combined tablet saves giving two separate tablets on treatment days and facilitates the use of both types of drug. Little was known about the tolerance of children to primaquine at the start of this study. We could not afford to leave children out of the trial because our surveys for many years on rural communities have always shown that the thick blood film rates in children are almost always twice or two and a half times as high as in adults, so we naturally wanted to include all ages. The tablets were scored so that they could be easily broken in half or even in quarters. The dosage was discussed with Dr. Alf Alving, Professor of Medicine, University of Chicago, and it was his opinion that the following dosage scheme would be tolerated by the dark skinned races of all ages and would probably be effective in preventing relapses due to vivax malaria. The composition of the new tablet is shown below in terms of primaquine base and chloroquine base, to be given in a single dose each week for about six months (Table 1).

We have used half a tablet each week for those weighing about 90 pounds, a quarter of a tablet for those under this weight but above six months of age; the adults were given a whole tablet each week.

We received the drug in June, 1952, but were delayed for some time before we could find a satisfactory location for the test. We wanted a place with a high rate of malaria where no control measures were in use, such as mosquito breeding control, house sprays with DDT and the use of antimalarial drugs in the schools. We investigated 15 places within a half day's motor car travel of Panama with-

TABLE 1

*Dosage of primaquine and Plaquenil used, in a combined tablet*

BODY WEIGHT, lb.	PRIMAQUINE, mg.	PLAQUENIL, mg.
15 or less.....	5	50
15 to 45.....	10	100
45 to 90.....	15	150
90 or over.....	30	300

out finding a suitable place although a few years ago all of these places had a high blood-film rate.

On August 6, 1952, we surveyed Rio Indio, a village about 20 miles up the Atlantic coast from the western boundary of the Canal Zone, located at the mouth of a river by the same name. Thick blood films were made from 92 people and 49, or 52.2 per cent revealed malarial parasites: *P. falciparum* in 36, *P. vivax* in 9, *P. malariae* in 3, and a mixture of *P. falciparum* and *P. vivax* in one. There were 42 adults and 50 children under 15 years of age. Fifteen adults and 34 children were positive for parasites. Treatments and taking of blood films weekly were begun September 11, 1952. Motor car transportation was provided by the Army from Panama City to Gatun where an Army jeep was used from Gatun to Salud; from this point to Rio Indio it was a two hours' walk on a sea-coast trail.

As the weekly visits were made, the names in the field record book increased until at the close of the period there were 186 names. However these people have their farms spread out over several miles of the river valley and attendance was very irregular for many of the people because of heavy rains and the planting and harvesting periods. There were 93 people with regular attendance on treatment days over a sufficient period, although many were not treated for the entire time. We have taken for our analysis those who were treated regularly from 20 to 26 weeks (Table 2).

It took about three weeks of suppressive treatment before most of the weekly blood-film surveys were reported as negative. After October 1 only six of the

TABLE 2

*Number of persons receiving drugs for each treatment period*

REGULAR TREATMENTS	NUMBER OF PERSONS SO TREATED
<i>weeks</i>	
26	15
25	14
24	17
23	16
22	11
21	5
20	15

regularly treated individuals were found positive for parasites. They are listed as follows:

1. Eduardo Lanson, age 2 years. On August 6, Sept. 10, 18 and 25 his blood was positive for *P. falciparum*. On October 10 he was again positive for the same parasite but was negative for the rest of the period.

2. Jacinto Lanson, age 1 year. On August 6 his blood film showed *P. falciparum* parasites, and on Sept. 11 and 25 his film contained both *P. falciparum* and *P. vivax*. He later became positive for *P. falciparum* November 6, Jan. 22 and Jan. 29. We have no way of knowing how many treatments this child retained and absorbed for as a rule he would immediately regurgitate the dose. He would do the same with small pieces of candy and pieces of soft sweet milk chocolate. The mother took some of his treatments home with her and occasionally he retained a dose.

3. Berta Valdez, age 3 years. On August 6 her blood film contained *P. falciparum* parasites, on Sept. 11 a mixed infection of *P. falciparum* and *P. vivax* was found while on Sept. 25 only *P. falciparum* appeared. On October 2 and 10 *P. falciparum* parasites were present but for the rest of the period no parasites were found.

4. José de la C. Valdez, age 16 years, was negative on all of the early surveys but on February 26, 1953, *P. vivax* parasites appeared in the film.

5. Marcela Vallejos, age 8 years. The initial survey on Aug. 6 revealed *P. vivax* parasites. On Sept. 11 some parasites of *P. falciparum* appeared. October 2 a few *P. falciparum* parasites were recorded but after that date all films were negative.

6. Miguel Vallejos, age 3 years. The initial survey of Sept. 25 showed few *P. falciparum* parasites and the same species appeared in the film on October 17. All others were negative.

During the period between October 2 and March 5, of those who had received regularly from 20 to 26 weekly treatments, 5 of 38 children (13.2%) and one of 12 adults (8.3%) showed positive films.

*Relapses or the reappearance of parasites during the period of treatment.* There were 6 cases, 3 with *P. falciparum*, 2 *P. falciparum* and *P. vivax* and one, *P. vivax*. The last case did not reveal parasites in the blood-film surveys until very late during the six months treatment.

The suppressive use of the drug ended March 5, 1953 but another blood film survey was made 16 weeks later on June 25, 1953, to obtain further information. This survey included 95 people and 19 of them (20 per cent) had parasites in their blood films. There were 53 children with 13 positives (24.5 per cent), and 42 adults, 6 of whom were positive (14.3 per cent). Fifteen of these positives had been regularly treated for from 20 to 25 weeks. All were children except one. The species of parasites found were 8 *P. falciparum* cases and 7 *P. vivax*.

#### DISCUSSION

During the six months course of treatment no toxic results were noted in these dark skinned people, either in children or adults. The treatment results

were good but no better than we would have expected to get with chloroquine alone. The parasites disappeared from thick blood-films in about three weeks except for the rare individual.

A letter dated March 11, 1953 was received from Col. John R. Wood in which he states that his early apprehensions regarding the use of this combined dosage in dark skinned races were unfounded. Dr. Alving in Chicago has since used the same combination of the drugs in the same dosage used at Rio Indio on 100 Negroes for nine months in Stateville Prison, Joliet, Ill. He was unable to detect any evidence of toxicity.

#### SUMMARY AND CONCLUSIONS

Ninety-three dark-skinned individuals (42 adults and 51 children) living in a highly malarious village in Panama, were given suppressive treatments weekly with a combination of primaquine and Plaquenil for from 20 to 26 weeks. After the first 3 weeks, only 6 were found positive for malaria parasites on weekly examination of thick blood-films, although the percentage of positives was 52.2% at the start. No toxic results were noted either in children or adults.

#### ACKNOWLEDGMENTS

Thanks are due to the Headquarters, U. S. Army, Caribbean, 25th Preventive Medicine Survey Detachment, for the motor car transportation provided for the technical staff from Panama to Salud and for the services of Hector Baxter, a technician from the office of Lt. Col. F. S. Blanton. Hector Baxter has for several years been personally acquainted with the inhabitants of Rio Indio and he served as the recorder of all these people who were under treatment and blood-film surveys.

The technicians of the Gorgas Memorial Laboratory who participated in the work were: Lionel de Sousa and Néstor González. Both of these men have had many years of experience in preparing and examining such blood films.