# PRELIMINARY SURVEY FOR CHLOROQUINE RESISTANT MALARIA IN PARTS OF NORTH SUMATRA, INDONESIA

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## INTRODUCTION

There is little published information on the status of chloroquine resistant malaria in Indonesia, particularly on the island of Sumatra. *Plasmodium falciparum* resistant to chloroquine occurs in the neighboring countries of Thailand (Bourke *et al.*, 1966; Cadigan *et al.*, 1968), Peninsular Malaysia (Sandosham *et al.*, 1967; McKelvey *et al.*, 1971; Andre *et al.*, 1972; Dondero *et al.*, in preparation), Sabah, North Borneo (C.M. Han, and Y.S. Huang pers. comm; Clyde *et al.*, 1973), and Singapore (Colbourne *et al.*, 1970). It therefore seemed reasonable to expect that such resistance may occur among the indigenous races in Indonesia. Indeed, recently a case of suspected chloroquine resistant *P. falciparum* in Central Java was reported (Hughes, 1974).

A preliminary survey for chloroquine resistant malaria was undertaken in several parts of North Sumatra.

## DESCRIPTION OF THE AREA

Although *P. vivax* was considered common in North Sumatra, little *P. falciparum* had been previously encountered except on Nias Island (Public Health Institute, pers. comm.). In April-May 1973, with the support of the provincial Health Department, four areas accessible from Medan were surveyed (see Map).

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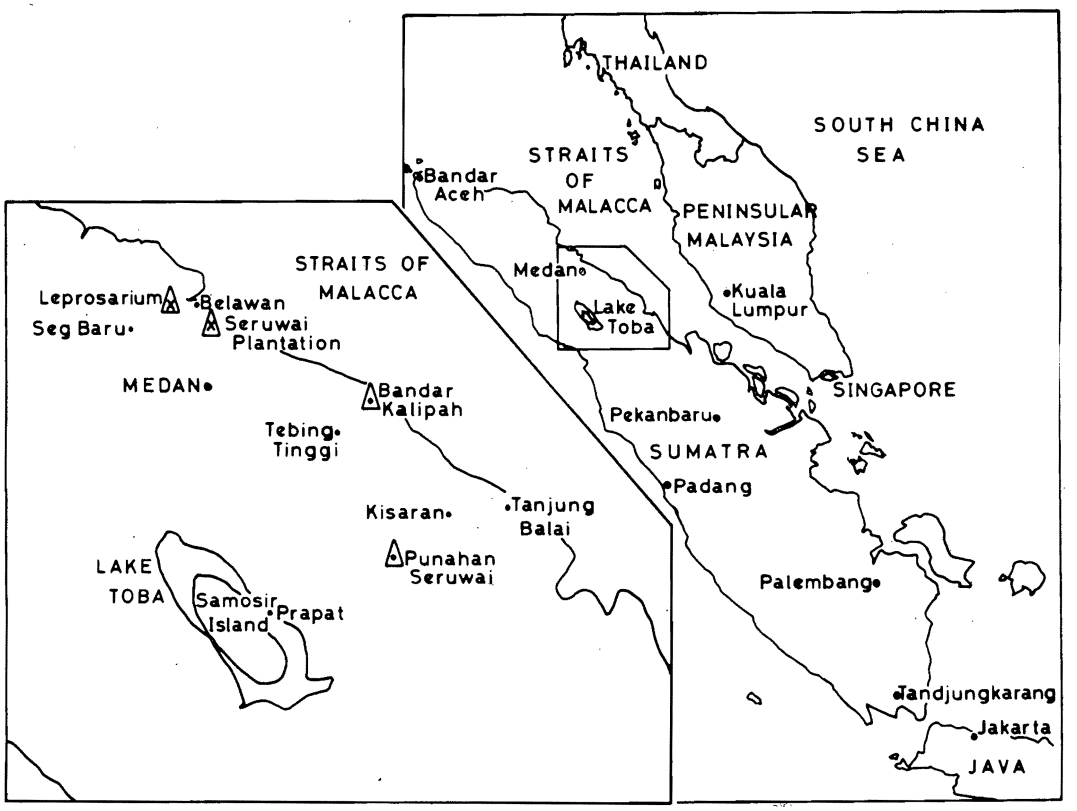
Seruwai Plantation in Labuan Deli, near the port of Belawan, 30 km north of Medan is a flat, low-lying coconut plantation of about 600 hectares, bordered on three sides by coastal mangrove swamp. Larval mosquito collections (Parsons *et al.*, in preparation), revealed numerous *Anopheles sundaicus* breeding in many areas of the plantation, including near the workers' houses. In addition the nearby government leprosarium with about 200 residents was examined during the second part of the study.

The second site, Kg. Seg Baru, in Hamparan Perak, about 35 km north west of Medan, is a riverine kampung where rice and fruit are raised. Kg. Bandar Kalipah, in Deli Serdang, near Tebing Tinggi, about 90 km south-east of Medan is a rice growing kampung. Punahan Seruwai, at Pemetang Siantar, is a large rubber plantation approximately 20 km interior from Kisaran and some 200 km south of Medan.

## MATERIALS AND METHODS

For preliminary surveys, thick blood smears were dried overnight, stained 45 min with dilute Giemsa (2% in buffered water, pH 7.2), and microscopically examined under oil immersion for 100 high powered fields. For resistance studies 200 fields were examined. Parasites were counted against leukocytes, assuming an average of 8500 leukocytes per c.mm. Personal data, including name, age, and house number were recorded for all subjects. Spleen rates were




Map of Sumatra, Indonesia, showing study area. (Triangles mark the survey sites.)

based on examination of children aged two through nine years.

Aside from the initial screening test in April 1973 at the time of the preliminary malaria survey, the proposed 28 day test was to have been conducted in January 1974. However, an unanticipated low malaria prevalence at that time and logistical considerations limited the study to a 7-day screening test, the WHO Standard Field Test (WHO, 1967; 1973), somewhat modified to suit local conditions. Subjects found positive for malaria were weighed and personally administered a 3 day, 25 mg/kg course of non-enteric coated chloroquine (Avloclor, Imperial Chemical Industries). Repeat duplicate thick blood smears were made just before treatment was initiated. Urine was collected before and on the last day of treatment and examined for chloroquine (Wilson and Edeson, 1954). Follow-up blood examination was made on day 7 in the preliminary survey, and on days 6 and 7 in the later survey. Asexual parasitaemia on day 7 in a subject who had been given full treatment and whose urine became positive for chloroquine, was considered to indicate chloroquine resistance.

Entomological surveys, especially with regard to anophelines, were conducted at the main study site, Seruwai Plantation, and in four other areas (Parsons *et al.*, in preparation).

## RESULTS

As shown in the table, in the initial survey only Seruwai Plantation had enough malaria

Results of malaria blood surveys, North Sumatra, Indonesia.

| Place + Date | Group composition | No. exam. | Malaria pos. | No. *falcip.* | No. *vivax* | Spleen rate |
|---|---|---|---|---|---|---|
| Seruwai Plantation, Labuan Deli (April, 1973) | 50 adults, plus all non-working children | 380 | 40 (10.5%) | 30 | 10 | 8.2% |
| Kg.Seg Baru, Hamparan Perak (April, 1973) | villagers of all ages | 145 | 0 (0%) | 0 | 0 | 0% |
| Kg. Bandar Kalipah Deli Serdang (April, 1973) | villagers of all ages | 252* | 7 (2.8%) | 3 | 4 | 1.5% |
| Punahan Seruwai Rubber Estate, near Kisaran (May, 1973) | children under 15 yrs | 240 | 5 (2.1%) | 0 | 5 | Not exam. |
| Seruwai Plantation, Labuan Deli (Jan, 1974) | entire estate population | 584 | 14 (2.4%) | 8 | 6 | 8.4% |
| Leprosarium, Belawan (Jan, 1974) | children | 58 | 2 (3.5%) | 0 | 2 | 2.7% |

*2 night blood found positive for *Brugia malayi*.

to warrant further study: 7.9% of the group had *P. falciparum*, 2.6% had *P. vivax*, and there was an 8.2% spleen rate.

**First Chloroquine Resistance Test:** Subjects found to have malaria in the initial survey at Seruwai Plantation were screened for chloroquine resistance.

Treatment and follow up of 28 cases of asexual *P. falciparum* parasitaemia met the test criteria although only 12 of these had parasite counts over 1000 per c.mm. Two additional subjects were excluded, one because of difficulty swallowing medications, one because of negative post treatment urine. Ten subjects with *P. vivax* were also tested. All blood samples were negative for asexual parasites on the 7th day.

**Second Chloroquine Resistance Test:** At the survey on Seruwai Plantation in January 1974, little malaria was found (see table). Eight subjects with *P. falciparum* trophozoites, including one with a mixed infection (only two with counts over 1000 per c.mm) and six with *P. vivax* were treated and followed up. All blood specimens were negative for parasites on days 6 and 7.

At the leprosarium no *P. falciparum* was found. The *P. vivax* rate was 3.4%. These cases were treated but not included in the study.

## DISCUSSION

The unexpectedly low prevalence of malaria at the time of the proposed 28-day study prevented a more definitive search for chloroquine resistance. A total of 36 subjects with asexual *P. falciparum* infections, only 14 of which had counts in excess of 1000 per c. mm., plus 16 subjects with *P. vivax* were treated and screened for asexual parasites after 7 days. In this limited series there was no evidence of chloroquine resistance in either species.

While a 7 day follow-up period can be expected to demonstrate the more serious R-II and R-III type resistance, it is inadequate to detect late recrudescing R-1 resistance, which is the type most commonly encountered in Peninsular Malaysia (Dondero *et al.*, in preparation). Moreover, old infections, as were some in this study - low density parasitaemia in generally asymptomatic hosts, are not good for demonstrating resistance *in vivo*, since minimal therapy may be sufficient.

If sufficient numbers of *P. falciparum* infections could be found in accessible areas of North Sumatra a test of their response to

chloroquine in a 28 day study could be most interesting. For in addition to the paucity of information on either resistance or sensitivity of *P. falciparum* in Indonesia generally, the parasites in this area probably have had little exposure to the drug. According to informal information, chloroquine seems not to have been long or heavily used in North Sumatra, quinine being a local product and more economical. Therefore it is suggested that little "chloroquine pressure" has been exerted, which might have encouraged the appearance of, or increased the natural frequency of resistance. The physicians in this study with local experience with chloroquine therapy have not encountered frequent treatment failures or early (2-3 weeks) "relapses". However, if and as chloroquine becomes more widely used in treatment, and particularly in prophylaxis, the emergence of chloroquine resistant strains may become more apparent, as it has in many parts of Southeast Asia.

## SUMMARY

Preliminary malaria prevalence rates were ascertained in four areas of North Sumatra accessible from Medan, in search of suitable sites for a 28-day chloroquine resistance study. Only one area had appreciable malaria, but even there the infection rate had dropped by the time of the resistance study.

Two short (7-day follow-up) *in vivo* field surveys for chloroquine resistance were conducted. Thirty-six *P. falciparum* infections including 14 with parasite counts greater than 1000 per c.mm plus 16 *p. vivax* infections were successfully tested, revealing no evidence of resistance to chloroquine, at least at the R-II or R-III level. Implications and limitations of this survey were discussed.

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