

Subtitle: A Preliminary Study of Diagnostic and Clinical Problems Associated with Mesoendemic Malaria in Southeast Thailand.

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A long-term longitudinal community-level study of malaria is planned. Preliminary to this, an investigation was carried in a mesoendemic area of Trad province, S.E. Thailand in order to determine some of the problems that might be encountered and to clarify the objectives of the larger study. In addition to the logistical and community relationship problems of such a study, information was sought on such factors as (1) the best method for microscopic detection of the parasite, (2) the correlation between presumptive clinical diagnosis and microscopic confirmation and (3) serum biochemical changes in the mild to moderate infections that would not normally warrant hospitalization.

Methods

Because of the brief time available a comprehensive epidemiologic study was not undertaken. At the community level, fever cases and controls were examined and a small survey of 61 schoolchildren carried out in two schools. The children in the first school were selected for those who the teacher said had not been feeling well and in the second school those that had an enlarged spleen as well as a history of chronic illness. In the village study a clinical work-up was obtained on 36 fever cases. The blood films were examined immediately and from those found positive, blood was drawn for serum chemistries (see Table II). Serum from controls was obtained at the same time. The clotted blood was centrifuged in the field and sera samples frozen in dry ice. The chemistries were carried out within a week of collection. For the schoolchildren only blood films and examination for splenomegaly were carried out.

Results and Discussion

1. Spleen rate in schoolchildren

Five of 26 children from the first school had an enlarged spleen. If this spleen rate in children was confirmed in a larger and unselected survey, then this area can be considered mesoendemic for malaria.

2. Parasitologic diagnosis.

For many years the accepted method of detecting plasmodia in low-density parasitaemias has been by examination of the thick blood film. Recently Dowling and Shute (1966) have questioned the efficacy of this technique. They reported that 60% to 90% of the parasites may be lost during dehaemoglobinization. Thus a thorough search of the thin film may reveal more scanty infections than thick film examination. These factors may be of extreme importance in detecting cases during the consolidation phase of malaria eradication as well as in confirming cases only clinically suspected to be malaria. For example, our examination of the records at Trad Provincial Hospital showed that on the average, 400 cases of malaria are treated each month although only about 100 of these are confirmed by blood smear.

In this present investigation a total of 82 smears (thick and thin) were obtained and stained by Romanowski's rapid method. Each slide was examined by three experienced microscopists. The first examination was made in the field with a search of the thin film only for 5 minutes. The second examination was in the laboratory with a thin film search of 20-30 minutes and independent confirmation of each positive. The third examination was carried out by a former Supervisor Microscopist of the Thai NMEP by searching the thick smear for 5-10 minutes (for method of detection used by the NMEP). The results are summarized in Table 1. It will be seen that the field examination of the thin films was as good or better than that of the thicks. The 20-30 minute search of the thin films was strikingly superior and revealed at least twice the number of parasitemias. Of the 20 positives 2 were P. vivax and these were picked up by all three methods.

However, gametocytes were found more frequently by thick smear examination (6 positive for gametocytes by thick smear and 4 positive by 20 minute thin smear examination).

Future study should resolve the question of what is the best method of examination for different purposes, e.g. survey, case finding, and detection of drug resistance. The problem of gametocyte carriers also deserves study. In this survey all were children (P. falciparum gametocyte carriers). Does this age group constitute the main reservoir in this region? What gametocyte density and other factors are involved in infecting the mosquito host?

3. Clinical Diagnosis of Malaria: Of the 36 patients evaluated clinically, 18 were felt to have malaria on the basis of fever, chills, headache anorexia, nausea, and/or orthostatic hypotension. Eight out of these 18 had positive smears for malaria. A negative malaria smear in those patients with findings suggestive of malaria may be explained by treatment with antimalarial drugs, parasites too scanty on the day of study or other diseases mimicking malaria. The finding that of 18 patients considered to have a disease other than malaria 4(3 with URI, 1 with mumps) had circulating parasites is disturbing and raises the possibility that presumptive treatment should be given to a larger group of patients, accepting that many will eventually prove not to have malaria. Formulation of the problem: In an area of known chloroquine-resistant falciparum malaria, where presumptive therapy is probably inadequate and may potentially increase the problem of chloroquine resistance how can the case identification best be carried out? Radical treatment may have to include drugs such as quinine and because of expense and side effects would necessitate good case identification. Possible questions to be answered in the field:

- 1) How many patients with the clinical diagnosis of malaria but with negative smears will prove to have malaria if smears are taken on subsequent days?
- 2) How many patients with clinically identified diseases other than malaria, actually have malaria either alone or in addition to the other disease?
- 3) In a community subject to mesoendemic malaria and where the majority of infected individuals have scanty parasitemias what is the rate of asymptomatic infections? At what rate and under what conditions do the asymptomatic convert to a clinically active disease?
- 4) What is the response of falciparum malaria to presumptive and radical treatment with chloroquine in this area?

4. Serum Biochemical Changes: Other studies of serum biochemical changes in malaria have usually studied a hospitalized population. Our aim was to evaluate changes resulting from a milder disease. The only significant changes caused by mild malaria were a lower serum cholesterol and albumin (Table II.) These changes have been observed in more severe malaria and in animal malarias.

The etiology of these abnormalities has not been studied. The serum sodium, potassium, and chloride were all normal, whereas in more severe disease they are low. One patient with vivax malaria had an elevated BUN (27.5 mg/100 ml), creatinine (1.5 mg/100 ml) and SGPT (51. S.F. units). One patient with falciparum malaria had an elevated SGOT (64 S.F. units). However because these values were normal in the great majority, the averages were not significantly different. In this small sample it would not be valid to necessarily attribute these individual changes to malaria. The gamma globulin was not significantly different, although in other studies it has been shown to be elevated. It may be that in an endemic area the level of gamma globulin is high in the entire population as shown in this small sample.

Table I — The readings on 82 malaria smears by 3 methods.

	Smear+	Smear—	% positive
Field examination of thin smear for 5 minutes	12*	70	15
Thick smear for 5—10 minutes	7*	75	9
Thin smear for 20 minutes	20*	62	24

* Two patients by each method had P. vivax. The rest were P. falciparum.

TABLE II — The Comparison of Average Serum Biochemistries between Malaria Patients and Healthy Controls in a Thai Village.

	Malaria Patients	Healthy Controls	"p" Value
Number	10	7	
Average age	30.7	33.6	
Hematocrit (%)	40.3	41.4	N.S.
Serum Sodium (mEq/L)	138.7	140.6	N.S.
Serum Potassium (mEq/L)	3.94	3.89	N.S.
Serum Chloride (mEq/L)	102	103	N.S.
Serum Creatinine (mg/100 ml)	0.92	1.0	N.S.
BUN (mg/100 ml)	13.1	10.8	N.S.
Serum Cholesterol (mg/100 ml)	126	159	<0.02
SGOT (S.F. Units)	30.7	27.0	N.S.
SGPT (S.F. Units)	18.3	14.9	N.S.
Serum Alkaline Phosphatase (Sigma Units)	3.33	2.30	N.S.
Thymol Turbidity (Units)	7.23	8.43	N.S.
Bilirubin — Total (mg/100 ml)	0.55	0.40	N.S.
Direct (mg/100 ml)	0.11	0.16	N.S.
Total Serum Protein (g/100 ml)	7.45	7.46	N.S.
Serum Albumin (g/100 ml)	3.36	3.68	<0.01
Serum, α_1 Globulin (g/100 ml)	0.32	0.26	N.S.
Serum α_2 Globulin (g/100 ml)	0.59	0.59	N.S.
Serum β Globulin (g/100 ml)	0.85	0.84	N.S.
Serum γ Globulin (g/100 ml)	2.39	2.09	N.S.