

Title: Study of Hemorrhagic Diathesis in Malaria

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OBJECTIVE: Although purpura and other bleeding manifestations have been noted in malaria patients in the past, every few studies have been done on the pathophysiology of these disorders. A detailed study of clotting factors, disturbances in coagulability as well as other hemostatic mechanisms was instituted, using previously untreated patients with P. falciparum infections at Phrabuddhabat Hospital in central Thailand. Control subjects were relatives or friends of the malaria patients who had accompanied them to the hospital. Except that they were asymptomatic at the time of study, no health data are available on the control subjects.

PROGRESS: Forty-two malaria patients were studied on admission and twenty-six of these were studied at intervals throughout hospitalization. The patients were predominantly males (83%). Twenty-three control subjects were studied on whom 48% were males. The laboratory tests are incomplete at the moment but the following data are available.

Jaundice was noted in ten patients, palpable liver and spleen in twenty-four. The tourniquet test was positive in three patients (two male, one female) and bleeding occurred in five male patients (only one of whom had a positive tourniquet test). Of the five who bled, three had epistaxis, one had subconjunctival hemorrhage, one (with positive tourniquet test) had purpura and bleeding from the mouth. Approximately 25% were treated with chloroquine alone, 37% with quinine alone and 37% with chloroquine plus quinine.

The mean hematocrit of the patients is lower on admission than in the control group (Table 1). The mean value in patients continues to decrease through the fifth hospital day (Table 2). In only six of the forty-two patients did it rise by the fifth day of hospitalization.

An abnormal level of reticulocytosis was found in nine cases, most of which had marked anemia. Although the mean reticulocyte counts of the patients were within the normal range, 79% of the patients had a count greater than 0.1% compared to 26% of the controls. High reticulocyte counts were observed at the time of admission and they continued to rise throughout hospitalization.

Prolonged bleeding time was demonstrated in four out of forty-two cases; all four had marked thrombocytopenia. Venous clotting times were within the upper limit of normal.

A screening coagulogram has been done in ten cases of malaria and in eight controls (Table 3). There were abnormalities in the prothrombin time and partial thromboplastin time of patients but the thrombin time was within normal limits. Recalcification time were within normal limits. These data reflect defects in the first and second stage of the blood clotting mechanism, possibly in the prothrombin complex. Assay of the individual clotting factors is being done.

Indirect platelet counts were done on the first thirty patients and, after a phase microscope became available, direct counts were done on the other twelve patients. As can be seen from Tables 1 and 2, the

mean platelet count of the patients was markedly reduced on admission but increased rapidly into an almost normal range about one week after initiation of anti-malarial therapy. (Table 2).

Chemistry determinations have only been completed on eleven cases. Of these, seven had increase bilirubin (chiefly in the direct value), eight had increased thymol turbidity, only one had a slight rise in alkaline phosphatase, ten had a rise in SGOT, and three in SGPT. The levels of SGPT were considerably lower than those of SGOT.

Table 1

Hematology Values of Malaria Patients and Controls

	Male		Female	
	Control (11)	Patients (36)	Control (12)	Patients (8)
Mean values				
Hematocrit	38.4	33.4	35.3	29.1
Reticulocytes	0.1	0.49	0.15	0.56
Bleeding time	3'17"	4'23"	2'59"	5'19"
Clotting time	7'13"	8'16"	6'36"	9'6"
Platelets—indirect	510,000	212,000*	472,000	298,000***
—direct	261,000	77,000**	240,000	85,000****

* 27 patients
 ** 3 patients
 *** 8 patients
 **** 4 patients

Table 2

Mean hematology values during hospitalization of twenty-six malaria patients

	Hospital Day			
	1	2	4	8
<u>Males (21)</u>				
Hematocrit	34.5	31	28.2	26.4
Reticulocytes	0.49	0.54	0.57	1.1
Bleeding time	5'16"	4'51"	4'16"	3'54"
Clotting time	8'52"	8'34"	8'3"	7'37"
Platelets*				
indirect	167,000	167,000	197,000	443,000
direct	77,000	106,000	138,000	215,000
<u>Females (5)</u>				
Hematocrit	29.1	25.4	20.5	23
Reticulocytes	0.56	0.56	1.23	1.2
Bleeding time	6'15"	5'43"	4'25"	3'51"
Clotting time	10'8"	8'53"	8'37"	7'46"
Platelets**				
indirect	298,000	298,000	308,000	342,000
direct	85,000	89,000	115,000	237,000

* 13 studied by indirect method, 8 by direct method

** 2 studied by indirect method, 3 by direct method

Table 3

Mean Values of Screening Coagulogram

	Control (8)	Patient (10) Hospital Day			
		1	2	4	8
Prothrombin time	100%	64%*	71%	71%	79%
Partial thromboplastin time	81.5"	105.3"	95.4"	110.5"	98.4"
Recalcification time	91.0"	103.3"	107.7"	106.4"	88.0"
Thrombin time	3"	3"	3"	3"	3"

* 4 out of 10 cases had prothrombin activity below 60% of normal control.