

## The Fate of Fibrinogen in Malaria

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**OBJECTIVE:** There is growing evidence that intravascular coagulation may be important in the pathogenesis of malaria. The objective of the present study is an evaluation of fibrinogen disappearance in Plasmodium coatneyi infected monkeys. If evidence for intravascular coagulation is found, efforts to study the phenomenon histologically will be made.

**DESCRIPTION:** Rhesus monkeys (Macaca mulatta) were used. Fibrinogen, prepared from the plasma of normal monkeys by the method of repeated salt fractionation by 2.05 M ammonium sulfate, was labelled with radioactive iodine (I-131) and injected intravenously into the monkeys to be studied. Blood samples were taken at various intervals for the determination of plasma radioactivity. Further details of the procedure were presented in the SMRL Annual Report 1969. Plasma volume and fibrinogen concentration were determined by standard methods. To obtain estimates of the amount of fibrinogen being degraded, fibrinogen turnover rates were calculated according to the expression  $V_p C_f K_f$  where  $V_p$  is the plasma volume,  $C_f$  the plasma fibrinogen concentration, and  $K_f$  the first order rate constant for I-131 fibrinogen disappearance. Urine samples were also collected for radioactivity measurements.

**PROGRESS:** A control study of fibrinogen metabolism was done in six normal monkeys. Plasma radioactivity, expressed as the percentage of the initial value at zero time (by extrapolation) was shown to have a biological half life between 30-39 hours. The cumulative radioactivity excreted in the urine (expressed as the percentage of the injected dose) in 6 days varied from 42% to 77% of the injected dose.

In three monkeys (MS67, PK20 and PK28), infected with Plasmodium coatneyi, the study was performed at 13, 15 and 16 days after the infection respectively. The parasitemias were 0.7%, 0.8% and 0.8% and the hematocrits 23%, 29% and 20%. Plasma radioactivity was shown to have a biological half life of 24, 32 and 34 hours; i.e., two of the three monkeys gave values within the normal range. The plasma volumes, fibrinogen concentrations and fibrinogen turnover rates for the normal and infected animals are given in Table I. Both plasma volume and plasma fibrinogen concentrations were higher in two of the three infected animals. Earlier studies (SMRL Annual Report 1968) also indicated expanded plasma volumes during chronic coatneyi malaria. Thus it appears that on a weight basis, more fibrinogen was degraded in the infected animals than in the controls; this is expressed in the table in terms of fibrinogen turnover rates. More data is required to determine whether or not these changes are representative of P. coatneyi infected monkeys in general.

Urinary excretion of I-131 in the infected monkeys was similar to that in the controls. Thus, in six days, 72%, 54% and 58% of the injected dose was excreted by the three monkeys.

**SUMMARY:** Fibrinogen turnover rates were greater in three monkeys with P. coatneyi infections than in control animals. These findings can be interpreted in terms of increased fibrin formation in the infected monkeys. Further study is needed to evaluate the generality of the observation.

Table I. Fibrinogen turnover in normal and Plasmodium coatneyi infected monkeys.

Monkey No.	Weight Kg.	Plasma volume ml/kg	Plasma fibrinogen concentration mg/ml	Fibrinogen turnover rate mg/kg/hr
<b>Normal</b>				
MS 91	2.25	28.5	4.3	2.8
MS 92	2.40	46.5	3.0	2.7
MS 93	2.65	36.5	3.7	2.7
MS 95	2.70	35.3	2.3	1.9
PK 20	4.20	30.4	3.8	2.5
PK 28	4.90	40.7	2.1	1.5
<b>Infected</b>				
MS 67	6.83	44.5	3.5	4.2
PK 20	3.95	80.1	4.5	7.9
PK 28	4.90	57.7	11.4	13.4