

3. Title: The fate of fibrinogen in malaria.

Principal Investigators: Tan Chongsuphajsiddhi, M.D., Ph.D.
Ratanaporn Kasemsuthi, B.Sc.
Kanjika Devakul, M.D., Ph.D.

Associate Investigator: Prapit Vevatanasesth, M.D.

OBJECTIVE

There is growing evidence that intravascular coagulation may be important in the pathogenesis of severe malaria and also probably in drug resistance. This work was carried out to investigate further this phenomenon in monkey malaria and to relate it to other events of the infection such as the levels of plasma haemoglobin and liver and renal functions.

DESCRIPTION

Six rhesus monkeys (*Macaca mulatta*) were used in this experiment. Four were used for preparation of fibrinogen and the others were used in the study of fibrinogen metabolism. Fibrinogen, prepared from the plasma of normal monkeys, was labelled with radioactive iodine (I^{125} or I^{131}) and was then injected intravenously into other monkeys. Blood samples were taken at various intervals for the determination of plasma radioactivity.

Preparation of fibrinogen

Fibrinogen was prepared by the method of repeated salt fractionation by 2.05 M. ammonium sulfate.

Labelling of fibrinogen

Fibrinogen concentration in the solution was determined and then concentrated with carbowax to a concentration of about 40 mg per ml. The fibrinogen was labelled by mixing with iodine (I^{125} or I^{131}) at pH 8.5 adjusted by alkaline glycine buffer. The solution was then passed through an ion exchange resin column and dialysed against 1.62% trisodium citrate solution overnight at 2°C. Fibrinogen preparations were discarded when less than 90% of the protein was convertible to fibrin.

Radioactivity counting

The radioactivity of the plasma samples was counted in a well type scintillation counter.

Two monkeys, PK-3 and PK-35, were used in the study of fibrinogen metabolism. PK-35 was injected intravenously with 5 mg. of radioactive fibrinogen containing 20 μ c. of I^{131} . PK-3 was given drinking water containing 0.005% potassium iodide for 7 days before the experiment and was injected with I^{125} labelled fibrinogen.

PROGRESS

Only the study of normal control monkeys has been carried out to date.

Plasma activity in figures I and II is expressed as the percentage of the initial value at zero time (by extrapolation). In both monkeys there was a sharp fall in fibrinogen, during 6 hours to 24 hours. The half periods of fibrinogen in PK-3 and PK-35 were 57 and 24 hours respectively. This difference is probably due to the fact that in PK-35 we did not block the thyroid uptake of I^{131} with potassium iodide before the experiment.

The plasma volumes of PK-3 and PK-35 were 39.63 ml/kg and 39.3 ml/kg respectively. These figures are slightly lower than those of PK monkeys in a previous series determined by I^{131} labelled serum albumin (average=42.7 ml/kg).

Further investigations are in progress.

f this stud
other eve

dy on the
ed blood
ity seemec
estigate w
ere used :
P. coatney

blood vol
s monkey
gibbons, a
on. The
ff in one
rule out t
blood vo
n blood vo
and the l
level.

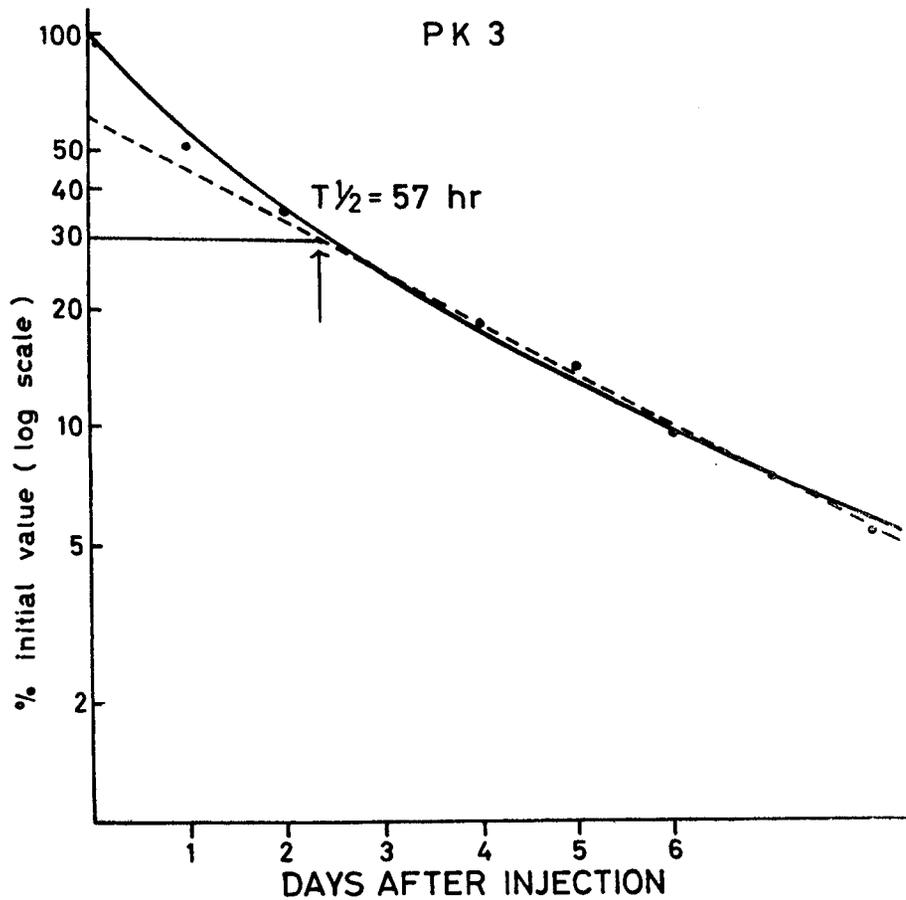


Fig. 1. Plasma I^{125} fibrinogen activity expressed as % of initial plasma activity

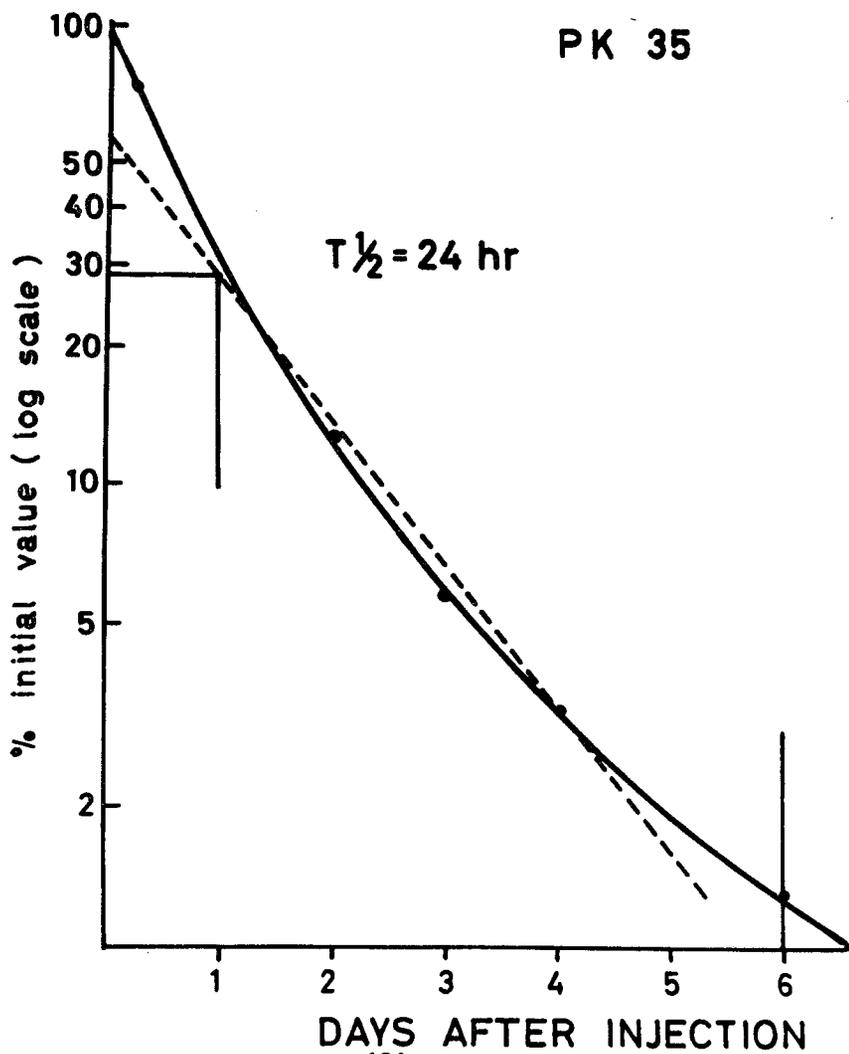


Fig.II. Plasma I¹³¹ fibrinogen activity expressed as % of initial plasma activity