

The Fate of Plasma Hemoglobin in Macaca mulatta Infected with Plasmodium coatneyi

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OBJECTIVE: The objective of this project is to study the fate of plasma hemoglobin in terms of the rate of removal from the plasma, the distribution in the liver, spleen, and bone marrow, and the urinary excretion in normal monkeys and in animals with Plasmodium coatneyi malaria.

DESCRIPTION: Rhesus monkeys (Macaca mulatta) were used in these experiments. The hemoglobin was labelled with Fe-59 or Cr-51; 120 μ c. of Fe-59 were injected intravenously into a donor monkey. After a suitable interval, 10-15 ml of blood were drawn and hemolyzed in distilled water. In the case of Cr-51, 10-15 ml of the recipient animal's blood was labelled with 50-80 μ c. of Cr-51 in vitro; after lysis, the hemoglobin concentration and the volume of hemoglobin solution were recorded. The labelled hemoglobin solution was injected intravenously to simulate intravascular hemolysis. Plasma radioactivity was measured at 10 minutes, 20 minutes, 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours and 24 hours after injection. The radioactivity of the spleen, the liver, the bone marrow and the urinary bladder was recorded by surface counting at 1/2 hours, 2 hours, 4 hours, 6 hours, 24 hours, 48 hours, 72 hours and 96 hours. Animals were kept in metabolic cages and urine was collected for 24-48 hours after the injection of labelled hemoglobin. The activity of the isotope excreted in the urine was calculated and expressed as the percentage of the dose given.

The monkeys were infected with P. coatneyi. Hemoglobin, hematocrit, red blood cell count and parasitemia in thick or thin blood smears were recorded daily. The study of hemoglobin metabolism was made when the hemoglobin and hematocrit decreased to about half of the initial value, usually about 20 days after the infection.

PROGRESS: The study was carried out in 9 rhesus monkeys (Macaca mulatta), 7 of which were normal and the other 2 infected with P. coatneyi. Two of the normal monkeys were injected with Fe-59 hemoglobin and all the others with Cr-51 hemoglobin.

It was found that in normal monkeys disappearance curves of Cr-51 and Fe-59 hemoglobin were similar. $T_{1/2}$ varied from 71 to 136 minutes. The activity of hemoglobin in the plasma 6 hours after injection was 6-11% of the administered dose and at 24 hours was 0-3.5% of the dose.

In two infected monkeys the study of hemoglobin metabolism was made at 19 and 21 days after infection when the parasitemia was 0.9% and 0.1% and hemoglobin was 5.5 and 6.9 gm% respectively. It was found that labelled hemoglobin seemed to leave the circulation more rapidly than in the normal animals ($T_{1/2}$ values were 63 and 69 minutes respectively). At 6 hours radioactive hemoglobin in the plasma was 10% and 5.9% of the administered dose and at 24 hours 3.7% and 2.5% respectively.

In the normal monkeys the activity over the liver and spleen rose rapidly during the first few hours after injection of hemoglobin and reached a maximum within 4 hours in every monkey; it then stabilized at about the same level up to 24 and 48 hours in two monkeys but decreased after 6 hours in five monkeys. There was not much activity in the bone marrow. Very high activity was detected over the urinary bladder at 6 hours but none could be detected at 24 hours.

In one infected monkey the result was similar to that observed in normal monkeys except that no activity could be detected in the liver at 48 hours. In the other infected animal there was some difference from

the normals. The activity over the spleen reached a maximum at 6 hours. The activity over the liver increased until 24 hours and then decreased to only about one-fifth of the 24 hour activity at 48 hours. The activity over the urinary bladder was low in comparison with that observed in the normal monkeys but activity could still be detected at 24 hours.

Studies on additional numbers of infected monkeys are in progress.

SUMMARY: Plasma hemoglobin clearance was compared in seven control normal and two P. coatneyi infected monkeys. Half life survival times in both infected animals were shorter than in any of the controls.