

## Red Cell Survival in Simian Malaria after Chemotherapy

Principal Investigators: Vithune Yuthasastr—Kosol, M.D.  
Carter L. Diggs, LTC, MC

Assistant Investigator: Thamma Sakulkaipeara

**OBJECTIVE:** Previous studies in this laboratory demonstrated shortening of red cell survival time in monkeys with chronic malaria due to Plasmodium coatneyi or Plasmodium inui. Erythroid hyperplasia of the bone marrow accompanied the accelerated erythrocyte destruction. The animals had very scanty parasitemias and it was suggested that the degree of red cell destruction was too great to be explained on the basis of direct destruction by parasites. However, since it is not possible to predict the degree of erythrocyte loss from the parasitemia data in quantitative terms, and because of the possibility of sequestered parasites not detectable in peripheral blood samples, the possibility of direct erythrocyte destruction by parasites could not be completely ruled out. The present study is designed to determine how long such accelerated destruction persists in the absence of parasitemia after chemotherapy; an abrupt return of erythrocyte survival time to normal values coincident with cessation of parasitemia would suggest direct destruction by parasites as a likely mechanism of red cell loss. On the other hand, persistence of accelerated destruction after cure would suggest a host mediated mechanism.

**DESCRIPTION:** Three chronic P. coatneyi infected rhesus monkeys, SP8, MS59, and PK21, and one chronic P. inui infected rhesus monkey, SP6, were studied for red cell survival before chemotherapy with chloroquine, 25 mg. base per kg. bodyweight intramuscularly over a three day period. Daily examinations for parasitemia were performed on each animal, and routine blood examinations were done on each animal once weekly. After the parasites completely disappeared from the peripheral blood smears, red cell survival studies were repeated periodically. (The techniques employed were the same as described in the SMRL Annual Report, 1968). Red cell survival was also studied in four normal control monkeys.

**PROGRESS:** Parasitemia disappeared after chemotherapy and daily blood films have remained negative up to the present. It is therefore assumed that radical cure was achieved.

The erythrocyte half-survival times ( $t_{1/2}$ ) in all animals at various times after cure are shown in Fig. 1. It can be seen that the values do not return to normal abruptly, but rather increase slowly over an extended period of time. Red cell survival is still abnormal in monkey MS59 at this time.

Other hematological changes were consonant with those in the erythrocyte survival times. Thus in the four animals, hematocrits ranged from 18–24% prior to therapy and range from 39–43% at present; hemoglobin rose from a range of 6.6–7.2 gms% to 13.3–13.6 grams% at present; reticulocytes, 7.5–14.2% prior to therapy, now range from 0.2–1.6%.

The red cell survival data (Fig. 1) suggested that survival times do not increase continuously after therapy, but that secondary decreases occurred during the observation period. The animals will therefore be studied further (until 200 post treatment days have elapsed) to determine whether or not the parameters measured are stable once normality is achieved.

These studies strongly suggest that the observed abnormal red cell destruction is not due to direct lysis by parasites but through some host mediated mechanism.

**SUMMARY:** Erythrocyte survival in four monkeys with chronic coatneyi or inui malaria returns to normal only gradually (130 days or more) after drug cure. It is suggested that this red cell destruction is not due to a direct lysis by the intracellular parasite.

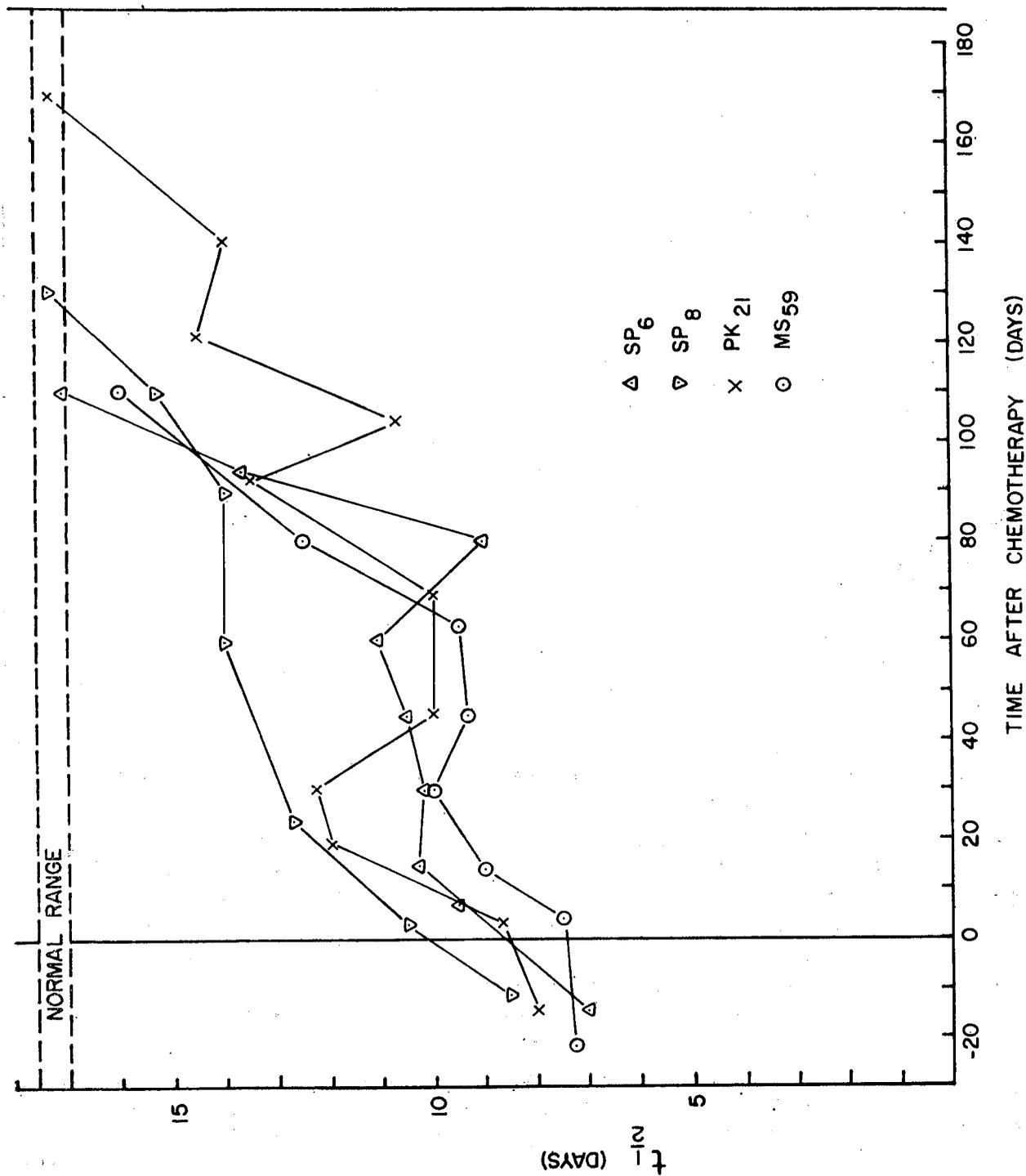


FIG. 1. ERYTHROCYTE SURVIVAL FOLLOWING CHEMOTHERAPY OF MALARIA IN RHESUS MONKEYS