

Title: HYPOCHOLESTEROLEMIA IN RODENT MALARIA (PLASMODIUM BERGHEI).

Principal Investigators: Robert S. Desowitz, Ph.D., D.Sc.

Bernhardt W. Langer, Jr., Ph.D.

Objective The occurrence of a hypocholesterolemia in primate malarias has been described by Desowitz et al., in a series of papers on the comparative pathology and host physiology of malarias (SEATO Ann. Prog. Report, 1967; Ann trop. Med. Parasit., 1968, 62, nos. 1 & 2). The decrease in serum cholesterol was particularly marked in malaria of the gibbon.

The cause of malaria-induced hypocholesterolemia is not known nor have any studies been carried out directed toward its elucidation. For obvious reasons, gibbons are unsatisfactory experimental animals for general use. The more convenient rodent malaria, P. berghei, was examined to determine whether it would be a suitable model.

Description The methods of parasite enumeration and serum cholesterol analysis have been given in previous reports (Desowitz et al., 1967, 1968 loc. cit.). I. Forty four adult white rats (weight: 100–175 gms) were inoculated intraperitoneally with infected rat blood containing approximately  $90 \times 10^6$  parasites. Groups of ten rats were killed on days 12, 19, 26 and 33 and a group of four rats on day 40. Ten uninfected rats were killed as controls on day 0. Heart blood was taken from each animal and the serum used for cholesterol analysis. II. Twenty rats were inoculated with approximately the same number of parasites as in Experiment I. In order to determine how rapidly cholesterol was reduced groups of rats were sacrificed at shorter intervals than in the first trial, i.e., five rats on days 3, 7, and 10. Ten uninfected rats again served as controls. III. Two hundred adult mice (weight: about 20 gms) were each inoculated with infected mouse blood containing  $1 \times 10^8$  parasites. Twenty five mice were sacrificed each day and blood obtained by cardiac puncture. Blood and serum from forty uninfected mice served as controls.

The principles of animal care as promulgated by the National Society for Medical Research were observed throughout these studies.

Progress The results of Experiments I & II (rat infections) are shown in figs. 1 and 2. The marked decrease in serum cholesterol to almost half the pre-infection level is apparent in both trials. The onset of the hypocholesterolaemia, sometime between the third and seventh days of infection (fig. 2) seems to be coincidental with the rise in parasitemia and consequent fall in hematocrit. After the 25th day the parasitemia was negligible and there was a progressive return of blood values towards normal. There was also a rise in cholesterol level but even by the 40th day it had still had not attained a pre-infection concentration.

In comparison to the rats, there was a wide variation in cholesterol levels between individual mice at all days of the experiment (fig. 3). In view of this, the decrease in cholesterol should be regarded as a trend rather than a significant change. Despite the much more severe course of infection and higher parasitemias in the mouse the average reduction in cholesterol was less than in infected rats (fig. 3). In the rat the average maximum reduction was to about 60% of the preinfection level while in mice it was approximately 77% of normal. The greatest decrease occurred between the 4th and 6th days.

Discussion It has been shown that anemia caused by a wide variety of etiologies, including malaria, is accompanied by a hypocholesterolemia (MacAdam and Shishkin, 1923, Quart. J. Med.; Rifkind and Gale,

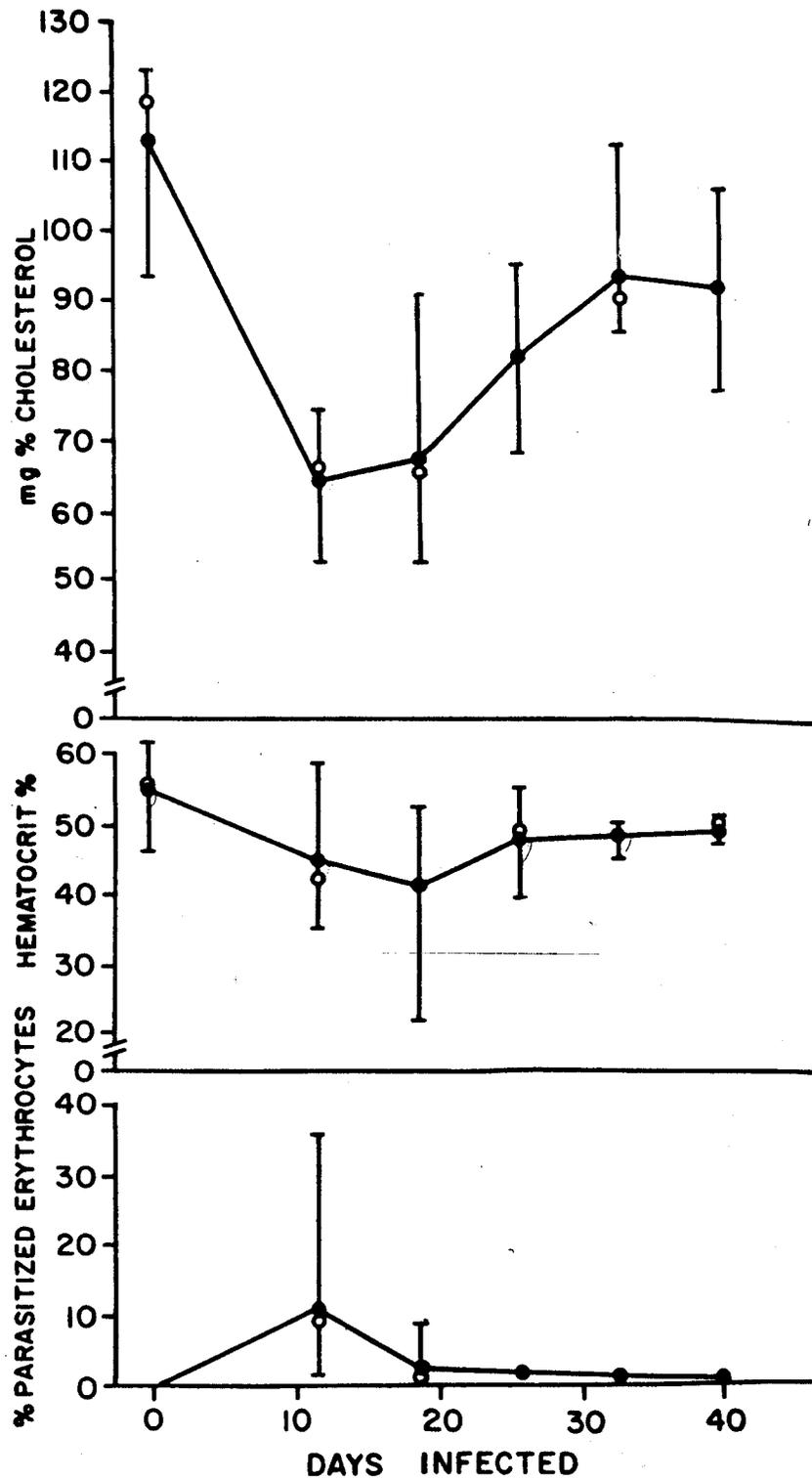


Figure 1. Experiment 1. Serum cholesterol, hematocrit and parasitemia during the course of *P. berghei* infection in rats.

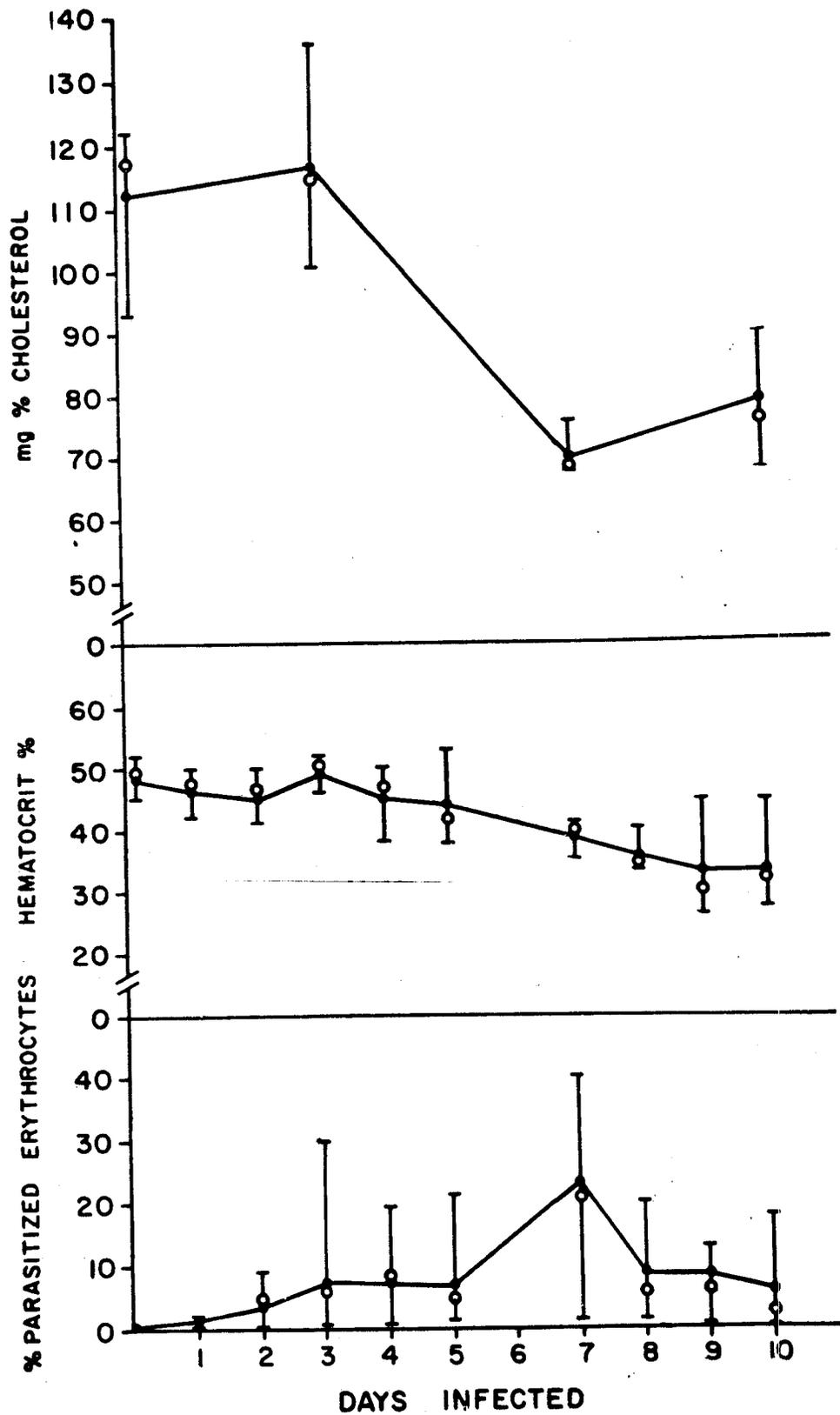


Figure 2. Experiment 2. Serum cholesterol, hematocrit and parasitemia during the course of *P. berghei* infection in rats.

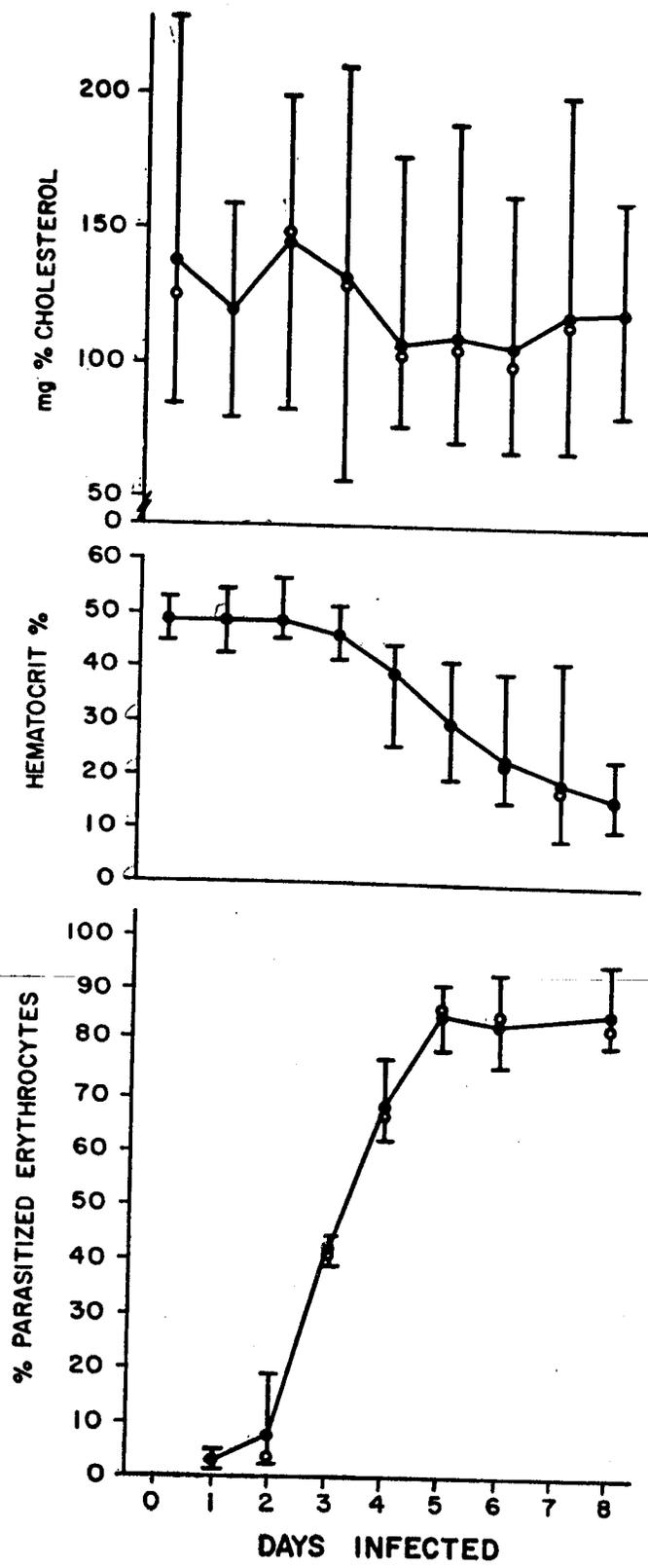


Figure 3. Experiment 3. Serum cholesterol, hematocrit and parasitemia during the course of *P. berghei* infection in mice.

Footnote to figures: | range  
 ● mean  
 ○ median

1967, Lancet). The mechanism responsible for lowering serum cholesterol in anemia is not known but its implications in the epidemiology of ischemic heart-disease have recently been discussed by Rifkind and Gale (loc. cit.). In underdeveloped countries there is a high incidence of anemia, much of it malaria-induced and the low incidence of ischemic heart disease in these tropical regions may be related to this. Elucidation of the underlying mechanism is therefore of obvious importance. The P. berghei infected rat which experiences a marked hypocholesterolemia for at least two weeks should provide a satisfactory experimental model for research in this direction.

Summary Serum cholesterol levels in rats and mice infected with Plasmodium berghei are described. There was a hypocholesterolemia in both animals but was more marked in the infected rat. The decrease in cholesterol appeared to be coincidental with fall in hematocrit.