

It was found that 10 mg/kg phenergan given to rabbits prior to intradermal inoculation of serum completely blocked PIF activity.

Discussion

It has been shown that the serum of monkeys infected with P. inui and P. coatneyi cause an increased vascular permeability when inoculated intradermally into the skin of the white rabbit. The permeability increasing activity of the serum was completely blocked by 10 mg/kg of an antihistamine, phenergan.

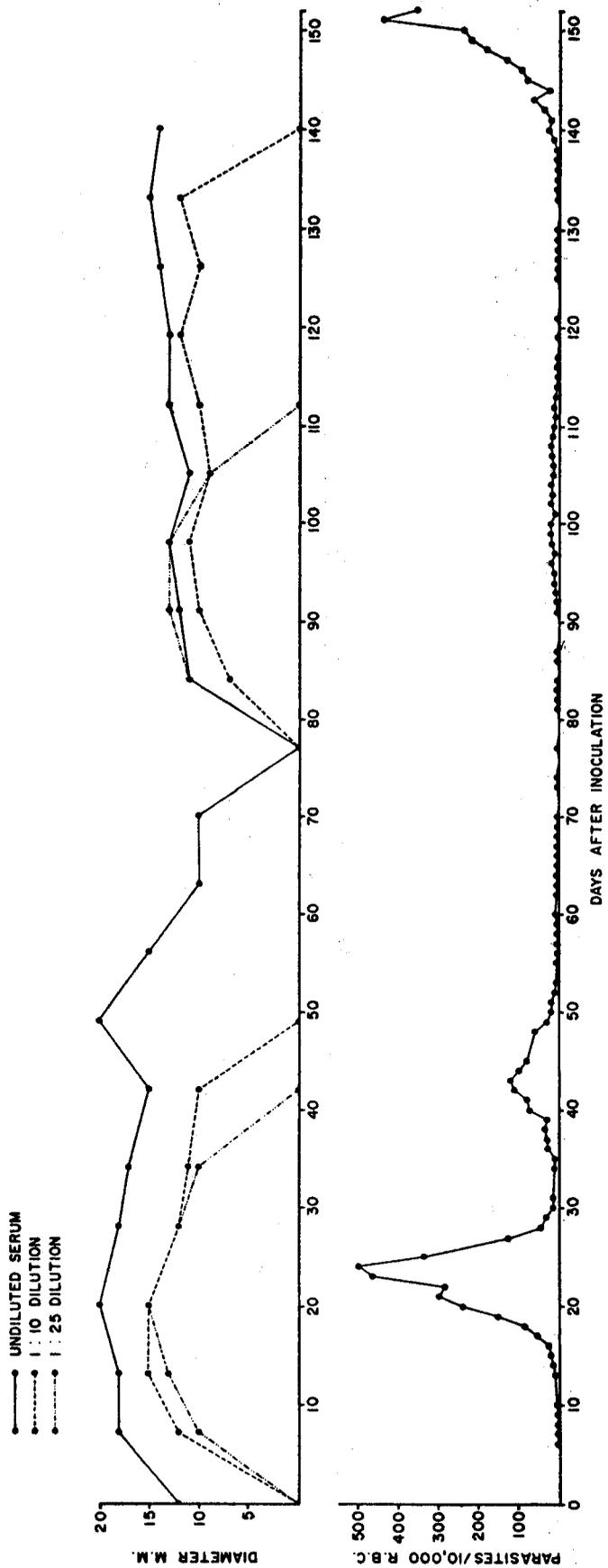
The factor responsible for causing the increased vascular permeability has not as yet been identified but may be a pharmacologically active peptide identical or related to the substances reported by Goodwin and Richards (1960) and Tella and Maegraith (1962, 1963). Whether the PIF is the same substance that is present in normal uninfected serum in low concentration or is a new substance that appears only with infection also is unknown. The possibility exists that the PIF may be induced by antigen-antibody complexes. That this may occur in parasitic infections has already been suggested in the report of the WHO expert committee on immunology and parasitic diseases (1965). Recently Ward and Conran (1966) demonstrated the presence of malaria antigen, γ -globulin and BIC-globulin deposited along the endothelial surfaces of the renal glomerulus. These authors suggest that the deposit might be antigen-antibody complexes that would cause a local increase of vascular permeability.

Further evidence of increased vascular permeability in malaria has been given by Malloy (pers. comm.) who found an alteration in fluid compartment physiology of P. falciparum-infected American soldiers in Vietnam. Our investigations on host physiology in primate malarias, of which a detailed account will be presented in subsequent communications, has shown a liver pathology with centrilobular necrosis in some P. coatneyi infected rhesus. It is possible that a PIF could cause a rapid decrease in plasma volume which might, in turn, induce shock and the consequent pathologic change in the liver. This is still highly conjectural but it would seem important to elucidate the possible participation of a PIF in the pathogenesis of malaria.

Summary

1. The sera of monkeys infected with P. inui or P. coatneyi caused an increased vascular permeability when inoculated into the skin of rabbits.
2. PIF activity in P. inui infected sera was reduced during the chronic stage of the infection but reappears during recrudescences. In acute infections a decrease in activity was observed immediately before or during the height of the primary parasitaemia.
3. The activity of infected sera was blocked when an antihistamine, phenergan was given to the rabbits.

Fig. 1. The course of infection and serum vascular permeability increasing activity in a *P. inui* infected rhesus (MS23)



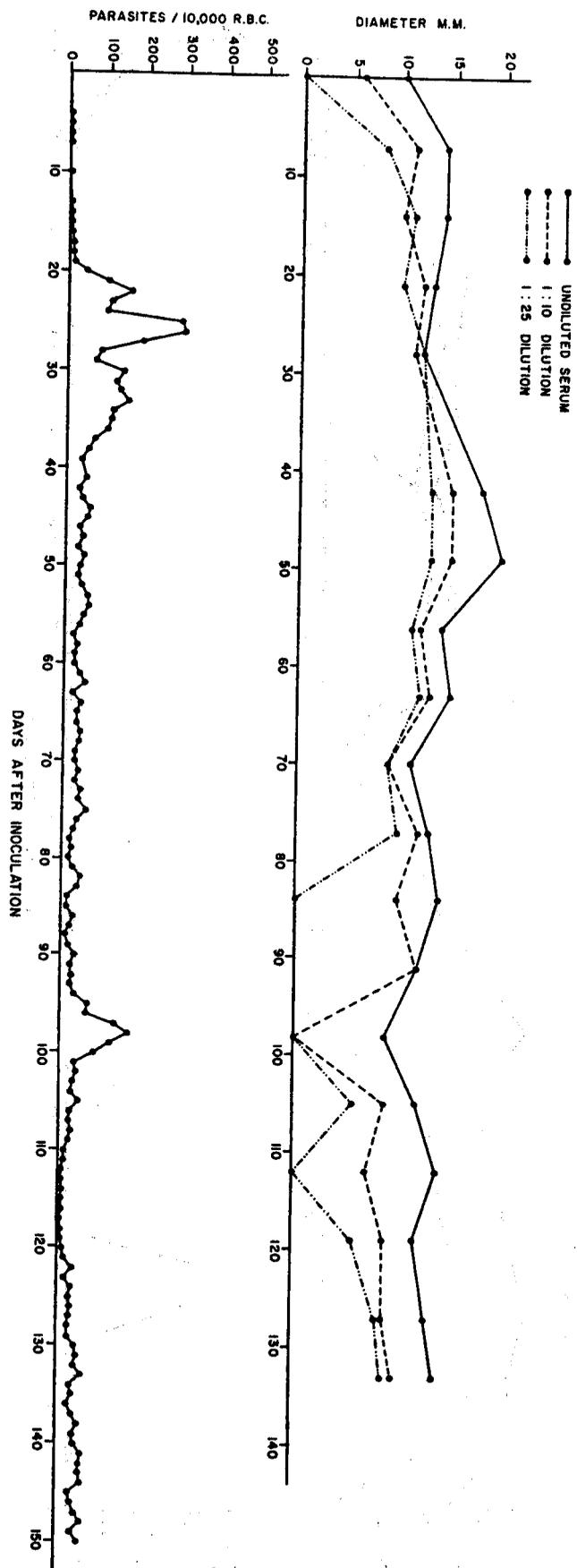


Fig. 2. The course of infection and serum vascular permeability increasing activity in a *P. inui* infected rhesus (SP2)

Fig. 3. The course of infection and serum vascular permeability increasing activity in a *P. inui* infected rhesus (SP4)

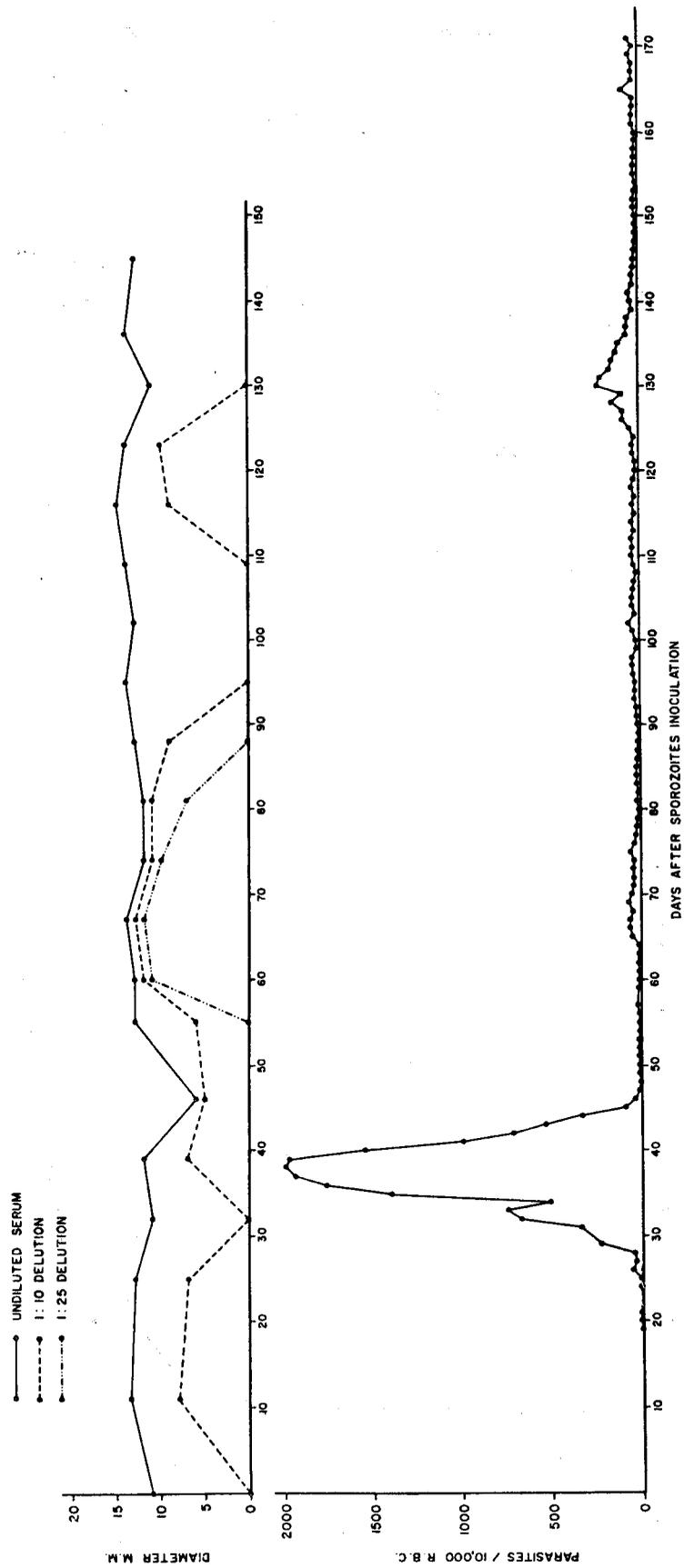


Fig. 4. The course of infection and serum vascular permeability increasing activity in a *P. inui* infected rhesus (MS24)

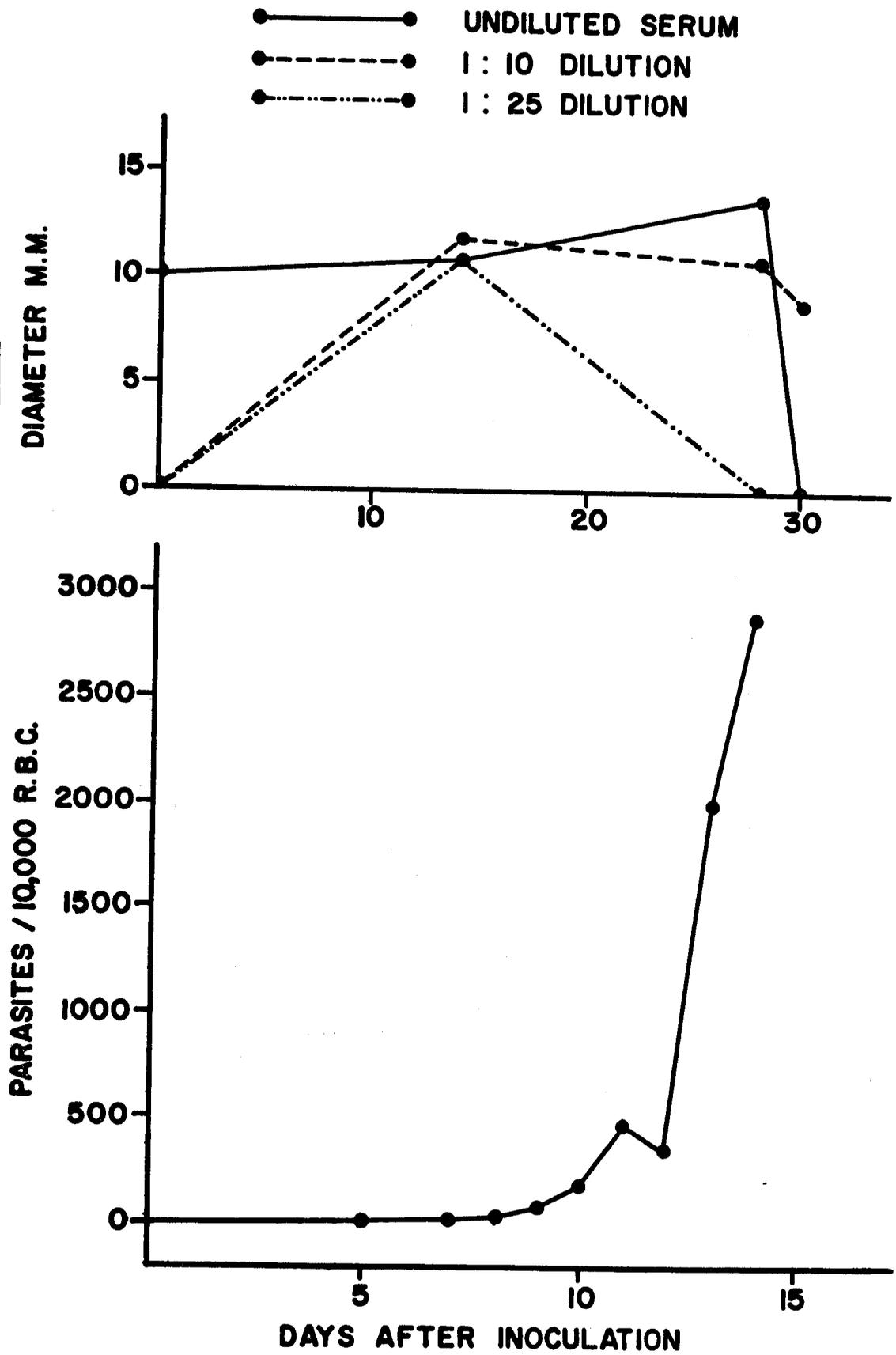


Fig. 5. The course of infection and serum vascular permeability increasing activity in a *P. coatneyi* infected rhesus (KL1)

