

6. Title: Plasmodium falciparum in the Gibbon (Hylobates lar)

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Objective: In the past, malaria research on the human malaria species has been severely hampered by the lack of a suitable non-human host. Except for the experience of Talliafero in the 1930's with howler monkeys, the first successful inoculation of a nonhuman primate with human malaria was that of Bray in the last decade. This work with chimpanzees marked the first successful work with an animal which could be used as a laboratory host and which would have adequate, albeit short lived, parasitemia. However, chimpanzees are scarce and expensive. It was therefore decided to evaluate the potential of the gibbon (Hylobates lar) as a host since these animals were plentiful and inexpensive in this country.

Description: Initially, six young gibbons were splenectomized and then moved to the study center adjacent to the Regional Malaria Eradication Center at Phrabuddhabat (approximately 90 miles north of Bangkok) where infected human blood was readily available from the Passive Detection Center and the District Hospital. The buildings and land which comprise the study center have been most generously loaned to us by the National Malaria Eradication Project. The six gibbons were negative on repeated testing for malarial parasites prior and subsequent to splenectomy. Nevertheless, as an added precaution, all animals were given full therapeutic courses of chloroquine and primaquine prior to experimental use. This same procedure has been followed in all subsequent work.

These six animals were inoculated with heparinized blood from infected humans. Each gibbon received approximately 6×10^6 to 10^8 trophozoites by the intraperitoneal or intravenous route. All subsequent work has been done by using the intravenous route only.

After a prepatent period of 2 to 20 days, all animals had small ring forms in the erythrocytes followed later by larger trophozoites characteristic of falciparum infection. All but one animal had gametocytes in the peripheral circulation four to twenty-five days after inoculation but these were virtually all immature morphologically. Peaks of parasitemia were as high as 150,000 parasites per cmm. The highest peak of gametocytemia was 9500 per cmm. Parasitemia persisted at detectable levels for 23-40 weeks. There was no definite cycle detected. Four other human strains of P. falciparum including one from Vietnam have been successfully inoculated into gibbons. Comparison of strain behaviour is not possible at this time.

Second passage of four strains has been successful. Preliminary examination of data suggests that magnitude and duration of parasitemia was dose dependent. Two animals which were subinoculated from animals with very low parasitemias had parasitemias of 14 weeks duration and never achieved high levels. Three which received blood from animals with high levels of parasites were positive for 24-27 weeks and with extremely high peaks.

Note

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Third passage has been successful but these animals have not been followed for a sufficient period to draw any conclusions.

Two non-splenectomized gibbons have been inoculated with blood from first passage gibbons. After a prepatent period of less than four days, both became positive and remained so for 23 and 29 weeks respectively. No gametocytes were seen.

Preliminary treatment studies with chloroquine reveal that all falciparum strains tested thus far are resistant to chloroquine therapy at a total dosage of 25 mg/kg. Two of these strains were shown to be resistant in humans, the others have presumptive evidence of resistance in humans. Evidence that chloroquine can be effective in these gibbons was shown by the successful treatment of P. vivax infection. Preliminary studies with quinine show a high relapse rate. Other trials with pyrimethamine and paludrine are insufficient for comment at this time.

Two splenectomized gibbons were successfully inoculated with sporozoites. This work is described below under the heading "Anopheles and Malaria".

Summary: The white-handed gibbon (Hylobates lar) has been shown to be an highly suitable laboratory host for P. falciparum, capable of both erythrocytic and exoerythrocytic infection and capable of maintaining infection for prolonged periods.