Falciparum Malaria: Transmission to the Gibbon by Anopheles balabacensis

Abstract. *The splenectomized gibbon* (Hylobates lar) *is susceptible to sporozoite-induced infection by sporozoites of* Plasmodium falciparum. *Two gibbons inoculated with sporozoites of* P. falciparum *from* Anopheles balabacensis *fed on humans with falciparum malaria developed parasitemia 48 and 46 days after infection.*

The splenectomized gibbon (*Hylobates lar*) is susceptible to blood-induced infection with *Plasmodium falciparum* (*1*). We now report that the splenectomized gibbon can also support the exoerythrocytic stage of *P. falciparum*. Thus, for immunologic and chemotherapeutic studies of falciparum malaria, its potential value as a laboratory host is extended. Until now, the splenectomized chimpanzee (*Pan satyrus*) was the only higher primate, aside from man, known to be susceptible to infection by sporozoites of *P. falciparum* (*2*).

Two gibbons (1 to 2 years old; body weight, 1.75 to 2.75 kg) were inoculated with sporozoites of *P. falciparum* from *Anopheles balabacensis* which had been reared in the laboratory and fed on malarious patients from Saraburi Province, Thailand. After the gibbons had been screened for natural malarial infections and had become acclimatized to colony conditions, they were splenectomized. One animal (S-1) was treated for possible latent malarial infections with chloroquine and primaquine as described previously (*1*), while the other animal (P-10) was untreated. Malarial parasites were seen in the blood of neither animal either before splenectomy or prior to inoculation. During the course of the experiment the gibbons were housed in quarters free of mosquitoes.

Two months after being splenectomized, gibbon P-10 was exposed to four *A. balabacensis* which were part of a group fed 16 days earlier on an adult patient who had, at the time of the feed, 1687 gametocytes per microliter of blood. Sporozoites were seen in the glands of other mosquitoes of this group dissected on day 15. As only one of the four mosquitoes fed to engorgement, all were ground up in 50 percent human serum (with isotonic saline as the diluent), and P-10 was inoculated intramuscularly with the supernatant from this suspension. Characteristic ring forms of *P. falciparum* were seen in the blood of this animal after a prepatent period of 47 days. Asexual parasites were continuously seen in P-10 until the end of the observation period on day 83. On day 64 a peak count of 3271 trophozoites per 500 white blood cells was observed (approximately 62,500 per microliter). The first gametocytes were seen on day 62 and were observed for 16 days thereafter. The maximum count of 50 gametocytes per 500 white blood cells (1000 per microliter) was observed on day 65. Of the asexual forms, only trophozoites were seen, while all of the gametocytes observed were young and either rounded or oat-shaped. Mature, sausage-shaped gametocytes were not seen.

Four months after it was splenectomized, gibbon S-1 was inoculated in the above manner with a suspension of 12 mosquitoes from a group of *A. balabacensis* fed 17 days earlier on a patient with 4536 *P. falciparum* gametocytes per microliter of blood. Sporozoites were seen in the salivary glands of other mosquitoes from this group on the day of inoculation. After a prepatent period of 45 days, small ring forms were seen in the blood of this animal. Gibbon S-1 continued to circulate asexual forms until the end of the observation period on day 73. Maximum counts of 130, 122, and 115 trophozoites were observed on days 50, 65, and 67, respectively. Asexual forms other than trophozoites were not seen, nor were gametocytes observed in the blood of this animal.

The prepatent period in these gibbons was considerably longer than that reported for humans infected with this parasite by way of mosquito bites; the medians in 161 cases ranged from 9 to 13 days (*3*). This longer period may be related to the relatively small number of sporozoites in the inoculum, to partial susceptibility of the gibbon to this parasite, or to an extended period of exoerythrocytic development of the parasite in this host species.

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References and Notes

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Drug-Induced Teratogenesis in vitro: Inhibition of Calcification by Different Tetracyclines

Abstract. *Inhibition of calcification in embryonic bone rudiments was studied in the presence of several tetracyclines at three different concentrations. Different criteria for calcification and different concentrations of tetracyclines yielded parallel results and showed significant differences in the inhibitory action of the various compounds. The clear-cut results indicate that the test-system that was developed may be useful for the comparison of various teratogens under simplified controllable conditions.*

Recent experience in testing the teratogenicity of drugs has shown that the conclusiveness of classic animal experiments is limited. Consequently, only large series performed on a number of different species can give reliable information. It was thought useful, therefore, to explore the possibilities of performing such tests in simplified model-systems in vitro, where side-effects could be determined more exactly. The tetracycline antibiotics were chosen for these tests. Both clinical experience and experimental results have shown that these drugs interfere with calcification of embryonic bones, in which the drug is selectively incorporated (*1*). The effect can be demonstrated and quantitated in organotypic cultures of embryonic bones (*2*), and hence this model-system was employed for certain comparative experiments. A variety of tetracyclines that are chemically closely related are in clinical use, and earlier experiments have indicated that