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PLASMODIUM VIVAX INFECTIONS IN THE SPIDER MONKEYS, *ATELES FUSCICEPS* AND *A. GEOFFROYI**

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ABSTRACT: Attempts to infect 11 black spider monkeys, *Ateles fusciceps*, and 1 red spider monkey, *A. geoffroyi*, with *Plasmodium vivax* by blood inoculations from man failed. However, 13 of 23 black spider monkeys and 4 of 6 red spider monkeys became infected after inoculation of vivax bloods from other monkeys. Black spider monkeys were infected with both the Achiote and Santa Rosa strains of *P. vivax* and red spider monkeys were infected with the Achiote strain. Black spider monkeys were infected from night monkeys, *Aotus trivirgatus*, and from other spider monkeys. The percentage of successes was higher when the donors were spider monkeys rather than night monkeys. Red spider monkeys were infected only from other spider monkeys but only 1 attempt was made from the night monkey. The infection has been through 4 serial passages in spider monkeys. Parasitemias developed after average prepatent periods of 12 days in black spider monkeys. Patency averaged 26 days and the maximum parasitemia averaged 23,700 and ranged up to 106,920 per mm³. In red spider monkeys, the prepatent period averaged 8 days and patency averaged 36 days. The maximum parasitemia averaged 12,840 and ranged up to 24,350 per mm³.

We previously reported that the black spider monkey, *Ateles fusciceps*, and the red spider monkey, *A. geoffroyi*, are susceptible to *Plasmodium vivax* (Young and Porter, 1969). Some characteristics of these infections follow.

MATERIALS AND METHODS

Materials and methods for handling primates, malarial bloods, and most immunosuppressant drugs were detailed previously (Porter and Young, 1966). Spider monkeys of either species were used indiscriminately as donors or recipients according to need and availability. Most spider monkeys used were juveniles. One *A. fusciceps* and one *A. geoffroyi* were administered Endoxan® (Asta-Werke Ag, Chemische Fabrik, Brackwede, Germany) (10 mg/kg) at the time of inoculation of the malarial blood. Neither developed an infection. All other spider monkeys inoculated, except one, were both splenectomized and administered Imuran® (Burroughs, Wellcome and Co., Inc., Tuckahoe, N. Y., USA) at doses previously detailed. The one, a black spider monkey, was splenectomized but not administered an immunosuppressant drug. It will be specifically mentioned in the results.

Spider monkeys are naturally infected with *P. brasilianum* (Dunn and Lambrecht, 1963; Porter et al., 1966). Because of the possibility of a natural occurring malarial infection being reactivated by the inoculation of human species of malarial parasites, all spider monkeys were followed by the examination of blood smears for long periods, most after splenectomy, to attempt to assure freedom from infection with *P. brasilianum*. Many monkeys also received primaquine for 11 to 14 days at the rate of 0.2 to 0.75 mg/kg prior to use as an added precaution to prevent the reactivation of a dormant *P. brasilianum* infection.

One black spider monkey was administered Thiobismol® (Parke, Davis and Company, Ann Arbor, Michigan) (3 mg/kg) to reduce the parasitemia without eradicating the infection.

RESULTS

None of 11 *A. fusciceps* or one *A. geoffroyi* became infected after the inoculation of vivax blood from man (Table I). Thirteen of 23 *A. fusciceps* and four of six *A. geoffroyi* did become infected after inoculation of vivax blood from monkeys. As noted in Table I, maximum parasitemias averaged 23,700 and reached 106,920 per mm³ in *A. fusciceps*. In *A. geoffroyi*, the respective figures were 12,840 and 24,350. The maximum parasitemia of 106,920 per mm³ occurred in the one splenectomized *A. fusciceps* that did not receive Imuran®. It received an inoculum of only 1×10^6 parasites, had a prepatent period of 10 days, and had a patent parasitemia of 17 days. If this infection had been excluded in the computation of the average maximum and the maximum parasitemias in the *A. fusciceps* infected from other monkeys (Table I), the respective maximums would have been 16,140

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TABLE I. Plasmodium vivax *blood-induced infections in* Ateles fusciceps *and* A. geoffroyi *from 1 January 1965 to 30 June 1968.*

Species of monkey	Suc.*/At.	Inoculum Range (10^6)	Prepatent period Range (days)	Prepatent period Avg	Patent period Range (days)	Patent period Avg	Parasitemia per mm³ Avg max	Parasitemia per mm³ Max	Patent day of avg max
	Man to monkey								
Ateles fusciceps	0/11	1–38		0		0	0	0	0
Ateles geoffroyi	0/1	?		0		0	0	0	0
	Monkey to monkey								
Ateles fusciceps	13/23†	1–300	2–56‡	12	3–36	26§	23,700|	106,920	15
Ateles geoffroyi	4/6	1–52	4–12	8	23–56	36	12,840	24,350	20

Suc./At. Successes/Attempts.

* Demonstrable parasitemia for at least 3 successive days.

Avg max Average maximum.

† One monkey that developed a mixed infection was excluded from further computations.

‡ One monkey became patent 2 days postinoculation. The primary parasitemia was < 10 per mm³ and extended for only 4 days. The secondary parasitemia, a more significant parasitemia, was used in computing the patency and maximum parasitemia.

§ Two monkeys died with patent parasitemias. If the two had been excluded, the average patency would have been 27 days.

| One monkey treated with Thiobismol® at maximum parasitemia of 39,790 per mm³.

and 39,790, which are reasonably similar to the figures for *A. geoffroyi*. Maximum parasitemias occurred between the 13th and the 19th day of patency in six of 12 *A. fusciceps* and three of four *A. geoffroyi*.

Splenectomized spider monkeys that developed *P. brasilianum* infections in our laboratory often had high parasitemias but apparently were not seriously affected by parasitemias below 200,000 per mm³. The spider monkey that developed the maximum vivax parasitemia of 106,960 per mm³ on the 13th day of patency died 4 days later. A second monkey developed a rapidly rising parasitemia of 39,790 per mm³ on the 9th day of patency. It was treated with Thiobismol® at that time but died 10 days later. Both monkeys were infected with the 13th *Aotus* passage of the

TABLE II. Plasmodium vivax *blood-induced infections, distributed by strain and primate donor, in* Ateles fusciceps *and* A. geoffroyi *from 10 March 1966 to 30 June 1968.*

Strain	Donor	Suc.*/At.	Inoculum Range (10^6)	Prepatent period Range (days)	Prepatent period Avg	Patent period Range (days)	Patent period Avg	Parasitemia per mm³ Avg max	Parasitemia per mm³ Max	Patent day of max parasit.
				Ateles fusciceps						
Achiote	*Aotus trivirgatus*	3/7	1–300	6–23	13	19–26	23	15,090	39,790‡	9
	Ateles fusciceps	6/6†	1– 80	2–11§	7	17–36	29	37,980	106,920	13
	Ateles geoffroyi	1/2	28– 86		6		3	<10	<10	1
Santa Rosa	*Aotus trivirgatus*	1/3	78–194		56		27	11,070	11,070	19
	Ateles fusciceps	2/3	18– 63	3– 4	4	30–33	32	19,050	25,350	22
Emperador	*Aotus trivirgatus*	0/1	92		0		0	0	0	0
	Saguinus geoffroyi	0/1	85		0		0	0	0	0
				Ateles geoffroyi						
Achiote	*Aotus trivirgatus*	0/1	1		0		0	0	0	0
	Ateles fusciceps	1/1	1		12		23	5,250	5,250	15
	Ateles geoffroyi	3/4	1– 52	4–11	7	27–56	40	15,370	24,350	29

Suc./At. Successes/Attempts.

* Demonstrable parasitemia for at least 3 successive days.

Avg max Average maximum.

Max parasit. Maximum parasitemia.

† One monkey that developed a mixed infection was excluded from further computations.

‡ Treated with Thiobismol® at maximum parasitemia.

§ One monkey became patent 2 days postinoculation. Because the primary parasitemia was insignificant, the secondary parasitemia was used in computing the patency and maximum parasitemia.

TABLE III. *Serial passage of blood-induced* Plasmodium vivax *infections in* Ateles *spp. from 10 March 1966 to 30 June 1968.*

Passage	Suc.*/At.	Inoculum Range (10^6)	Prepatent period Range (days)	Prepatent period Avg (days)	Patent period Range (days)	Patent period Avg (days)	Parasitemia per mm³ Avg max	Parasitemia per mm³ Max	Patent day of max parasit.
Aotus trivirgatus to *Ateles* spp.	4/12	1–300	6–56	24	19–26	24	14,080	39,790‡	9
1st: *Ateles* spp. to *Ateles* spp.	6/6†	1– 80	2–12§	7	17–36	28	33,730	106,960	13
2nd: *Ateles* spp. to *Ateles* spp.	3/3	18– 63	3–11	8	27–32	30	21,220	30,230	16
3rd: *Ateles* spp. to *Ateles* spp.	2/3	18– 41	2– 4	3	29–37	33	22,980	24,350	29
4th: *Ateles* spp. to *Ateles* spp.	2/3	28– 86	5– 6	6	3–56	30	600	1,190	17
5th: *Ateles* spp. to *Ateles* spp.	0/1	1		0		0	0	0	0

Suc./At. Successes/Attempts.

* Demonstrable parasitemia for at least 3 successive days.

Avg max Average maximum.

Max parasit. Maximum parasitemia.

† One monkey that developed a mixed infection was excluded from further computations.

‡ Treated with Thiobismol® at maximum parasitemia.

§ One monkey became patent 2 days postinoculation. Because the primary parasitemia was insignificant, the secondary parasitemia was used in computing the patency and maximum parasitemia.

Achiote strain. No other monkey developed a parasitemia in excess of 30,230 per mm³ or died during patency.

Table II shows that both species of monkeys became infected with the Achiote strain, the first vivax strain passed serially in monkeys (Porter and Young, 1966). It also shows that *A. fusciceps* became infected with the Santa Rosa strain, the first strain passed from man to monkey to man to monkey (Young et al., 1966). The two *A. fusciceps* tried were not infected by the Emperador strain, a strain that caused high parasitemias in the Panamanian marmoset, *Saguinus geoffroyi* (Porter and Young, unpublished data). Three of seven *A. fusciceps* were infected with the Achiote strain from night monkeys, *Aotus trivirgatus*, and one of three was infected with the Santa Rosa strain from the same donor. The one attempt to infect *A. geoffroyi* from an *Aotus*, infected with the Achiote strain, failed. Higher percentages of *A. fusciceps* were infected with both the Achiote and the Santa Rosa strains from *Ateles* than from *Aotus* donors. The same was true for *A. geoffroyi* with respect to the Achiote strain. Significant average maximum and maximum parasitemias resulted in most cases. As shown, with the one exception of < 10 per mm³, average maximum parasitemias ranged from 5,250 to 37,980 per mm³ and maximum parasitemias from 5,250 to 106,920 per mm³.

Table III summarizes the results of serial passages of *P. vivax* in spider monkeys. The infection has been through four serial passages in *Ateles* species. The prepatent period averaged 24 days in the *Aotus* to *Ateles* passages but, in serial passages in *Ateles*, the average ranged from 3 to a maximum of only 8 days. The patent period for the *Aotus* to *Ateles* passages averaged 24 days; for the *Ateles* serial passages, the average ranged from 28 to 33 days. The average maximum parasitemia for the *Aotus* to *Ateles* passage was 14,080 per mm³; for the spider monkey serial passages, the averages ranged from 600 to 33,730 per mm³. If the maximum parasitemia of 106,920 per mm³ that occurred in the first serial passage in *Ateles* had been excluded, the average maximum parasitemia for this serial passage would have been only 15,440 per mm³. Using this latter figure, the average maximum parasitemias in the first three *Ateles* serial passages would have ranged only from 15,440 to 22,980 per mm³. The two parasitemias that resulted in the fourth serial passage were low; one was

TABLE IV. *Serial passage of blood-induced* Plasmodium vivax *infections in* Ateles *spp. distributed by strain and passage number in the* Aotus trivirgatus *donor from 10 March 1966 to 30 June 1968.*

Passage in *Ateles* spp.	Suc.*/At.	Inoculum: Range (10^6)	Prepatent period: Average (days)	Patent period: Average (days)	Parasitemia per mm³: Avg max	Parasitemia per mm³: Maximum	Patent day of max parasit.
		Achiote (13th passage in *Aotus*)					
Aotus to *Ateles*	1/1	138	6	19	39,790	39,790‡	9
1st: *Ateles* to *Ateles*	4/4†	1– 80	8§	25	41,980	106,920	13
2nd: *Ateles* to *Ateles*	1/1	25	11	27	20,570	20,570	17
3rd: *Ateles* to *Ateles*	1/1	41	4	37	24,350	24,350	29
4th: *Ateles* to *Ateles*	2/3	28– 86	6	30	600	1,190	17
5th: *Ateles* to *Ateles*	0/1	1	0	0	0	0	0
		Achiote (19th passage in *Aotus*)					
Aotus to *Ateles*	1/1	79	23	26	560	560	17
		Achiote (52nd passage in *Aotus*)					
Aotus to *Ateles*	1/1	124	11	23	4,910	4,910	14
1st: *Ateles* to *Ateles*	1/1	12	9	30	17,400	17,400	25
2nd: *Ateles* to *Ateles*	1/1	18	11	32	30,230	30,230	16
3rd: *Ateles* to *Ateles*	1/1	80	2	29	21,600	21,600	9
		Santa Rosa (20th passage in *Aotus*)					
Aotus to *Ateles*	1/2	78–194	56	27	11,070	11,070	19
1st: *Ateles* to *Ateles*	1/1	25	4	34	25,330	25,330	22
2nd: *Ateles* to *Ateles*	1/1	63	3	30	12,860	12,860	19
3rd: *Ateles* to *Ateles*	0/1	18	0	0	0	0	0

Suc./At. Successes/Attempts.

* Demonstrable parasitemia for at least 3 successive days.

Avg max Average maximum.

Max parasit. Maximum parasitemia.

† One monkey that developed a mixed infection was excluded from further computations.

‡ Treated with Thiobismol® at maximum parasitemia.

§ One monkey became patent 2 days postinoculation. Because the primary parasitemia was insignificant, the secondary parasitemia was used in computing patency and parasitemia.

< 10 and the other 1,190 per mm³. The one attempt to transfer this serial passage failed but only a relative small inoculum was given.

Table IV details the infections that occurred in the *Ateles* inoculated from three different *Aotus* infected with the Achiote strain and from one infected with the Santa Rosa strain. High parasitemias resulted from inoculations of the 13th and 52nd passage of the Achiote strain and the 20th passage of the Santa Rosa strain in the *Aotus*. This indicates that long serial passage in the *Aotus* did not eliminate the infectivity of the parasite to the *Ateles*.

Gametocytes were produced and proved infective to *Anopheles albimanus* mosquitoes. Sporozoite transmission attempts were successful (Baerg et al., 1969).

DISCUSSION

All attempts to infect *A. fusciceps* or *A. geoffroyi* with *P. vivax* parasites directly from man failed but we infected the spider monkeys in four of 12 attempts after passage through *Aotus trivirgatus*. The malaria, in contrast, was transferred readily by blood inoculations within and between the two *Ateles* species during the initial serial passages. Two of three strains were infective to *A. fusciceps* and one to *A. geoffroyi*. Most resulting parasitemias were similar in the two species. Maximum vivax parasitemias were generally more moderate than brasilianum infections in splenectomized monkeys; however, the two monkeys with the highest maximum vivax parasitemias died. In contrast, monkeys infected with similar brasilianum parasitemias probably would have lived. A shortage of spider monkeys limited our investigations.

Because of natural occurring malaria in *Ateles* species, it is necessary to take precautions that are not necessary with night monkeys or marmosets before inoculating blood. *Ateles* species, however, do offer compensatory advantages. They generally have maximum parasitemias ranging from 5,000 to 30,000 per mm³ which they withstand well. Their large

size makes it possible to obtain large volumes of blood or other biological materials when desired. They readily adjust to captivity; thus they can be followed for several years post-infection if long-term studies are desired. *A. fusciceps* and *A. geoffroyi* should be considered, along with the previously reported *Aotus trivirgatus* (Young et al., 1966) and *Saguinus geoffroyi*, the Panamanian marmoset (Porter and Young, 1966), as laboratory hosts for *P. vivax* infections.

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