Humoral immune response in capuchin monkeys (*Cebus apella*) after vaccination with inactivated suckling mouse brain rabies vaccine: comparison of two schedules of immunization

Estevão de Camargo PASSOS[1]
Pedro Manuel Leal GERMANO[2]
José Daniel Luzes FEDULLO[3]
Cleide Aschenbrenner CONSALES[1]
Maria Luiza CARRIERI[1]
Ricardo CARDOSO[4]
Margareth de Andrade GONÇALVES[5]

[1] Instituto Pasteur, São Paulo - SP
[2] Faculdade de Saúde Pública da Universidade de São Paulo, São Paulo - SP
[3] Fundação Parque Zoológico de São Paulo, São Paulo - SP
[4] Centro Universitário das Faculdades Metropolitanas Unidas, São Paulo - SP
[5] Secretaria da Educação do Governo do Estado de São Paulo, São Paulo - SP

Correspondence to:
ESTEVÃO DE CAMARGO PASSOS
Instituto Pasteur
Av. Paulista, 393, Cerqueira César
01311-000 - São Paulo - SP
estevaopqc@yahoo.com.br

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Abstract

Two groups of adult capuchin monkeys (*Cebus apella*) were vaccinated i.m. against rabies with inactivated suckling mouse brain rabies vaccine (SMBV), at the Zoo Park Foundation in São Paulo, SP, Brazil. The animals had not been immunized against rabies at any time before. Group I consisted of nine animals, to which were given three 1.0mL doses on days 0 and 30, plus a booster on day 210. Group II comprehended ten animals, to which were given two 1.0mL doses: one, on day 0 and, another, a booster, on day 210. The blood samples were collected on days 0, 30, 60, 90, 150, 210, 240, 300 and 365, being the titrated neutralizing antibodies determined by the simplified fluorescent focus inhibition technique. The vaccine induced immune responses with neutralizing antibody titers above 0.5 IU/m in both groups of capuchin monkeys; however, they were short, lasting 54.9 ± 57.0 days and 36.1 ± 60.2 days in Groups I and II, respectively, after primo-vaccination, and 62.6 ± 74.0 and 86.4 ± 61.5 days in Groups I and II, respectively, after a booster. No statistically significant differences were observed out between the two groups studied ($p > 0.05$).

Key-words:
Rabies.
Vaccination.
Capuchin monkeys (*Cebus apella*).
Suckling mouse brain rabies vaccine (SMBV).
Neutralizing antibodies.

Introduction

In Brazil, according to the National Health Fund data, 17 diagnosed cases of human rabies transmitted by monkeys were registered. The *Callithrix jacchus* were found to be responsible for rabies transmission in eight of these human cases, between the years of 1991 and 1998[1]. Laboratory diagnoses of rabies both in wild monkeys and in those kept as pets have been routinely carried out in some Brazilian states[1,2,3].

The inactivated suckling mouse brain rabies vaccine (SMBV) presents an adequate antigenic mass, producing immunity with few adverse side effects in the majority of the animal population[4]. Since a low immunogenic response had been observed in studies undertaken with individuals and animals immunized with the inactivated suckling mouse brain rabies vaccine, a booster dose was found necessary[5,6,7,8,9]. The SMBV is used in Brazilian national vaccination campaigns against rabies, in dogs and cats, carried out, annually, in September. Considering just the São Paulo State, 4,168,337 dogs and 581,722 cats were vaccinated during the last campaign, in 2001, covering about 90.0% of the estimated canine population.

Brazilian sanitation authorities, besides having little access to information

on the efficacy of this vaccine for Neotropical primates, strongly disapprove the maintenance of these animals as pets. Since primates are frequently vaccinated during the annual rabies vaccination campaigns, their owners believe they do not need to seek out medical services in case a vaccinated primate bites them.

The Pasteur Institute of São Paulo, State of São Paulo, Brazil, carried out an antirabies post-exposure treatment in 61 persons attacked by monkeys during 2001, representing 1.7% (61/3,576) of the population there attended to.

Taking in view the lack of information on capuchin monkeys (*Cebus apella*) regarding their humoral immune response induced by SMBV, as well as the difficulties in handling these animals, two protocols of immunization were simultaneously carried out in the present research. The first one simulated the antirabic vaccination protocol carried out in veterinary clinics, where a booster dose is recommend 30 days after the first dose of the vaccine had been taken. The second protocol adopted was that used in vaccination campaigns against rabies, sponsored by national health agencies, in which only one dose of the vaccine is annually administered.

The goal of the present paper was to compare two new protocols of antirabic immunization in capuchin monkeys as well as to characterize the humoral immunity stimulated after vaccination during a one-year period.

Methods

Two groups of adult capuchin monkeys *Cebus apella*, each with nine and 10 animals respectively, were housed at the Zoo Park Foundation, in São Paulo, SP, Brazil. Vaccination trials were conducted from June 1995 to June 1996. The animals were in good health and had not been immunized against rabies at any time before. Numbers tattooed on their inner thighs uniquely identified the researched animals. Twice a day they were fed with the São Paulo Zoo's primate formula ration, with water being given to them *ad libitum*. Each group were maintained in a 3.0 x 2.0 x 4.0 meter-enclosure with iron bars, wire netting, and cemented floor, for 12 months.

Each animal was anesthetized with a i.m. 4.4 mg/kg tiletamine and zolazepam (Zoletil 50, Virbac do Brasil Ind. e Com. Ltda., São Paulo, Brazil, 04696-000) to facilitate vaccination, blood sampling and veterinary care. The inactivated suckling mouse brain rabies vaccine (SMBV)[10] (VARC Vacina Anti-Rábica Fuenzalida Modificada, uso veterinário, TECPAR, Curitiba, PR, Brazil, 80035-050), presenting a $10^{5.8}$ DP50/0.03mL titer in the Habel potency test [11] was used. Each animal received a dose of 1.0 mL, i.m. Group I comprised nine animals, which were vaccinated on days 0 and 30, plus receiving a booster on day 210. Group II comprised 10 animals, which were vaccinated on day 0, and were given a booster on day 210.

Ten mL of blood were collected via a femoral venipuncture on days 0, 30, 60, 90, 150, 210, 240, 300, and 365. Samples were centrifuged under refrigeration at 2,000 rpm for 15 min and the sera were stored at –20°C in plastic tubes (Eppendorf Safe-Lock, Sigma-Aldrich Química Brasil Ltda, São Paulo, SP, Brazil, 01239-010).

The simplified fluorescent focus inhibition test (SFFIT)[12] is the national serological reference test for searching out antibodies in persons submitted to rabies virus pre- and post-exposure treatment, being chosen for determining the dosage of antibodies to rabies present in the sera of the animals under study. A rabies anti-nucleocapsid fluorescent conjugate (Diagnostic Pasteur, Marnes-la-Coquete, France, 92430) was used, there following the fluorescent microscope reading procedure. The comparison between the results obtained with the serum test and the standard hyper immune serum presented titers equivalent to 282 IU/mL, serving as a basis for obtaining the titers expressed in IU/mL. According to the World Health Organization[13], human subjects, are considered as immunized after

presenting seroconversion to a titer of at least 0.5 IU/mL. The same criterion was adopted for non-human primates in this experiment.

The statistical analyses employed in this study were based on the Student's t test[14], comparison of two independent averages, with a 5.0%.

Results

Results obtained during the trial can be seen on tables 1 and 2 showing the kinetics, production and titers of rabies neutralizing antibodies in capuchin monkeys vaccinated with the SMBV, during a twelve-month period. The animals presented a humoral immune response, characterizing an individual variability, sometimes an irregular response. No adverse side effects were observed after vaccination.

Table 2, "Persistence of neutralizing antibodies", was drawn up on the basis of an extrapolation of data obtained in table 1. The determination by days of the persistence of neutralizing antibodies was based on a straight-line equation, where the value 0.5IU/mL was considered as the cut-off point for both positive sera presenting increasing antibody titers and for these same positive sera presenting decreasing antibody titers down to the 0.5 IU/mL value. The distance between the two points crossing this value (0.5 IU/mL), at the intersection of the X axis (abscissa), has enable us to extrapolate the number of days in which the animals remained with neutralizing antibodies, with titers equal to or higher than 0.5IU/mL. Therefore, the construction of table 2 has permitted us to visualize the total days in which the capuchin monkeys showed the persistence of neutralizing antibodies during the trial.

During the studied period, the animals # 26 and # 30 from Group I and # 70 from Group II have never given a humoral immune response with titers equal to, or higher than, 0.5IU/mL.

After the second dose, the animals of Group I developed neutralizing antibodies with titers above 0.5IU/mL in 55.5% (5/9) of the animals, but their immune response persisted for only 54.9 $\pm$ 57.0 days. By day 210, no animal presented any neutralizing antibodies, having received, at that time, a booster, which produced neutralizing antibodies titers above 0.5 IU/mL in 66.6% (6/9) of the animals. At day 365, only 25% (2/8) of the studied population had neutralizing antibodies titers above 0.5 IU/mL. Before the end of the experiment, monkey # 21 died during confinement, due to injuries caused by bites it suffered, when fighting for group hierarchy. After booster, the animals' immune response persisted for only 62.6 $\pm$ 74.0 days. After the first dose of

Table 1 - Antibody titers expressed in IU/ml, detected by the SFIT methods, in capuchin monkeys belonging to Group I submitted to three doses of SMB rabies vaccine administered on days 0, 30 and 210, and to Group II submitted to two doses of SMB rabies vaccine administered on days 0 and 210

	Days	0	30	60	90	150	210	240	300	365
Group I	Monkey 1	0.18	0.35	0.53	0.35	0.18	0.18	1.06	1.06	1.41
	Monkey 10	0.18	0.35	0.71	1.06	0.53	0.26	1.06	0.71	0.53
	Monkey 11	0.18	0.53	0.26	0.18	0.35	0.26	0.53	0.35	0.18
	Monkey 15	0.18	0.26	0.71	0.53	0.71	0.18	0.71	0.53	0.35
	Monkey 21	0.18	0.53	0.53	0.53	0.53	0.26	0.71	0.71	Died
	Monkey 26	0.18	0.26	0.26	0.26	0.35	0.18	0.18	0.18	0.18
	Monkey 30	0.18	0.26	0.18	0.18	0.18	0.18	0.26	0.18	0.18
	Monkey 43	0.35	0.71	0.18	0.18	0.18	0.18	0.26	0.26	0.26
	Monkey 98	0.18	0.71	1.06	0.53	0.26	0.18	1.06	0.35	0.18
Group II	Monkey 7	0.18	0.35	0.53	1.41	1.41	1.06	1.41	1.06	1.06
	Monkey 16	0.18	0.71	ND	0.18	0.35	0.18	1.06	0.71	0.18
	Monkey 22	0.18	0.53	0.35	0.26	0.35	0.26	4.23	1.41	1.06
	Monkey 38	0.18	0.26	0.18	0.26	0.35	0.18	1.41	0.53	0.71
	Monkey 48	0.18	0.26	0.18	0.35	0.18	0.18	0.35	0.18	0.18
	Monkey 59	0.18	0.53	0.26	0.35	0.26	0.18	0.71	0.53	0.18
	Monkey 70	0.18	0.26	0.18	0.18	0.18	0.18	4.23	0.18	0.18
	Monkey 71	0.35	0.35	0.53	0.18	0.26	0.18	0.18	0.35	0.18
	Monkey 73	0.18	0.53	0.35	0.18	0.18	0.18	1.06	0.18	0.18
	Monkey 97	0.35	0.71	0.53	0.71	0.53	0.18	1.06	0.71	0.53

the vaccine, the animals of Group II developed neutralizing antibodies with titers above 0.5 IU/mL in 50% (5/10) of them; however, their immune response persisted for only 36.1 ± 60.2 days. By the day 210, only the monkey # 7 had neutralizing antibodies. At that time, all animals received a booster, producing neutralizing antibody titers above 0.5 IU/mL in 80% (8/10) of the animals. At the 365th. day, 30% (3/10) of the animals had neutralizing antibody titers above 0.5 IU/mL. After a booster, their immune response persisted for only 86.4 ± 61.5 days.

A statistical comparison was carried out using the Student's T test. No statistically significant differences were found out between the two groups studied ($p>0.05$).

Discussion

In areas where rabies occurs endemically, the immunization of animals belonging to zoos must be considered; above all, when the colonies present a high risk of exposure to the rabies virus [12, 15, 16], avoiding, this way, the dissemination of the disease among exposed animals as well as among different species of susceptible mammals, there including man.

In more complex and riskier circumstances, bats that were being handled by gibbons, *Hylobates lar* [20] and capuchin monkeys, *Cebus apella* [14] within the primates' premises were captured. Laboratorial examination of these chiropters disclosed the presence of the rabies virus. After vaccination, all those monkeys had been exposed produced neutralizing antibodies presenting titers higher than 0.5 IU/mL

Taking into account the SMBV prescribed for dogs and cats, have been administered either subcutaneously or intramuscularly in different species of Neotropical primates as well as in monkeys of the Old World with the purpose of verifying the immunization schedules adopted to, which resulted in a humoral immune response. After a single dose of the SMBV vaccine, the production of neutralizing antibodies to rabies was observed in *Callithrix spp* in 16.6% (1/6)[20] and 100% (7/7)[21] of the animals; in 100.0% (3/3) of the *Saimiri* spp[15]; in 80.0% (8/10) in *Macaca mulatta*[16]; and, in 80.0% (4/5) in *Macaca mulatta*[22]; after two doses of the vaccine, it was observed in 33.3% (2/6) of the *Callithrix* spp specimens[20] and, in 100.0% (10/10) in *Macaca mulatta*[16]; after three doses of the vaccine, it was observed in 100.0% (8/8) of the *Cebus apella* specimens[8]; and, after four doses of the vaccine, it was observed in 100.0% (6/6) of the *Callithrix* spp specimens[20].

As conclusive results regarding the value of rabies antibody titers for non-human species were not found in the literature, it is worth emphasizing that, in the present paper, we have used the values of the humans'

Table 2 - Persistence of neutralizing antibodies evaluated in days, with titers equal to or higher than 0.5IU/mL in capuchin monkeys (*Cebus apella*) belonging to Groups I and II after being submitted to an initial vaccination plus a booster dose, afterwards, with a SMB rabies vaccine

Group I			Group II		
Monkey #	After two doses, 0 and 30 days	After booster, 210 days	Monkey #	After one dose, 0 day	After booster, 210 days
1	10	152	7	155	150
10	114	188	16	36	103
11	6	13	22	7	148
15	128	82	38	0	87
21	129	Died	48	0	0
26	0	0	59	6	93
30	0	0	70	0	0
43	29	0	71	8	47
98	78	66	73	7	57
			97	142	179
Average	54.9	62.6		36.1	86.4
Standard error	57.0	74.0		60.2	61.5

immune humoral response to the vaccine after antirabies treatment pre and/or post-exposure to the rabies virus, according to WHO[13], individuals with human antibody titers reaching values equal to, or higher than, 0.5 IU/mL are considered as protected.

The monkeys # 26, 30 and 70 that have never given a satisfactory humoral immune response probably did so either because they were anergic, bad responder animals, or for being constantly submitted to stressing factors such as unskilled or excessive handling, or maybe for being engaged in fights for territorial domain within the study premises.

The variation obtained when determining neutralizing antibodies titers in the same animal might have been caused by factors inherent to the very technique employed. It should be mentioned that all sera were two-fold examined and, although more than three times replied, some situations continued to present always the same results.

No description of experimental trials, employing capuchin monkeys vaccinated against rabies and challenged to the rabies virus, could be found out in the literature. For this reason, it was not possible for the authors to establish levels of protective antibodies against rabies for being used with the capuchin monkeys of the present study. Operational difficulties for carrying out this procedure and not counting with the authorization of the Brazilian Environmental and Natural Recoverable Resources Institute for doing so, were the two main motives responsible for the rabies virus being not challenged in the present trial. Therefore, some animals presenting antibody titers below the accepted 0.5 IU/mL value might have survived the rabies virus inoculation.

The comparison of data concerning the capuchin monkeys' serological trials of this study to previously published works turned out to be a difficult task, since scientific papers dealing with this primate species are rare in the literature.

Conclusions

Taking in mind the above-mentioned reasons, it is believed that the SMBV is inadequate for immunizing capuchin monkeys *Cebus apella*, either the ones brought-up as pets or those kept in zoos. In order to estimate the variations of intensity and duration concerning the immune response to the rabies virus in capuchin monkeys, the authors advocate that new protocols of vaccination should be tested for, along with different types of inactivated rabies vaccine, prepared in cell culture.

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Resposta imune humoral de macacos-pregos (*Cebus apella*) após vacinação com vacina anti-rábica inativada produzida em cérebros de camundongos lactentes: comparação de dois esquemas de imunização

Resumo

Foram vacinados contra a raiva, dois grupos de macacos-pregos adultos, com a vacina inativada preparada em cérebros de camundongos lactentes, administrada pela via intramuscular, na Fundação Parque Zoológico de São Paulo. Os animais em momento algum haviam sido imunizados contra a raiva. O grupo I consistia de nove animais, que receberam três doses de 1,0 mL nos dias 0, 30 e uma dose de reforço aos 210 dias, e o grupo II continha 10 animais que receberam duas doses de 1,0 mL no dia 0 e uma dose de reforço aos 210 dias. As amostras de sangue foram colhidas aos

Palavras-chave:
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Vacina anti-rábica produzida em cérebros de camundongos lactentes

0, 30º, 60º, 90º, 150º, 210º, 240º, 300º e 365º dias, e os anticorpos neutralizantes titulados pela técnica simplificada da inibição de focos fluorescentes. A vacina induziu uma resposta imune de curta duração com títulos de anticorpos neutralizantes acima de 0.5 UI/mL em ambos os grupos; entretanto a resposta imune persistiu por apenas 54,9 $\pm$ 57,0 e 36,1 $\pm$ 60,2 dias nos Grupos I e II respectivamente após a primo vacinação, e, por apenas 62,6 $\pm$ 74,0 e 86,4 $\pm$ 61,5 dias nos Grupos I e II respectivamente após o reforço. Não houve diferença estatística significante entre os grupos estudados ($p > 0,05$).

(Fuenzalida & Palacios). Anticorpos neutralizantes.

References

1 FAVORETTO, S. R.; DE MATTOS, C. C.; MORAIS, N. B.; ARAÚJO, F. A. A.; DE MATTOS C. A. Rabies in marmosets (Callithrix jacchus), Ceará, Brazil. **Emerging Infectious Diseases,** v. 7, n. 6, p. 1062-1065, 2001.

2 GAMBETA, W. R.; CHAMELET, E. L. B.; SOUZA, L. T. M.; AZEVEDO, M. P. **Instituto Pasteur de São Paulo, 75 anos de atividade (1903-1978):** análise historica de sua atuação técnica e científica na profilaxia da raiva. São Paulo: Coordenadoria de Serviços Técnicos Especializados da Secretaria de Estado da Saúde de São Paulo, 1979. 37 p.

3 PICCININI, R. S.; FREITAS, C. E. A. Experiences with rabies control in Brazil. In: KUWERT, E.; MÉRIEUX, C.; KOPROWSKI, H.; BÖGEL, K. **Rabies in the tropics.** Berlin: Spring-Verlag, 1985. p. 737-741.

4 GERMANO, P. M. L.; SILVA, E. V.; SILVA, E. V.; PRETO A. A.; CORDEIRO, C. F. Avaliação em camundongos de vacinas anti-rábicas inativadas frente a variantes antigênicas do vírus da raiva. **Arquivos de Biologia e Tecnologia,** v. 33, n. 3, p. 551-560, 1990.

5 ALBAS, A.; NOGUEIRA, R. M. B.; FONTOLAN, O. L.; ALBAS, K. S.; BREMER NETO, H. Efeito do congelamento sobre a imunogenecidade da vacina contra a raiva produzida em tecido cerebral de camundongo. **Revista da Sociedade Brasileira de Medicina Tropical,** v. 34, n. 1, p. 49-52, 2001.

6 ALMEIDA, M. F.; AGUIAR, E. A.; MARTORELLI, L. A.; PRESOTTO, D.; BRANDÃO, M. M.; PEREIRA, O. A. Resposta imune humoral de cães a vacina inativada , de cérebro de camundongos lactentes, utilizada nas campanhas anti-rábicas no Brasil. **Revista de Saúde Pública,** v. 31, n. 5, p. 502-507, 1997.

7 HIRAYAMA, N.; JUSA, E. R.; NOOR, M. A. R.; SAKAKI, K.; OGATA, M. Immune state of dogs injected with rabies vaccines in West Java, Indonesia. **Japanese Journal of Veterinary Science,** v. 52, n. 5, p. 1099-1101, 1990.

8 PASSOS, E. C.; GERMANO, P. M. L.; GUIMARÃES, M. A. B. V.; FEDULLO J. D. L.; CORRÊA, S. H. R.; CONSALES, C. A.; CARRIERI, M. L.; GONÇALVES, M. A. Inactivated suckling mouse brain rabies vaccine provides short-term immunity in capuchin monkeys (*Cebus apella*) **Journal of Zoo and Wildlife Medicine,** v. 32, n. 1, p. 55-57, 2001.

9 ZANETTI, C. R.; CONSALES, C. A.; RODRIGUES DA SILVA, A. C.; TOYOSHIMA, Y.; PEREIRA, O. A. C. Short duration of neutralization antibody titers after pre-exposure rabies vaccination with suckling mouse brain vaccine. **Brazilian Journal of Medical and Biological Research,** v. 31, n. 10, p. 1275-1280, 1998.

10 FUENZALIDA , E.; PALACIOS, R. Un metodo mejorado en la preparacion de la vacuna antirrabica. **Boletin del Instituto Bacteriologico de Chile,** v. 8, p. 3-10, 1955.

11 HABEL, K. Habel test for potency. In: MESLIN, F. X.; KAPLAN, M. M.; KOPROWSKI, H. **Laboratory techniques in rabies.** 4. ed. Geneva: World Health Organization, 1996. p. 369-373.

12 FAVORETTO, S. R.; CARRIERI, M. L.; TINO, M. S.; ZANETTI, C. R.; PEREIRA, O. A. C. Simplified fluorescent inhibition microtest for the titration of rabies neutralizing antibodies. **Revista do Instituto de Medicina Tropical,** São Paulo, v. 35, p. 171-175, 1993.

13 WHO Expert Committee on Rabies. **8. report**. Geneva: World Health Organization, 1992. (WHO-Technical Report Series, 824).

14 BERQUÓ, E. S.; SOUZA, J. M. P.; GOTLIEB, S. L. D. **Bioestatística**. 2. ed. São Paulo: EPU, 2001. p. 215-232.

15 HAIGH, J. C.; FIELD, M. F. Rabies vaccination in a small zoo: antibody titers studies. **Journal of Zoo and Animal Medicine,** v. 12, n. 1, p. 17-20, 1981.

16 KESSLER, M. J.; SUMMER, J. W.; BAER, G. M. Evaluation of killed rabies vaccine for Rhesus monkeys (*Macaca mulatta*). **Journal of Zoo and Animal Medicine,** v. 13, n. 2, p. 74-77, 1982.

17 NIEVES, P.; RODRIGUEZ, J. F.; KESSLER, M. J.; BERCOVITCH, F. Subcutaneous rabies vaccination of pigtail macaques. **Journal of Medical Primatology,** v. 25, n. 1, p. 14-16, 1996.

18 SMITH, R. E.; PIRIE, G. J.; ENGLAND, J. J. Rabies vaccination of captive white-handed gibbons potentially exposed to wild rabies virus. **Laboratory Animal Science,** v. 37, n. 5, p. 668-669, 1987.

19 KENNY, D. E.; KNIGHTLY, F.; BAIER, J.; MOORE, S. M.; GORDON, C. R.; DAVIS, R. D.; HELLER, A. C.; BRIGGS, D. J. Exposure of hooded capuchin monkeys (*Cebus apella* cay) to a rabid bat at a zoological park. **Journal of Zoo and Wildlife Medicine,** v. 32, n. 1, p. 123-126, 1999.

20 ANDRADE, M. C. R.; OLIVEIRA, A. N.; ROMIJN, P. C.; KIMURA, L. M. S. Resposta imune produzida por vacinas anti-rábicas em sagüis (*Callithrix* sp). **Revista da Sociedade Brasileira de Medicina Tropical,** v. 32, n. 5, p. 533-540, 1999.

21 CABRERA, M. A. A.; FIGUEIREDO, M. J.; SILVA, W. C.; FERRER, D.; TEIXEIRA, R. H.; CAVALHEIRO, M. L. J.; ANDRADE, M. C. R.; FERNANDES, R. C.; MOURA, W. C. Antibody response to a inactivated rabies vaccine in some species of Brazilian monkeys. In: WORLD VETERINARY CONGRESS, 24., 1991, Rio de Janeiro, Brazil. **Abstracts...** Rio de Janeiro: World Veterinary Congress, 1991. p. 322.

22 SIKES, R. K.; CLEARY, W. F.; KOPROWSKI, H.; WIKTOR, T. J.; KAPLAN, M. M. Effective protection of monkeys against death from street virus by post-exposure administration of tissue-culture rabies vaccine. **Bulletin World Health Organization,** v. 45, p. 1-11, 1971.