# Lethal infection by Herpes simplex virus 1 (HSV-1) in a captive Azara's Owl Monkey (*Aotus azarae*) in Paraguay

## *Infección letal por Herpes simplex virus 1 (HSV-1) en Marikiná de Azara (Aotus azarae) cautivo en Paraguay*

## *Infecção letal pelo vírus Herpes simplex 1 (HSV-1) em Marikiná de Azara (Aotus azarae) em cativeiro no Paraguai*

J. Richard Vetter[1,2]; Marlene Florentín-Morel[3]; María-Graciela Riera-Domínguez[4]; Ricardo G. Cañiza[1*]

[1]*Departamento de Recursos Faunísticos y Medio Natural, Facultad de Ciencias Veterinarias, Universidad Nacional de Asunción, Paraguay.*
[2]*Refugio Silvestre Urutaú, Paraguay.*
[3]*Clinica Veterinaria Diego Dacak, Paraguay.*
[4]*Departamento de Investigación y Docencia, Laboratorio Meyer Lab, Paraguay.*

[*] **Corresponding author:** Departamento de Recursos Faunísticos y Medio Natural, Facultad de Ciencias Veterinarias, Universidad Nacional de Asunción, Highway PY02, km 13,5, San Lorenzo 111421, Paraguay. E-mail: jvetter@vet.una.py

***Received:*** *December 10, 2023.* ***Accepted:*** *August 30, 2024*

***To cite this article:***

Vetter JR, Florentín-Morel M, Riera-Domínguez MG, Cañiza RG. Lethal infection by Herpes simplex virus 1 (HSV-1) in a captive Azara's Owl Monkey (Aotus azarae) in Paraguay. Rev Colomb Cienc Pecu. *Year, Vol, number, and pages pending.* DOI: https://doi.org/10.17533/udea.rccp.v38n3a5

## Abstract

**Anamnesis**: A 2-year-old male *Aotus azarae* was brought to the wild animal clinic. The animal weighed 975 grams and was in poor body condition. The individual was kept in close contact with the caretakers, and it was fed to a large extent by the people in the household, sharing their meals. As reported by the caretaker, the animal was asthenic and anorexic since approximately 2 days ago. **Clinical and laboratory findings:** On clinical inspection, the animal was weakened, with pale oral mucosa and hyperemic pharynx, and a rectal temperature of 34.2°C. Dry crusts were observed in the perinasal region, and a slight dyspnea was perceived. The patient died during the inspection. The hemogram was suggestive of normocytic normochromic anemia, leukopenia, hypoproteinemia, and thrombocytopenia. The observed result of molecular analysis was detectable for HSV-1. **Conclusion:** Data obtained through anamnesis and clinical history, as well as hematologic findings and the PCR results, confirmed the diagnosis of HSV-1 infection. To the authors best knowledge, this is the first report of the disease in a non-human primate in Paraguay.

**Keywords:** *Anthropozoonosis; Aotus azarae; cross-transmission; Herpes simplex virus; Herpesvirus; HSV-1; New World primate; Owl monkey; PCR; Platyrrhini.*

## Resumen

**Anamnesis**: Un *Aotus azarae* macho de 2 años fue llevado al Consultorio de Animales Silvestres. El animal pesaba 975 gramos y presentaba baja condición corporal. El individuo se mantenía en estrecho contacto con los cuidadores y era alimentado en gran medida por las personas de la casa, compartiendo sus comidas. Según informó el cuidador, el animal estaba asténico y anoréxico desde hacía aproximadamente 2 días. **Hallazgos clínicos y de laboratorio:** En la inspección clínica, el animal estaba debilitado, con la mucosa oral pálida y la faringe hiperémica, y la temperatura rectal de 34,2ºC. Se observaron costras secas en la región perinasal y se percibió una ligera disnea. El paciente falleció durante la inspección. El hemograma fue sugestivo de anemia normocítica normocrómica, leucopenia, hipoproteinemia y trombocitopenia. El resultado observado al análisis molecular fue detectable para VHS-1. **Conclusiones:** Los datos obtenidos a través de la anamnesis y la historia clínica, así como los

hallazgos hematológicos y los resultados de la PCR confirmaron el diagnóstico de infección por VHS-1. Según el entender de los autores, este es el primer reporte de la enfermedad en un primate no humano en Paraguay.
**Palabras clave:** *Antropozoonosis; Aotus azarae; Herpesvirus; Herpes simplex virus; HSV-1; Mono búho; PCR; Platirrino; primate del Nuevo Mundo; transmisión cruzada.*

**Resumo**

**Anamnese:** Um *Aotus azarae* macho de 2 anos de idade foi trazido para a clínica de animais selvagens. O animal pesava 975 gramas e estava em baixa condição corporal. O indivíduo estava em contato próximo com os cuidadores e era principalmente alimentado pelas pessoas da casa, compartilhando suas refeições. De acordo com o cuidador, o animal estava astênico e anoréxico há aproximadamente dois dias. **Achados clínicos e laboratoriais:** Na inspeção clínica, o animal estava debilitado, com mucosa oral pálida e faringe hiperêmica, e temperatura retal de 34,2ºC. Crostas secas foram observadas na região perinasal e uma leve dispneia foi percebida. O paciente morreu durante a inspeção. O hemograma foi sugestivo de anemia normocítica normocrômica, leucopenia, hipoproteinemia e trombocitopenia. O resultado observado na análise molecular foi detectável para HSV-1. **Conclusões:** Os dados obtidos na anamnese e na história clínica, bem como os achados hematológicos e os resultados da PCR confirmaram o diagnóstico de infecção pelo HSV-1. Para o conhecimento dos autores, este é o primeiro relato da doença em um primata não humano no Paraguai.
**Palavras-chave:** *Antropozoonose; Aotus azarae; Herpesvírus; HSV-1; Macaco coruja; PCR; Platirrino; Primata do Novo Mundo; transmissão cruzada; Vírus herpes simplex.*

## Introduction

Herpesviruses are enveloped DNA viruses with complex genomes that infect a wide variety of vertebrate species, with many primates and humans being natural hosts (Ludlage and Mansfield, 2003; Casagrande, 2014). Formerly classified within the family Herpesviridae, now in three families within the Order Herpesvirales: the family Herpesviridae, which retains all mammalian, avian and reptile herpesviruses; the new family Alloherpesviridae, comprising fish and frog viruses; and the new family Malacoherpesviridae, containing the viruses of bivalves. The family Herpesviridae is again divided into three subfamilies, among which are the 39-known species of human and non-human primate Herpesviruses (Casagrande, 2014).

The genus *Simplexvirus*, of the subfamily Alphaherpesvirinae, contains five species of New World Primate herpesviruses (NWP), as well as two species of human herpesviruses: *Herpes*

*simplex virus* 1 (HSV-1) and *Herpes simplex virus* 2 (HSV-2). Many human and non-human primates carry their own species of Herpesviruses of this genus, which normally do not cause clinical disease in the immunocompetent natural host (Casagrande, 2014). Humans are the only primate species infected by two distinct herpes simplex viruses: HSV-1 and HSV-2 (Wertheim *et al.*, 2014). Herpesviruses have been infecting and co-diverging with their vertebrate hosts for hundreds of millions of years (Wertheim *et al.*, 2014), however, when these viruses infect different primate species, they can cause significant and often fatal clinical disease (Casagrande, 2014).

Unlike Old World Primates (OWP), which have a generally self-limiting infection, like infection in humans, NWPs are more susceptible to HSV-1 infection, usually developing a generalized and fatal disease, characterized by anorexia, dermatitis, pruritus, depression, and ulcerative lesions in the oral cavity and gastrointestinal tract (Casagrande, 2014; Fortman *et al.*, 2018). The disease produced by these viruses has already been described in captive NWPs of the genus *Cebus* (Zinsser, 1929; Souvignet, 2019), *Aotus* (Katzin, 1967; Barahona *et al.*, 1976; Meignier *et al.*, 1990; Gozalo *et al.*, 2008; Kreutzer *et al.*, 2011), *Callithrix* (Huemer *et al.*, 2002; Mätz-Rensing *et al.*, 2003; Hatt *et al.*, 2004; Casagrande, 2007; Sekulin *et al.*, 2010; Imura *et al.*, 2014; Araújo *et al.*, 2016), and *Pithecia* (Schrenzel *et al.*, 2003; Lapid and Eshar, 2017). Primates of the genus *Aotus* are known for their high susceptibility to HSV infection, in whom the virus apparently has a predilection for the cerebral cortex, causing encephalitis (Calle and Joslin, 2015), which is why they are also used as a model for the study of the pathogen (Katzin *et al.*, 1967; Todo *et al.*, 2000; Roth *et al.*, 2014).

Because of the frequent but unapparent spread of herpesviruses, careful handling of the animals should be recommended, and certain hygienic restrictions should be applied for the sake of both owners and pet monkeys, whereas standard veterinary practice is to consider whether diseases of primates that have been in close contact with humans may have been caused by human viruses (Huemer *et al.*, 2002). In addition to considering the transmission of NWP Herpesviruses, such as CeHV-1, to a human host, where it can develop potentially fatal encephalitis (Casagrande, 2007), the potential link between a wild animal and an acquired infection from a human host should be highlighted, considering that humans in contact with the animal will not necessarily demonstrate signs of disease (Huemer *et al*, 2002) because herpesviruses do not usually cause serious infections in healthy members of their natural host species, as most of these infections are asymptomatic (Eberle and Jones-Engel, 2017). A distinctive feature of herpesviruses is their ability to establish latent infections that persist throughout the life of the host without clinically apparent signs of infection (Eberle and Jones-

Engel, 2017). The objective of the present work is to report a case of lethal infection by *Herpes simplex virus* 1 (HSV-1) in a captive Azara's owl monkey (*Aotus azarae*) in Paraguay.

**Patient Examination**

*Anamnesis*

A 2-year-old male pet *Aotus azarae* was brought to the Wild animal clinic in the Faculty of Veterinary Sciences, National University of Asunción. The animal weighed 975 grams and was in poor body condition. The individual was kept in close contact with the caretakers: either loose inside the house or tied at waist level with a nylon leash and on the caretakers' shoulders; and it was fed to a large extent by the people in the household, sharing their meals, even practicing mouth-to-mouth feeding. As reported by the caretaker, the animal was asthenic and anorexic since approximately 2 days ago.

*Clinical findings*

On clinical inspection, the animal was observed weakened, with pale oral mucosa and hyperemic pharynx, and a rectal temperature of 34.2°C (hypothermia). Dry crusts were observed in the perinasal region, and a slight dyspnea was perceived. The patient was placed in an oxygenation chamber and died after one hour.

*Diagnostic aids used*

Immediately after confirming the death of the animal, 3 ml of blood was extracted by cardiac puncture. Of the blood extracted, 1 ml was placed in a vial with EDTA, for a hemogram, and 2 ml in a vial without anticoagulant, for molecular diagnostics, and both were refrigerated at 4°C until processing. The caretaker refused to send the patient’s body for routine post-mortem studies.

The blood sample for hemogram was processed by the following methods: (a) Counting of figured elements and hemoglobin by manual methods; (b) Differential counting of leukocytes in blood smears with Giemsa staining; (c) Morphological evaluation of blood cells in blood smears with Giemsa staining; (d) Determination of total plasma protein level by refractometry. The results, shown in Table 1, were suggestive of normocytic normochromic anemia, leukopenia, hypoproteinemia, and thrombocytopenia, being indicative of viremia.

160 **Table 1.** Hematological results from a sample taken from an *Aotus azarae* infected by HSV-1.

| Analyte (unit) | Results | Reference* |
|---|---|---|
| Hematocrit (%) | 24.0 | 34.1 – 53.6 |
| Hemoglobin (g/100 ml) | 8.6 | 12.0 – 19.4 |
| Red blood cells ($10^6$/mm$^3$) | 3.2 | 4.56 – 7.06 |
| Mean corpuscular volume (fl) | 75 | 71 – 83 |
| Mean corpuscular hemoglobin (pg) | 26 | 23 – 30 |
| Mean corpuscular hemoglobin concentration (gr/dl) | 35 | 32 – 39 |
| White blood cells ($10^6$/mm$^3$) | 4300 | 4900 – 21000 |
| Segmented (µ/l) | 989 | 910 – 7190 |
| Lymphocytes (µ/l) | 3311 | 3140 – 10600 |
| Monocytes (µ/l) | -- | 0 – 302 |
| Eosinophils (µ/l) | -- | 94 – 4062 |
| Basophils (µ/l) | -- | 0 – 411 |
| Platelets ($10^3$/µl) | 2.0 | 3.7 – 24.5 |
| Total proteins (g/L) | 4.2 | 6.9 – 8.1 |

161 *Takeshita *et al*. (2011)

162

163 From the blood sample, RNA extraction was performed with the commercial kit Ribospin vRD
164 (GeneAll), following the manufacturer's instructions. The primers used for HSV-1 detection:
165 HSV-1 Forward: 5' GCAGTTTACGTACAACCACATACAGC 3', Reverse: 5'
166 AGCTTGCGGGCCTCGTT 3' and the probe: CGGCCCAACATATCGTTGACATGGC. The
167 primers used for HSV-2 detection: Forward: 5' TGCAGTTTACGTATAACCACATACAGC
168 3', Reverse: 5' AGCTTGCGGGCCTCGTT 3' and the probe:
169 CGCCCCAGCATGTCGTTCACGT. The conditions used in the BioRad CFX96 thermal
170 cycler were: Activation: 95°C for 2 minutes, then 40 cycles of denaturation: 95°C, for 5 seconds
171 and, finally, 60°C extension for 20 seconds. The observed result was detectable for HSV-1, and
172 not detectable for HSV-2.

173

174 **Discussion**

175 Given that humans and nonhuman primates (NHPs) are genetically and physiologically similar,
176 it is not surprising that some herpesviruses from NHPs can infect humans, and vice versa.

Although most of these cross-species infections are probably abortive (i.e., the virus cannot complete its replicative cycle to produce an active or latent infection or cause clinically apparent disease), some herpesviruses produce severe or lethal infections when transmitted to a non-natural host species (Eberle and Jones-Engel, 2017).

The clinical signs reported in captive primates of the genus *Aotus* infected with HSV-1 partially coincide with the case reported in the present work, mentioning severe dyspnea, apathy, hypothermia and lethargy that gradually worsened until the death of the animal in a period of 4 to 7 days (Melendez *et al.*, 1969; Kreutzer *et al.*, 2011). Reports also mention lesions in the oral cavity, including vesicles, mucous exudate, necrotic plaques, moderate multifocal gingival defects and ulcers in the oral mucosa and tongue, which may extend into the pharynx, esophagus and trachea (Melendez *et al.*, 1969; Gozalo *et al.*, 2008; Kreutzer *et al.*, 2011). All cases report infection with high case fatality (Melendez *et al.*, 1969; Meignier *et al.*, 1990; Gozalo *et al.*, 2008; Kreutzer *et al.*, 2011).

In *Callithrix* spp. another group of NWPs, an acute course of infection is also reported, with an evolution between 1 to 8 days (Juan-Sallés *et al*., 1997; Huemer *et al.*, 2002; Mätz-Rensing *et al.*, 2003; Hatt *et al.*, 2004; Casagrande, 2007). Clinical signs are similar, reporting prostration, paresis, hyporexia, hypersalivation, vomiting, diarrhea, aggressiveness, seizures, nystagmus, anisocoria and dyspnea (Huemer *et al*., 2002; Hatt *et al.*, 2004; Casagrande, 2007; Imura *et al.*, 2014). Associated with the neurological signs, most animals present small ulcers covered by crusts on the skin of the face, extensive ulcers covered by whitish fibrinous material on the oral mucosa and tongue, and conjunctivitis may occur (Mätz-Rensing *et al*., 2003; Hatt *et al*., 2004; Casagrande, 2007; Sekulin *et al.*, 2010; Araújo *et al*., 2016). Some animals present neurological alterations without skin and mucosal lesions (Juan-Sallés *et al*., 1997; Casagrande, 2007; Imura *et al.*, 2014), or do not present clinical manifestations, being found dead (Mätz-Rensing *et al.*, 2003; Hatt *et al*., 2004; Casagrande, 2007). In *Pithecia pithecia*, outbreaks of acute and fatal infection have also been reported, with animals dying between 48 and 96 hours after the onset of signs, being similar to the cases in *Aotus* spp. and *Callithrix* spp. (Schrenzel *et al.*, 2003; Lapid and Eshar, 2017).

In terms of diagnostic methods, the use of serological testing for the diagnosis of herpesvirosis should be approached with caution because many primates are asymptomatic carriers of various species of herpesviruses. When histopathological examinations are performed, alterations are non-suppurative meningoencephalitis with necrotizing vasculitis, and the presence of typical intranuclear inclusions, although it does not allow determination of the species of herpesvirus. In contrast, if immunohistochemistry is performed using monoclonal antibodies, it is possible

to differentiate several species, although antiHSV-1 and antiHSV-2 antibodies are polyclonal and cross-labeled with each other (Casagrande, 2014).

Currently, PCR is the technique of choice for the definitive diagnosis of the herpesvirus species involved in diseases of humans and NHPs, although the use of the technique must be associated with the clinical presentation and lesions of the patient. Swabs of lesions or blood from diseased animals can be used, as well as organs obtained during necropsy (Casagrande, 2007; Casagrande, 2014). The reports by Schrenzel *et al.* (2003), Casagrande (2007), and Sekulin *et al.* (2010) present the primers used for the detection of HSV-1 in *Pithecia pithecia* and *Callithrix jacchus* specimens, respectively.

Treatment with acyclovir does not prevent death from encephalitis in HSV-1-infected animals, although it remains the antiherpetic drug of choice in humans (Casagrande, 2014; Kukhanova *et al*., 2014). Other drugs used in humans are valacyclocir and ganciclovir, which could be used in NHPs (Casagrande, 2014). There is a single report of a *Callithrix jacchus* that survived a natural HSV-1 infection, and recovered spontaneously without any treatment (Hatt *et al*., 2004). It should be noted that HSV-1 infection in NHPs is an anthropozoonosis, and the present report coincides with acute spontaneous HSV-1 infections described in fatal cases in *Aotus* spp. and *Callithrix* spp. after contact with a person carrying HSV-1 (Mätz-Rensing *et al.*, 2003), kept as a pet in close contact with the owners (Juan-Sallés *et al.*, 1997; Huemer *et al.*, 2002; Hatt *et al.*, 2004; Kreutzer *et al.*, 2011; Imura *et al.*, 2014), or even sharing food with the animal (Araújo *et al.*, 2016). HSV-1 infection in NWPs has already been widely reported in Brazil, being observed in animals from zoos, conservation and breeding centers, research centers, as well as cases reported by veterinarians in pet patients, but mainly in primates of the *Callithrix* genus (Casagrande, 2007). A work conducted in Peru with primates kept in homes reports that 50.4% go for consultation with an infectious disease, and 11.4% go for an infectious and non-infectious disease at the same time (Nolasco, 2017), highlighting the potential impact of household primate ownership on public health.

## Conclusions

Data obtained through anamnesis and clinical history, as well as observable signs during the physical examination, the hematologic findings, and the PCR results confirmed the diagnosis of HSV-1 infection that caused the death of a captive Azara's owl monkey. To the authors best knowledge, this is the first report of the disease in a non-human primate in Paraguay.

## Declarations

*Aknowledgements*

A special thanks to Thomas Goossen (Asociación Paraguaya de Mastozoología), Lorena Núñez and Lourdes Narváez (División Laboratorio de Biotecnología Animal, Departamento de Clínicas Veterinarias, FCV-UNA), Nicolás Aguayo.

*Funding*

This study was financed by the authors' own resources. There was no financial support by any of the companies mentioned in this manuscript.

*Conflicts of interest*

The authors declare they have no conflicts of interest regarding the work presented in this report.

*Author contributions*

J. Richard Vetter: study conception, data collection, wrote the paper. Marlene Florentín-Morel: data collection, critical review of the paper. MaríaGraciela Riera-Domínguez: data collection, wrote the paper. Ricardo G. Cañiza: data collection, critical review of the paper.

*Use of artificial intelligence (AI)*

No AI or AI-assisted technologies were used during the preparation of this work.

**References**

Araújo JL, Frade MTS, Melo CMF, dos Santos Carneiro R, Galiza GJN, Olinda RG, Lucena RB & Dantas AFM. Infecção sistêmica por herpesvírus simples em um sagui-de tufo-branco (*Callithrix jacchus*) no semiárido da paraíba. Veterinária e Zootecnia 2016; 23(2):203–208. https://pesquisa.bvsalud.org/portal/resource/pt/vti-762783

Barahona H, Melendez LV, Hunt RD, Daniel MD. The owl monkey (*Aotus trivirgatus*) as an animal model for viral diseases and oncologic studies. Lab Anim Sci. 1976; 26(6):1104–1112. https://pubmed.ncbi.nlm.nih.gov/190472/

Calle PP, Joslin JO. New world and old world monkeys. In: Miller E, Fowler M, editors. Zoo and Wild Animal Medicine. 8th ed. St Louis: Elsevier Saunders; 2015. p.301–335. https://doi.org/10.1016/B978-1-4557-7397-8.00037-2

277 Casagrande RA. Herpesvirus simplex Tipo 1 (HSV-1) em sagüis (*Callithrix jacchus* e
278 *Callithrix penicillata*)-Caracterização anatomopatológica e molecular (Doctoral dissertation).
279 Universidade de São Paulo; 2007. https://doi.org/10.11606/D.10.2007.tde-20082007-133334
280 Casagrande RA. Herpesviroses em Primatas. In: Cubas ZS, Ramos Silva JC, Catao-Dias JL,
281 editors. Tratado de Animais Selvagens. 2nd ed. Rio de Janeiro: Roca; 2014. Pp. 1321–1336.
282 Eberle R, Jones-Engel L. Understanding primate herpesviruses. J Emerging Dis Virol
283 2017; 3(1). https://doi.org/10.16966%2F2473-1846.127
284 Fortman JD, Hewett TA, Halliday LC. The laboratory nonhuman primate. 2nd ed. Florida: CRC
285 Press; 2018. https://doi.org/10.1201/9781315117065
286 Gozalo AS, Montoya EJ, Weller RE. Dyscoria associated with herpesvirus infection in owl
287 monkeys (*Aotus nancymae*). J Am Assoc Lab Anim Sci. 2008; 47(4):68–71.
288 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2694719/
289 Hatt JM, Grest P, Posthaus H, Bossart W. Serologic survey in a colony of captive common
290 marmosets (*Callithrix jacchus*) after infection with herpes simplex type 1–like virus. J Zoo
291 Wildl Med. 2004; 35(3):387–390. https://doi.org/10.1638/03-041
292 Huemer HP, Larcher C, Czedik-Eysenberg T, Nowotny N, Reifinger M. Fatal infection of a pet
293 monkey with human herpesvirus 1. Emerg Infect Dis. 2002; 8(6):639.
294 https://doi.org/10.3201%2Feid0806.010341
295 Imura K, Chambers JK, Uchida K, Nomura S, Suzuki S, Nakayama H, Miwa Y. Herpes simplex
296 virus type 1 infection in two pet marmosets in Japan. J Vet Med Sci. 2014; 76(12):1667–1670.
297 https://doi.org/10.1292/jvms.14-0374
298 Juan-Sallés C, Ramos-Vara JA, Prats N, Solé-Nicolás J, Segalés J, Marco AJ. Spontaneous
299 herpes simplex virus infection in common marmosets (*Callithrix jacchus*). J Vet Diagn Invest.
300 1997; 9(3):341–345. https://doi.org/10.1177/104063879700900325
301 Katzin DS, Connor JD, Wilson LA, Sexton RS. Experimental herpes simplex infection in the
302 owl monkey. Proc Soc Exp Biol Med. 1967; 125(2):391–398.
303 https://doi.org/10.3181/00379727-125-32100
304 Kreutzer R, Kreutzer M, Günther CP, Mätz-Rensing K, Wohlsein P. Systemic herpesvirus
305 infection in an Azara's Night Monkey (*Aotus azarae*). J Med Primatol. 2011; 40(3):197–199.
306 https://doi.org/10.1111/j.1600-0684.2011.00469.x
307 Kukhanova MK, Korovina AN, Kochetkov SN. Human herpes simplex virus: life cycle and
308 development of inhibitors. Biochem (Mosc). 2014; 79:1635–1652.
309 https://doi.org/10.1134/S0006297914130124

Lapid R, Eshar D. Fatal Herpes simplex virus 1 (HSV-1) infection in a group of zoo-kept white-faced saki monkeys (*Pithecia pithecia*) in Israel. Isr J Vet Med. 2017; 72:51–55. https://www.ijvm.org.il/node/529

Ludlage E, Mansfield K. Clinical care and diseases of the common marmoset (*Callithrix jacchus*). Comp Med. 2003; 53(4):369–382. https://www.ingentaconnect.com/content/aalas/cm/2003/00000053/00000004/art00006

Mätz-Rensing K, Jentsch KD, Rensing S, Langenhuyzen S, Verschoor E, Niphuis H, Kaup FJ. Fatal Herpes simplex infection in a group of common marmosets (*Callithrix jacchus*). Vet Pathol. 2003; 40(4):405–411. https://doi.org/10.1354/vp.40-4-405

Meignier B, Martin B, Whitley RJ, Roizman B. In vivo behavior of genetically engineered herpes simplex viruses R7017 and R7020. II. Studies in immunocompetent and immunosuppressed owl monkeys (*Aotus trivirgatus*). J Infect Dis. 1990; 162(2):313–321. https://doi.org/10.1093/infdis/162.2.313

Melendez LV, Espana C, Hunt RD, Daniel MD, Garcia FG. Natural herpes simplex infection in the owl monkey (*Aotus trivirgatus*). Lab Anim Care. 1969; 19(1):38–45. https://pubmed.ncbi.nlm.nih.gov/4304237/

Nolasco Chumpitaz CE. Estudio retrospectivo de las historias clínicas de primates atendidos en el consultorio de animales silvestres y exóticos de la Facultad de Medicina Veterinaria, Universidad Nacional Mayor de San Marcos, durante el período 2005-2014 (Undergraduate dissertation). Universidad Nacional Mayor de San Marcos; 2017. https://hdl.handle.net/20.500.12672/7254

Roth JC, Cassady KA, Cody JJ, Parker JN, Price KH, Coleman JM, Peggins JO, Noker PE, Powers NW, Grimes SD, Carroll SL, Gillespie GY, Whitley RJ & Markert JM. Evaluation of the safety and biodistribution of M032, an attenuated herpes simplex virus type 1 expressing hIL-12, after intracerebral administration to *Aotus* nonhuman primates. Hum Gene Ther Clin Development. 2014; 25(1):16–27. https://doi.org/10.1089/humc.2013.201

Schrenzel MD, Osborn KG, Shima A, Klieforth RB, Maalouf GA. Naturally occurring fatal herpes simplex virus 1 infection in a family of white-faced saki monkeys (*Pithecia pithecia pithecia*). J Med Primatol. 2003; 32(1):7–14. https://doi.org/10.1034/j.1600-0684.2003.01040.x

Sekulin K, Jankova J, Kolodziejek J, Huemer HP, Gruber A, Meyer J, Nowotny N. Natural zoonotic infections of two marmosets and one domestic rabbit with herpes simplex virus type 1 did not reveal a correlation with a certain gG-, gI-or gE genotype. Clin Microbiol Infect. 2010; 16(11):1669–1672. https://doi.org/10.1111/j.1469-0691.2010.03163.x

344 Souvignet T, Giorgiadis M, Drouet B, Quintard B. EAZA Best Practice Guidelines capuchin
345 monkeys (*Sapajus* and *Cebus* sp.). Mulhouse: European Association of Zoos and Aquaria;
346 2019.
347 Takeshita RSC, Monteiro FOB, de Miranda Lins e Lins FL, da Silva GA, Faturi C, Coutinho
348 LN, Monteiro MVB, Kugelmeier T, de Castro PHG & Muniz JAPC. Hematological, hepatic,
349 and renal evaluation in *Aotus azarai infulatus*. J Med Primatol. 2011; 40(2):104–110.
350 https://doi.org/10.1111/j.1600-0684.2010.00452.x
351 Todo T, Feigenbaum F, Rabkin SD, Lakeman F, Newsome JT, Johnson PA, Mitchell E,
352 Belliveau D, Ostrove JM & Martuza RL. Viral shedding and biodistribution of G207, a
353 muitimutated, conditionally replicating herpes simplex virus type 1, after intracerebral
354 inoculation in *Aotus*. Mol Ther. 2000; 2(6):588–595. https://doi.org/10.1006/mthe.2000.0200
355 Wertheim JO, Smith MD, Smith DM, Scheffler K, Kosakovsky Pond SL. Evolutionary origins
356 of human herpes simplex viruses 1 and 2. Mol Biol Evol. 2014; 31(9):2356–2364.
357 https://doi.org/10.1093/molbev/msu185
358 Zinsser H. Herpes encephalitis in Cebus monkeys. J Exp Med. 1929; 49(4):661.
359 https://doi.org/10.1084%2Fjem.49.4.661