

# NONHUMAN PRIMATE DERMATOLOGY: RESEARCH AND ADVANCES

Bernstein, JA<sup>1</sup>

<sup>1</sup>Long Green Animal Dermatology Center, P.C., 13515 Long Green Pike, Baldwin, MD 21013

## INTRODUCTION AND KEY POINTS

The study of dermatologic diseases in nonhuman primates (NHP) has been neglected almost entirely by veterinary dermatologists. The scientific literature regarding this subject is disparate and unorganized. In “Nonhuman primate dermatology: a literature review” in 2009, this author attempted to gather wide-ranging case reports and studies into a more cohesive format to provide a baseline reference point for the veterinary dermatologist interested in the study of NHPs.<sup>1</sup> The aim of this discussion is to provide encouragement to members of the American College of Veterinary Dermatology (ACVD) to participate in NHP case work and research in conjunction with the primatologists of the Association of Primate Veterinarians (APV). The following key points will be discussed:

- Basic Taxonomy
- Health requirements and safety precautions for the dermatologist preparing to work in a facility housing NHPs
- Update on NHP dermatologic research in the past two years focusing on NHP alopecia
- Recommended reading

## TAXONOMY

The order Primata includes more than 200 species divided into two sub-orders; the Haplorhini (tarsiers, Old World and New World monkeys, apes and humans) and the Strepsirhini (bushbabies, lorises and lemurs). The Groves classification system is the most commonly used and can be referred to for a detailed primate taxonomy.<sup>2</sup> Rhesus (*M. mulatta*) and cynomolgus (*M. fascicularis*) macaque species are the most commonly studied NHPs in biomedical research.

## HEALTH AND SAFETY PRECAUTIONS

Because of the close phylogenetic relationship between non-human primates and humans, zoonotic and reverse-zoonotic diseases caused by a number of pathogenic organisms are of concern. Essential aspects of an institution’s Occupational Health and Safety Programme (OHSP) include: health screening of animals and personnel, risk assessment of infectious and non-infectious hazards and personal protective equipment requirements determined by the primate species, health status and work environment.<sup>3</sup>

- Tuberculosis: TB testing (intradermal PPD) is typically required every 6 months to work with NHP patients.
- Recommended (sometimes required depending on institution) vaccinations for clinicians: Measles, Rabies, Hepatitis A, Hepatitis B

- Personal protective equipment can range from dedicated clothing, footwear and gloves to a more typically encountered higher level of barrier protection including mask, hat, goggles and/or face visor. This can make dermatologic examination uncomfortable and sometimes difficult.
- Engineering controls (crush backs and tunnel catching systems), as well as chemical controls (sedation typically with ketamine 10-15 mg/kg IM) are used to prevent bites and scratches, as well as exposure to bodily fluids.

The most significant zoonotic concern for clinicians and keepers is “Herpes B Virus (BV)”. Formerly named *Cercopithecine herpesvirus 1*, it has recently been renamed by the International Committee on Taxonomy of Viruses in the 2008 overhaul of the classification system as *Macacine herpesvirus 1* (McHV-1).<sup>4</sup> In its reservoir hosts (*Macaca* genus), this organism produces a mild clinical infection similar to HSV in humans followed by latency in sensory nerve ganglia. Typical clinical signs are erythema and vesicles on mucocutaneous junctions. Transmission to its non-natural hosts (humans, African monkeys and New World monkeys) usually results in a fatal encephalitis. Despite the development of specific pathogen-free (SPF) macaque colonies, due to issues with reliability of assessment of viral status by antibody assay, all macaques should be considered potentially infected.

## **UPDATE ON NHP DERMATOLOGIC RESEARCH- FOCUS ON ALOPECIA**

The majority of efforts in recent dermatologic investigations in captive NHP species have focused on the causes of alopecia. The disproportionate amount of research energy being devoted has been spurred by regulations promoting the psychological well-being of captive NHPs and a recent focus by USDA regulators on alopecia. A default diagnosis of psychogenic alopecia (trichotillomania) is often presumed on inspections of facilities without an evidence-based diagnostic approach. As in companion animal patients, alopecia can be either a primary or secondary lesion; and numerous factors and causes have been reported in the NHP.<sup>5-12</sup> An excellent comprehensive review article published in 2009 (Novak MA and Meyer JS) summarized causes of alopecia including: seasonal variation, aging, nutritional and hormonal imbalances, immunologic and genetic factors, bacterial, parasitic, fungal, allergic and psychologic factors.<sup>13</sup> Recommendations for an organized diagnostic assessment of cases were made as well as management strategies.

The researchers of the New England Primate Research Center (NEPRC), Harvard Medical School worked in 2010 on clinical and dermatopathologic evaluation of different presentations of alopecia in a large colony of Indian-origin rhesus macaques. In the first of the two alopecia studies undertaken by the NEPRC group, a group of rhesus macaques with varying degrees of alopecia were biopsied to assess underlying pathology. Twenty-five affected individuals were sampled along with 11 control animals chosen for normal hair coats. Twenty-four of the affected animals had clinical dermatitis associated with the alopecia. Alopecia was associated with perivascular mononuclear cell infiltrate, acanthosis, hyperkeratosis, and edema. Immunohistochemical and metachromatic stains revealed increased numbers of mast cells, CD3+ lymphocytes, CD 163+ histiocytes and dendritic cells. The immunophenotypic analysis showed a statistically significant difference between the affected and control patients. Complete blood count, chemistry panels, cortisol levels and thyroid function tests showed no significant differences between affected and unaffected animals. Pathologic findings in this study led to the conclusion that the affected patients likely had a chronic hypersensitivity reaction or atopic dermatitis-like disease.<sup>14</sup>

The follow-up study focused on a subset of alopecic rhesus macaques with low grade alopecia localized to the forearms or lower legs. This clinical subset (n=17) had no evidence of

excoriation or dermatitis but anecdotally caretakers had reported hair picking and pulling behaviors in the affected anatomic areas. Skin scrapes, surface cytologies, and bacterial and fungal cultures revealed no evidence of parasitism, bacterial or fungal infection. Biopsies were taken from affected and unaffected areas on the same limb. Skin biopsies demonstrated little difference between alopecic and non-alopecic areas. Features of trichotillomania in humans<sup>15</sup> were rarely noted: increased catagen follicles (n=2), reduced numbers of hair follicles (n=1), trichomalacia (n=3), and intrafollicular hemorrhage (n=2). No bulbar inflammation or folliculitis was noted and no perivascular inflammation, acanthosis or dermal edema were noted as compared with the patients in the previous study. Mast cell and CD3+ lymphocyte counts were the same in affected and unaffected skin samples. The authors proposed that this focal presentation of self-inflicted limb alopecia, unlike the presentations in the prior study, was most consistent with a psychogenic self-inflicted alopecia (accepted for publication January 2011, Kramer, J, Mansfield, KG, Simmon, J, Bernstein, JA. Psychogenic alopecia in rhesus macaques presenting as focally extensive distal limb alopecia. Comparative Medicine.)

### RECOMMENDED READING

Wolfe-Coote, S, The Laboratory Primate. Elsevier, 2005

Voevodin, AF, Marx, PA. Simian Virology, 1<sup>st</sup> Edition. Wiley Blackwell, 2009.

Wolfensohn, S, Honess, P. Handbook of Primate Husbandry and Welfare, Blackwell Publishing, 2005.

Nonhuman Primate Drug formulary on APV website- [www.primatetvets.org](http://www.primatetvets.org)

### REFERENCES

1. Bernstein, JA, Didier PJ. Nonhuman primate dermatology: a literature review. Veterinary Dermatology. 2009; 20: 145-156.
2. Groves, CP. Order Primates. IN: Wilson, DE and Reeder DM (eds), Mammal Species of the World: A Taxonomic and Geographic Reference. 3<sup>rd</sup> Edition. Baltimore, Johns Hopkins University Press, 2005, pp 111-184.
3. Wolfensohn, S, Honess, P. Handbook of Primate Husbandry and Welfare, Blackwell Publishing, 2005, pp. 33-42.
4. Voevodin, AF, Marx, PA. Simian Virology, 1<sup>st</sup> Edition, Wiley Blackwell, 2009, p 267.
5. Beisner, BA Isbell LA. Factors influencing hair loss among female captive rhesus macaques (*Macaca mulatta*). Applied Animal Behavior Science. 2009; 119: 91-100.
6. Beisner, BA, Isbell LA. Ground substrate affects activity budgets and hair loss in outdoor captive groups of rhesus macaques (*Macaca mulatta*). American Journal of Primatology. 2008; 70: 1160-1168.
7. Ahmad, W, Ratterree, MS, Panteleyev, AA, Aita, VM, Sundberg, JP, Christiano, AM. Atrichia with papular lesions resulting from mutations in the rhesus macaque (*Macaca mulatta*) hairless gene. Laboratory Animal. 2002; 36: 61-67.
8. Beardi, B, Wanert, F, Zoller, M, Freyshmidt-Paul, P, Bodemer, W, Kaup, FJ. Alopecia areata in a rhesus monkey (*Macaca mulatta*). Journal of Medical Primatology. 2007; 36: 124-130.
9. Honess, P, Gimpel, J, Wolfensohn, S, Mason, G. Alopecia scoring: the quantitative assessment of hair loss in captive macaques. Alternatives to Lab Animals. 2005; 33: 193-206.
10. Horenstein, VD, Williams LE, Brady AR, Abee, CR, Horenstein, MG. Age-related diffuse chronic telogen effluvium-type alopecia in female squirrel monkeys (*Samiri boliviensis boliviensis*). Comparative Medicine. 2005; 55: 169-174.

11. Steinmetz, HW, Kaumanns, W, Dix, I, Heistermann, M, Fox, M, Kaup, FJ. Coat condition, housing, condition, and measurement of faecal cortisol metabolites- a non-invasive study about alopecia in captive rhesus macaques (*Macaca mulatta*). *Journal of Medical Primatology* 2006: 35: 3-11.
12. Steinmetz, HW, Kaumanns, W, Neimeier, KA, Kaup, FJ. Dermatologic investigations of alopecia in rhesus macaques (*Macaca mulatta*). *Journal of Zoo and Wildlife Medicine*. 2005: 36: 229-238.
13. Novak, MA, Meyer, JS. Alopecia: possible causes and treatments, particularly in captive nonhuman primates. *Comparative Medicine*. 2009: 59: 18-26.
14. Kramer, J, Fahey, M, Santos, R, Carville, A, Wachtman, L, Mansfield, K. Alopecia in rhesus macaques correlates with immunophenotypic alterations in dermal inflammatory infiltrates consistent with hypersensitivity etiology. *Journal of Medical Primatology*. 2010: 39: 112-122.
15. Muller, SA. Trichotillomania: a histopathologic study in sixty-six patients. *Journal of the American Academy of Dermatology*. 1990: 23: 56-62.