

# Nonhuman primate dermatology: a literature review

Joseph A. Bernstein\* and Peter J. Didiert

\*Long Green Animal Dermatology Center, P.C. P.O. Box 61, 13515 Long Green Pike, Baldwin, MD 21013, USA

†Divisions of Comparative Pathology, Microbiology, Tulane National Primate Research Center, Tulane University, Covington, LA, USA  
Correspondence: Joseph A. Bernstein, Long Green Animal Dermatology Center, P.C., P.O. Box 61, 13515 Long Green Pike, Baldwin, MD, USA. E-mail: drjoe@lganimalderm.com

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## Abstract

**In general, veterinary dermatologists do not have extensive clinical experience of nonhuman primate (NHP) dermatoses. The bulk of the published literature does not provide an organized evidence-based approach to the NHP dermatologic case. The veterinary dermatologist is left to extract information from both human and veterinary dermatology, an approach that can be problematic as it forces the clinician to make diagnostic and therapeutic decisions based on two very disparate bodies of literature. A more cohesive approach to NHP dermatology – without relying on assumptions that NHP pathology most commonly behaves similarly to other veterinary and human disease – is required. This review of the dermatology of NHP species includes discussions of primary dermatoses, as well as diseases where dermatologic signs represent a significant secondary component, provides a first step towards encouraging the veterinary community to study and report the dermatologic diseases of nonhuman primates.**

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## Introduction

Veterinary dermatologists in general do not have extensive experience of nonhuman primate (NHP) dermatoses. With exceptions, the literature does not provide an organized evidence-based approach to the NHP dermatologic case, leaving the veterinary dermatologist to draw from both human and veterinary dermatology. The authors have found this approach to be essential in the investigation of such dermatoses in an organized fashion, but it can be frustrating because of the need to extrapolate from two very disparate bodies of medical knowledge. This review of the literature was undertaken to compile the extant information in an organized format to enable the veterinary

dermatologist to participate in and or undertake disease investigations with an understanding of the available resources and their limitations. This represents a first step in providing a base for future specific studies of NHP dermatologic diseases. The investigation of dermatological conditions in NHPs presented from zoological and research collections or as pets should merit a multidisciplinary approach that may involve veterinarians from a number of disciplines including the zoological or research facility communities, as well as physicians trained in human dermatology.

## Overview

Any exploration of the scientific literature concerning NHP dermatology quickly becomes problematic for the clinician seeking practical reference as there is a paucity of organized literature regarding primary dermatologic disease in either captive or wild NHPs. The predominant source of reference consists of case reports. Some assert that this is because of an infrequency of spontaneous skin disorders in these species<sup>1</sup> attributed to the following factors:

- 1 Natural selection is an efficient means of removing individuals with genetic mutations that adversely affect the organism's susceptibility to infectious and parasitic disease and the function of the skin to protect the organism from the external environment.
- 2 Captive NHPs are only a few generations removed from wild stock.
- 3 Captive animals with dermatologic disease are removed from the breeding pool unless a specific model is being sought for study
- 4 Reduced importation of feral animals has reduced the prevalence of infectious and parasitic disease
- 5 Improved preventative screening by exporters in the countries of origin

These explanations are not entirely satisfactory as the assertions regarding the relative advantage or disadvantage of feral stock is contradictory. Other discussions of NHP dermatology in the literature assert that clinical dermatologic disease in NHPs is relatively common.<sup>2</sup> How then can the absence of coherent veterinary dermatologic literature on the subject be explained?

A brief overview of the extant scientific research enables the relevant studies to be divided into three main categories:

- 1 The study of diseases in which the NHP has been found to be a good model for human diseases.
- 2 The search for diseases in which the NHP could be a potential comparative model for human disease.
- 3 The study of diseases of primary concern to the NHP, with no obvious application in human dermatology or medicine.

Not surprisingly it is the first and second groups that make up the bulk of the rigorous scientific work. Examples of subjects from the comparative literature include the healing of skin wounds,<sup>3</sup> initial changes in burns,<sup>4</sup> dermatographism,<sup>5</sup> chloracne,<sup>6</sup> geriatric dermatologic changes,<sup>7</sup> treatment of facial wounds with Botox,<sup>8</sup> Lyme disease,<sup>9</sup> treatment of pressure sores,<sup>10</sup> and male pattern baldness.<sup>11</sup>

The third group consists primarily of case reports predominantly based on ad hoc observational work. These reports are valuable, but are rarely used to draw conclusions about dermatologic disease in general or provide an organized approach to diagnosis and therapy in the NHP.

It is widely accepted that 'most lesions [in the NHP] are similar in appearance and clinical progression to those seen in humans and other animals, and therapies that work well in these species are usually satisfactory in NHP.'<sup>2</sup> However, this represents a pervasive attitude towards review of the case reports, which is not always borne out by the scientific evidence. It is a broad assumption, *ex pede herculem*, in which NHP dermatology is extrapolated from other veterinary and medical knowledge. In cases where the NHP is a good model for human or other mammalian dermatologic disease, this assumption can result in logical and successful medical conclusions. Where this assumption is unfounded, the results could potentially be deleterious to both the advancement of scientific study and the clinical assessment and care of NHP patients. It is with this in mind that the authors have undertaken a review of the relevant literature and information regarding primary NHP dermatologic diseases as well as those diseases in which dermatologic signs represent a significant secondary component.

### Taxonomy and dermatology

In discussing diseases of the NHP, it is worth noting that the Order Primates (prosimians, monkeys and apes) includes approximately 240 species including *Homo sapiens*. This number varies depending on whether closely related groups are considered to be varieties of each other or distinct species. They range in size from the 160-kg male mountain gorilla to the 100-g pygmy marmoset. In addition to great variation in size and other anatomy, evolutionary divergence has resulted in variable dermatologic appearance. The general evolutionary trend includes refinement of the hands and feet for grasping (flat nails instead of claws, sensitive pads). There is great variation in the colour, length and density of hair coats amongst the species. Variation in the histology of the skin (e.g. sweat glands) has also been described.<sup>12</sup> The presence of sexual skin also varies with some genera (*Cercocebus*, *Macaca*, *Papio*, *Theropithecus*, *Miopithecus* and *Mandrillus*) having perianal engorgement and oestrous-dependent reddening of skin. A prominent difference between New World and Old World monkeys includes the New World evolutions of prehensile tails and the old world predominance of ischial callosities of the buttocks, hairless, keratinized areas on which they sit (Figure 1).<sup>13</sup> Recognition of red sexual skin and ischial callosities as normal features in simian anatomy is important, as new students of primatology may mistake these for pathologic lesions.



**Figure 1.** The normal red sexual skin and prominent ischial callosities in a female rhesus monkey (*Macaca mulatta*).

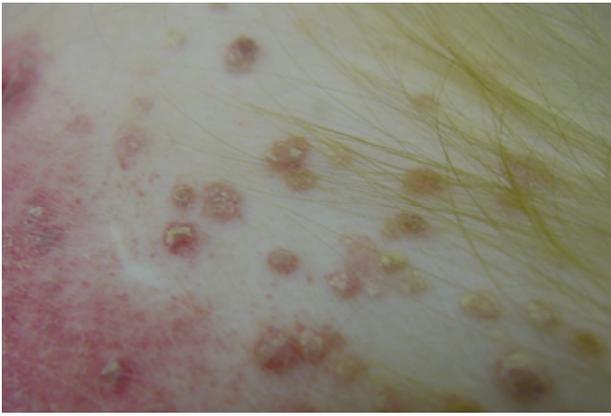
### Bacterial infections

It is anecdotally understood that the dermatologic presentation most commonly encountered by the NHP veterinarian is the opportunistic secondary bacterial skin infection associated most commonly with fight wounds and trauma, but also with environmental causes and immunodeficient states.<sup>1,2</sup> Clinical disease can result from overgrowth of normal skin flora (*Staphylococcus* and *Streptococcus*) or introduction of nonresident pathogens.<sup>1</sup> Lesions range from superficial impetigo and moist pyoderma to deeper cutaneous and subcutaneous infections with the possibility of extensive cellulitis and draining tracts.<sup>1,2,14-16</sup> Most routine cutaneous bacterial infections in an NHP facility are managed with appropriate wound care (debridement, closure or second-intention healing) and antibiotics. Failure to perform culture and sensitivity tests may result in some of the more unusual aetiologies being missed.<sup>17</sup>

Opportunistic bacterial infection from trauma (iatrogenic or bite wound) is widely recognized by NHP veterinarians as the most common dermatologic presentation,<sup>1,2</sup> although there is no body of literature specifically addressing this. In support of this review, an analysis of skin cultures performed in 2005 by one of the authors (P. Didier) yielded 61 bacterial isolates. All were associated with trauma, 52 were associated with indwelling catheters placed for a single ongoing research project, the remaining isolates were from wounds.

#### Staphylococcus

The usual aetiology is *Staphylococcus aureus*, which is commonly carried asymptotically in the nose and throat. Infections occur in damaged skin<sup>15</sup> and indwelling catheters can be a common source of infection.<sup>16</sup> *S. aureus* can cause pustular dermatitis in young animals, which can lead to cellulitis and abscess formation (Figure 2). Serious infections can potentially lead to systemic involvement including visceral abscess formation, endocarditis, and septicemia.<sup>14-17</sup> Although methicillin-resistant *S. aureus* is noted in clinical practice, the present authors are unaware of any organized attempt to investigate the incidence of carriage or dermatologic infection in NHPs, handlers or veterinary personnel. Given the current volume of ongoing research in veterinary and human medicine, this appears to be a glaring omission in the NHP research field.



**Figure 2.** Pustular dermatitis of the inguinal area of a female macaque caused by *S. aureus*.

#### Streptococcus

*Streptococcus pyogenes* and other species have been isolated in numerous skin infections, including an impetigo-like moist pyoderma of nursery reared macaques attributed to the moist environment of incubators. This is a condition that readily responds to appropriate antibiotics and environmental changes.<sup>1</sup>

#### Pseudomonas

*Pseudomonas aeruginosa* and *Pseudomonas pseudomallei* have been isolated from both captive and wild NHPs. *P. aeruginosa* is predominantly a problem in immunocompromised, debilitated, burned and neutropenic patients. Commonly reported causes of immunosuppression include chronic steroid use and radiation. The hallmark lesions of *P. aeruginosa* in the NHP are abscesses and vasculitis without thrombosis. *P. pseudomallei* is a cause of disease in animals and humans from Southeast Asia and results in meliodiosis, characterized by abscessation, recurrent fistulas and pneumonia.<sup>18–20</sup>

#### *Mycobacterium leprae*

Numerous examples of experimentally-induced leprosy exist in NHP. Naturally occurring disease has been reported in only three species – chimpanzees, sooty mangabeys, and cynomolgous monkeys.<sup>21</sup> The route of transmission is unclear. Only the lepromatous form of leprosy has been reported. Lesions occur on the cooler parts of the body (ears, face, distal extremities, tail, scrotum, etc.) The skin is thickened and often ulcerated with dermal and subcutaneous histiocytic inflammation focusing on peripheral nerve bundles.<sup>22</sup> Lesion appearance and histopathology are well characterized in the literature because of their similarity to human lepromatous leprosy.<sup>21–27</sup>

#### Other bacterial diseases

Other bacterial species reported to cause cutaneous infections include: *Pasteurella multocida* and *Pasteurella haemolytica*, *Corynebacterium* spp., *Erysipelothrix*, *Proteus*, *Mycobacterium tuberculosis* and *Mycobacterium bovis*, *Chromobacterium*, *Clostridium*, *Salmonella typhimurium*, *Actinomyces* spp. and *Dermatophilus congolensis*.<sup>1,2,17,28–30</sup> The reports range widely in quality and documentation.



**Figure 3.** *Candida* paronychia in a macaque.

## Fungal infections

#### *Dermatophytosis*

The most common aetiologies include *Microsporum canis* and *Trichophyton mentagrophytes*. Infections with other *Microsporum* and *Trichophyton* species occur less commonly. In captive settings, infections are usually associated with contact with humans or domestic pets. Typical clinical signs include hyperkeratotic circumscribed alopecic areas. Some sources associate infection with rapid spread in group housing,<sup>1</sup> whereas others suggest the opposite.<sup>31</sup> Reports describing dermatophytosis in the wild are poorly described and characterized. Diagnoses based on clinical appearance without cultures have been used to evaluate the efficacy of therapeutic agents. A recent evaluation of the efficacy of lufenuron in wild chimpanzees is a good example of diagnosis and treatment without culture.<sup>32</sup>

#### *Candida*

*Candida albicans* is a ubiquitous, opportunistic infection typically occurring in debilitated and immunocompromised patients. Superficial infection of the mucous membranes and skin has been reported,<sup>33,34</sup> and paronychia and preputial inflammation were noted in one report of a rhesus monkey.<sup>35</sup> One of the authors (J. Bernstein) has also diagnosed candidal paronychia in a rhesus macaque (Figure 3).

#### *Others*

*Histoplasma capsulatum* var. *duboisii*, *Sporothrix schenckii* and *Coccidioides immitis* have all been reported with infrequent cutaneous manifestations. The ulcerated granulomatous nodules of histoplasmosis among African baboons have responded well to surgery.<sup>36</sup> Several NHP species in endemic areas of the United States have

developed coccidiomycosis, which responded poorly to treatment and was frequently lethal.<sup>37,38</sup> Sporotrichosis, often associated with penetrating injury, is an infrequent cause of cutaneous nodules and ulceration.<sup>1</sup>

### Viral infections

Viral diseases represent a large and clinically important group of diseases affecting NHP in both captivity and the wild.<sup>1,2,17</sup> Some present with primary dermatologic lesions whereas others have secondary dermatologic signs as markers of systemic infection. Recognition of the classic viral dermatologic lesions in NHP is essential, and appropriate precautions must be taken because of the high number of recognized and potentially serious zoonoses in this group. In addition, viral diseases that may be subclinical in one NHP species may cause a fatal disease in others, necessitating separation of species in laboratory and other facilities.

#### *Herpes B (Cercopithecine herpesvirus 1)*

This organism produces a mild clinical or latent infection in its reservoir hosts, members of the genus *Macaca*, but may cause fatal encephalitis in humans infected by a shedding macaque. Infection of African green monkeys, gibbons, owl monkeys, marmosets and patas monkeys is fatal. NHP species should not be mixed in housing for this reason. Transmission may be via bites and scratches or venereal. The virus is shed in oral and genital secretions as well as vesicular fluid. In macaques the primary dermatologic lesions are vesicles and ulcers of the oral cavity, lips and conjunctiva (mucocutaneous junctions). Herpetiform lesions can also occur on the genitalia. Latent infection is common, and asymptomatic macaques can shed virus. One must assume that all macaques can shed virus and take proper precautions.<sup>39-42</sup>

In the United States the following contact may assist with diagnosis of such infection

Resource contact for clinicians:

**Herpes B-Virus Diagnosis: National Resource Laboratory, Department of Biology, Viral Immunology Center, Georgia State University**

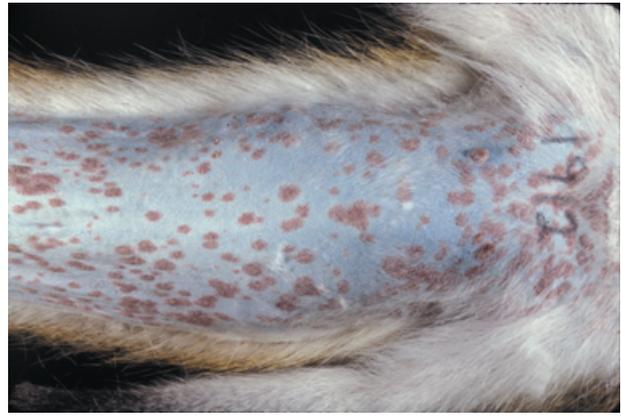
Package shipment: 50 Decatur Street, Atlanta, Georgia 30303 USA

**Mission:** To identify B-virus infections in humans and macaques and study basic pathogenesis mechanisms of this and other neurotropic herpesviruses; to develop control and prevention strategies of B-virus infections. All samples evaluated by the resource can be used in ongoing research studies.

**Key personnel:** Julia K. Hilliard, Ph.D; Principal investigator, phone: 404-413-6550; Fax-404-413-6556, E-mail: bvirus@gsu.edu, Website: www.gsu.edu/bvirus

#### *Herpesvirus papio 2 (Cercopithecine herpesvirus 16, HVP-2)*

HVP-2 is a simian alphaherpesvirus closely related genetically and antigenically to African green monkey SA8, Herpes B, and human herpes simplex viruses (HSV1 and HSV2). It is endemic in baboons (*Papio* species).



**Figure 4.** Multifocal to coalescing macules and papules associated with simian varicella infection.

Transmission appears to be venereal in adults, but in infants and juveniles the lesions are typically localized to the oral cavity. Oral, genital and cutaneous lesions are variably vesicular or ulcerative and usually resolve spontaneously. Like other members of the genus *Simplexvirus*, HVP-2 can establish latent infections in neuronal sensory ganglia and can reactivate to cause recurrence of clinical lesions or asymptomatic shedding. HVP-2 may be a good model for study of human simplex viruses. Although it is not thought to be virulent in humans, the zoonotic risk this virus poses to individuals working with baboons is not certain.<sup>43-46</sup>

#### *Simian varicella virus (SVV)*

Simian varicella belongs to a group of closely related herpesviruses that includes human varicella zoster and has been detected in *Patas* and African green monkeys and macaques (Figure 4). SVV has provided an animal model of varicella latency and pathogenesis in humans. The disease is highly contagious and is characterized by vesicular and maculopapular eruptions of the skin and oral mucous membranes with fever. Progression to hepatitis and pneumonia can occur. The disease may resolve within 2 weeks, but in some epizootic outbreaks, high morbidity and mortality have been noted. Although varicella zoster reactivation in humans is generally localized to one to three dermatomes, SVV reactivation may be generalized.<sup>47-52</sup> There is aerosol transmission and latency, but SVV is not zoonotic.<sup>53</sup>

#### *Herpesvirus tamarinus (Cebid herpesvirus 1)*

The natural host of this alphaherpesvirus is the squirrel monkey in which a high incidence of natural infection is found. Infection is usually inapparent, but oral vesiculation and periocular oedema may be noted. Infection in owl monkeys and marmosets is fatal. In these species, infection produces a generalized vesicular exanthema and ulceration with multi-organ necrosis.<sup>54,55</sup> For this reason, owl monkeys and marmosets are not housed with squirrel monkeys.

#### *Herpes simplex virus (herpes hominis)*

Humans are the natural reservoir of HSV, and transmission to the captive NHP is anthrozoönotic followed by

monkey to monkey transmission. Lesions vary from local to generalized vesicles and ulcers, conjunctivitis, encephalitis and death. Owl monkeys, lemurs, marmosets, gibbons, gorillas and tamarins have been reported with generalized disease (high morbidity and mortality), whereas chimpanzees usually have localized disease confined to the genitals, labia, skin and oral cavity.<sup>56,57</sup>

#### *Epstein-Barr virus (EBV)*

NHP-EBV-related herpesvirus is transmitted by contact usually resulting in a latent infection. In immunodeficient animals, it has been associated with B-cell lymphoma and squamous proliferations of the oral, genital and cutaneous surfaces resembling leucoplakia.<sup>58,59</sup> These B-lymphotropic herpesviruses related to but distinct from human EBV have been isolated from baboons, chimpanzees, orangutans, gorillas, green monkeys, cynomolgous monkeys and stump-tailed macaques.<sup>60</sup> This is not a zoonotic disease.

#### *Monkeypox virus*

Monkeypox is an orthopoxvirus currently endemic only in Central and West Africa and has a suspected rodent reservoir. It is not known whether NHPs also maintain the infection in the wild or are only incidental hosts. Clinical disease in monkeys and apes can be mild to fatal, with the cutaneous lesions consisting of papular to umbilicated pustular dermatitis. Severe cases can have facial oedema, oral ulcers, pneumonia and lymphadenopathy. Old and New World monkeys and apes are susceptible. Sporadic cases have been reported in wild and captive NHPs. The disease may be transmitted to humans from rodent and primate bites or contact with blood causing a syndrome clinically similar to smallpox. The first cases in humans in the western hemisphere were reported in June 2003 from contact with ill prairie dogs, which had been caged next to Gambian rats.<sup>42,61–67</sup>

#### *Yaba pox*

Yaba monkey tumour poxvirus causes benign histiocytomas and occurs as a natural infection in rhesus monkeys and baboons but can be a zoonosis.<sup>68</sup> Clinical lesions consist of rapidly growing nodules of the dermis and subcutis less than 4 cm in diameter on the head and limbs, which spontaneously slough and heal in 6–12 weeks. Unlike other poxviruses, Yaba infects subcutaneous mesenchymal cells rather than epithelial cells.<sup>69</sup> The mode of transmission is unclear, but arthropod vectors and trauma are suspected.

#### *Benign epidermal monkey pox (BEMP)*

Caused by a tana poxvirus, BEMP infects macaques and humans exposed to affected macaques, resulting in a multifocal macular crusting dermatitis of the face and arms that resolves spontaneously in 3–4 weeks. It was first noted in macaques and children in Kenya in the 1950s and later in imported captive macaques and their handlers in the United States. Histopathologically, this is a classic poxvirus with epithelial hyperplasia and necrosis with eosinophilic cytoplasmic inclusions.<sup>70,71</sup> There are no recent reports of the disease.

#### *Molluscum contagiosum*

Caused by molluscipoxvirus, this well-recognized disease entity in humans has been reported once in captive chimpanzees.<sup>72</sup> Cutaneous lesions of *Molluscum* in humans consist of smooth, waxy umbilicated papules, and can appear anywhere on the skin. Lesions in chimpanzees were noted primarily on the face with one case of inguinal lesions recorded.

#### *Human measles virus*

The aetiology of human measles in the NHP is a paramyxovirus/morbillivirus infection. The reservoir is humans, but transmission to NHP has been well described with apes, macaques, baboons, green and squirrel monkeys, and marmosets being affected in nature and more frequently in captivity. The transmission is by aerosol, and disease symptoms can range from a mild presentation to severe mortality. Typical lesions are a maculopapular eruption of the ventral abdomen and thighs. Vesicles are rare, but pustules have been noted in cases of secondary bacterial infection. One millimetre in diameter, elevated white papules on the oral mucosa (Koplik's spots) usually precede a more generalized rash. Facial oedema and erythema are common.<sup>73–75</sup>

#### *Papillomavirus*

Papillomaviruses have been implicated in the production of proliferative squamous epithelial lesions in NHP species but have not been reported with great frequency. Anecdotally, papillomaviruses are commonly implicated as the cause of genital warts that can lead to the euthanasia of breeding animals in captive NHP populations (Figure 5). It has been stated that they 'probably behave biologically in a manner similar to those infections in other mammalian species'.<sup>76</sup> Discussion of papillomavirus in the NHP is often based on case reports. In some of these reports there has been variable success in ascertaining the presence of papillomavirus utilizing immunohistochemistry, electron microscopy and polymerase chain reaction.<sup>77,78</sup>



**Figure 5.** Genital warts caused by papillomavirus in a macaque.

However, more than ten types of papillomaviruses from the reproductive tracts of rhesus monkeys have been classified using molecular techniques.<sup>79</sup> Papillomaviruses have been well documented in the colobus monkey and have been accepted as an animal model of human venereal papillomatosis.<sup>76,80,81</sup> Cervical and vaginal intraepithelial neoplasms in a series of cynomolgus macaques (*Macaca fascicularis*) were demonstrated to be caused by papillomavirus by morphologic features and selective staining with papillomavirus antibodies.<sup>82</sup> A papilloma-induced disease known as focal epithelial hyperplasia has been reported in chimpanzees (*Pan troglodytes*), pygmy chimpanzees (*Pan paniscus*) and a howler monkey (*Alouatta fusca*).<sup>83-87</sup> This is a condition characterized by well-circumscribed, soft papules of the oral mucosa, lips and gingiva. Prevalence studies have not been performed, and it has been suggested that this condition may be under-diagnosed because of its benign behaviour.<sup>88</sup>

#### *Hemorrhagic fever viruses*

Simian hemorrhagic fever virus (Arterivirus) and simian ebola filovirus are associated with epizootics in Africa and are therefore included in the differential diagnoses for all rapidly transmissible aetiologies that induce disseminated intravascular coagulation in primates. Affected animals exhibit dermatologic signs such as a maculopapular rash and generalized petechiation late in the course of the diseases.<sup>89,90</sup> Outbreaks in imported captive NHPs were documented in famous cases in Marburg, Germany, Virginia and Texas.<sup>91-95</sup> Mandatory testing and quarantine requirements were instituted after the 1989-1990 Reston outbreak.<sup>90</sup>

#### *Simian retroviruses (SRV)*

The family Retroviridae includes both immunosuppressive and oncogenic subsets. Dermatologic lesions are often secondary to systemic infections. SRV type 2, a simian type D retrovirus, can cause ischemic, necrotizing cutaneous lesions over the maxillary arcade in macaques involving the midline of the face (nose and lips).<sup>1,96,97</sup> This is not likely a direct viral effect but the result of secondary bacterial infection resulting from immune suppression. The virus is endemic in many captive colonies. Simian T-lymphotropic virus causes cutaneous lymphomas in Old World monkeys and apes.<sup>2,98</sup> There is active National Institutes of Health support for the establishment of research colonies free of these viruses because they confound experimental work. Simian immunodeficiency virus (SIV), an experimental infection, is an established model for research on HIV-induced AIDS. A maculopapular exanthema (localized and generalized) has been studied in SIV-infected macaques and has been demonstrated to be a good model for the cutaneous acute exanthema associated with human HIV.<sup>99</sup>

### **Parasitic infestations**

#### Demodicosis

*Demodex* spp. have been reported in captive-bred squirrel monkeys and tamarins.<sup>100-102</sup> Lesions have been described as nonpruritic, alopecic and hyperkeratotic with secondary

infection. One report concluded that treatment with Amitraz 250 p.p.m. dips every 2 weeks was effective, whereas ivermectin was not.<sup>101</sup> However, the doses of ivermectin given were never above 0.3 mg/kg every 2 weeks because of fear of toxicity. More recently, *Demodex* spp. were reported in the hair follicles of immunocompetent and immunocompromised rhesus macaques.<sup>103</sup> In this study, mites were found in the perineal and facial skin of 19 of 53 rhesus monkeys at necropsy regardless of age, sex or immune status. This newly discovered species was named *Demodex macaci*, and all its life-stages were described in a recent follow-up publication.<sup>104</sup>

#### Scabies

*Sarcoptes scabiei* has been reported to be a zoonosis of NHP on the basis of a report of a 1922 outbreak of scabies in a group of ten imported gibbons (*Hylobates* spp.) in a zoo. Nine died after suffering a severe hyperkeratotic pruritic dermatitis, which was also contracted by the handlers.<sup>105</sup> A case of scabies was also noted in a colony-born Bonnet macaque (*Macaca radiata*).<sup>106</sup> Recent reports of scabies infestation in human habituated free-ranging mountain gorillas in Bwindi Park, Uganda have led to suspicion that the apes were infested from contact with humans.<sup>107,108</sup> Intramuscular injections of ivermectin 1% (0.2 mg/kg) were successful in resolving the condition.

#### Psorergates

*Psorergates* mites, living in the epidermis and stratum corneum, have been reported to cause a pruritic papular dermatitis or a nonpruritic, alopecic crusting dermatitis. Transmission of *Psorergates cercopitheci* has been attributed to direct contact, but subclinical latent infestations have been recorded. Transmission from imported females to their offspring in captive colonies is suspected.<sup>109</sup> In stumptailed macaques with psorergatic infestations, ivermectin 1% (0.2 mg/kg weekly) and topical rotenone (weekly dips) were compared, with both modalities resolving the disease.<sup>110</sup>

#### Anatrichosoma

*Anatrichosoma cutaneum* is a nematode that causes dermatologic disease commonly in wild Old World monkeys. Embryonated eggs are deposited in nasal or cutaneous epithelia. Mild palmar and plantar exfoliative dermatitis is typical, but facial lesions have also been noted. Serpentine tracts with intense inflammation are seen occasionally. Skin scrapes and nasal swabs reveal ova and parasite fragments. The disease, which can be zoonotic, is rarely seen in captive animals that have been routinely treated with anthelmintics.<sup>2,111,112</sup>

#### *Other parasitic diseases*

Numerous other parasites have been reported in the NHP. Lice (several species of biting and sucking lice) have usually been found on debilitated caged animals. Ticks have been noted to be of importance primarily in the transmission of other diseases. *Dermacentor* and *Rhipicephalus* have been implicated in the transmission of *Rickettsia rickettsii*, the aetiologic agent of Rocky Mountain spotted fever. Lesions are characterized by a macular

eruption of the limbs, head, lower back and perineum.<sup>1</sup> *Ixodes dammini* ticks have transmitted *Borrelia burgdorferi* infection experimentally to rhesus monkeys, resulting in an infection that is an excellent model for human Lyme disease. The classic cutaneous lesion in humans, erythema migrans, which heralds the onset of this multi-system disease, is also demonstrated by rhesus monkeys.<sup>9,113</sup> To the authors' knowledge, this infection has only been transmitted to NHP in the laboratory setting.

### Alopecia

Alopecia resulting from a variety of aetiologies is a common dermatologic problem noted in NHP. The most common cause of focal alopecia is associated with overgrooming or barbering.<sup>114</sup> This can be self-inflicted or caused by other primates within a social group (allogrooming). Behavioural disorders and stereotypic behaviours are frequently encountered in the captive NHP in the laboratory setting.<sup>115</sup> NHP species often have complex behavioural and social systems, which are disturbed in the artificial environment of captive colonies. Coat damage resulting from behavioural stress, however, has become a default diagnosis in cases of alopecia of unknown aetiology. Recent papers have sought to investigate the pathogenesis of such cases of alopecia in captive rhesus macaques.<sup>116</sup> Hair loss was found to vary with both season and sex. A relationship between the hypothalamic-pituitary-adrenal (HPA) axis and hair loss was also suggested.<sup>117</sup> Other causes of focal alopecia include bacterial folliculitis, dermatomycoses, ectoparasitism, burns and scarring from wounds.<sup>1,2</sup>

Zinc and protein deficiencies in the captive NHP fed an inappropriate diet have been associated with hypotrichosis, lichenification, hyperkeratosis and increased fragility of the hairs.<sup>118</sup> Diagnoses of these dermatoses are based on evaluation of the diet and response to dietary supplementation. Typically inappropriate cereal-based diets result in concurrent protein-calorie malnutrition and zinc deficiency, caused by the high phytate content of cereals, which decrease zinc bioavailability.

Telogen effluvium has also been noted in the literature as a cause of diffuse alopecia. Age-related chronic telogen effluvium was noted in female squirrel monkeys (*Samiri boliviensis*) in which a systematic evidence-based diagnostic approach revealed a statistically significant correlation between age and telogen shedding.<sup>119</sup> This study proposed the potential use of female squirrel monkeys as a model for chronic telogen effluvium in the human female. It noted, however, that further study is necessary both in the captive and wild squirrel monkey to rule out chronic stress as a possible contributing aetiology of the described alopecia.

Endocrine disease as a cause of dermatologic lesions has been rarely reported in the NHP. Hypothyroidism has been reported as a cause of alopecia in a chimpanzee and an orangutan. In both cases, a sparse haircoat was seen in conjunction with obesity and lethargy.<sup>120,121</sup> However, hypothyroidism in a gorilla was not associated with any dermatologic manifestations.<sup>122</sup>

Perhaps the most widely encountered alopecia in the literature is the common pattern baldness of the stump-tail macaque (*Macaca arctoides*), which is a genetically inherited trait (Figure 6). The reason for the plenitude of research



**Figure 6.** Androgenetic alopecia in the stump-tail macaque (*M. arctoides*) is a model for male pattern baldness in the human.

has nothing to do with any health complications for the macaque, as the alopecia is only a cosmetic problem. Rather, it is because the macaque is the best model for studying male pattern (androgenetic) baldness in the human. Androgenetic alopecia occurs in chimpanzees, stump-tail macaques and South American uakaris. However, the stump-tail macaque has the most prominent appearance and greatest incidence of frontal scalp alopecia (nearly 100%). Inhibitors of 5- $\alpha$  reductase (e.g. Propecia®) prevent post-adolescent alopecia in both male and female macaques.<sup>11</sup> Even surgical hair transplantation procedures were developed using the stump-tail model.

### Allergy, seborrheic dermatitis and psoriasis

The quest for adequate animal models for human atopic dermatitis, seborrheic dermatitis and psoriasis has involved some of the fringe work in NHP research. Most of the case reports come from the early 1980s.

In a group of monkeys with IgE-mediated asthma, two were found to have chronic, steroid-responsive, relapsing, pruritic dermatitis with flexural lichenification, immediate skin reactivity and recurrent skin infections. These cases were suggested to be an analogue of human atopic dermatitis.<sup>123</sup> Of related interest, the use of *in vivo* and *in vitro* allergy testing in a chimpanzee with inhalant dermatitis was reported and may provide a basis for anecdotal reports of such testing for allergic dermatosis in the NHP.<sup>124</sup> Intradermal allergy testing of an olive baboon with presumed environmental allergies was also recently reported.<sup>125</sup> In addition, the first use of cyclosporine for the treatment of atopic dermatitis was reported in a macaque with an analogue of human atopic dermatitis.<sup>126</sup>



**Figure 7.** Seborrheic dermatitis in a rhesus macaque.

A rhesus monkey was diagnosed with a seborrheic dermatitis clinically and histopathologically similar to human idiopathic seborrheic dermatitis. The monkey had erythematous, variably pruritic, focally exudative lesions primarily of the face and intertriginous areas. The condition was exacerbated by stress, and was treated successfully with topical hydrocortisone. The difficulty of performing this topical treatment with a squeeze cage was noted and there was no reported long-term follow-up with which to assess the success of the therapy.<sup>127</sup> One of the authors (J. Bernstein) also diagnosed seborrheic dermatitis in macaques with clinical and histopathologic characteristics identical to the case report (Figure 7).

A dermatosis was described in a lone rhesus monkey with the characteristic features clinically and histopathologically of human psoriasis vulgaris. No animal model for this human disease exists. Lesions consisted of erythematous scaling plaques on the scalp, face, dorsal back and lateral extremities. Histopathology demonstrated regular acanthosis with supra-papillary thinning and parakeratosis. Dermal changes consisted of inflammatory infiltrate in the papillary dermis and vascular dilatation. Improvement with topical steroids and subsequent rebound recurrence of the condition were consistent with human psoriasis. This monkey would have been extremely valuable for further study, however, she died of 'accidental deprivation of water' before she could provide offspring to confirm any hereditary links.<sup>128,129</sup> A similar single case was noted in *M. fascicularis*.<sup>130</sup>

Latex contact hypersensitivity has also been studied in the rhesus monkey.<sup>131</sup> The patient had a history of repeated latex exposure during nursery rearing and its use in research projects. The report indicated that latex sensitivity and contact dermatitis in general should be included in the differential diagnoses for any NHP with acute or chronic allergic dermatitis.



**Figure 8.** Multifocal subcutaneous nodules associated with mammary carcinoma.

### Neoplasia

Case reports of a variety of malignant and benign neoplastic disease of the skin exist. Benign tumours include haemangiomas, sebaceous gland adenomas, fibromas, lipomas and basal cell tumours among others. Malignant tumours have been reported both as primary and metastatic lesions (Figure 8). Basal cell carcinomas, squamous cell carcinomas, fibrosarcomas, adenocarcinomas, lymphomas and melanomas have been reported.<sup>2</sup> Lymphomas caused by simian T-lymphotropic virus or SIV infection may be found in the subcutis.<sup>1</sup> The relationship between actinic (solar) damage and BCCs, SCCs and melanomas has been well established and would be well worth considering when housing NHP in outdoor shelters. This lesson was learned in 2003 with the passing of the famous albino gorilla, Snowflake, at Barcelona Zoo from melanoma after a lifetime of sun exposure.<sup>132</sup> There is little organized discussion of the treatment of cutaneous malignancies in the NHP, and most of the early discussion of neoplastic disease in the NHP came from case reports. An attempt to clarify the literature was made in a recent review of spontaneous neoplasia in baboons, which provided a comprehensive list of baboon neoplasia and found that integumentary tumours represented 13% of the cases reported.<sup>133</sup> Although papers of this scope represent a sorely needed addition to the literature, it is difficult to make much practical use of this study, given the problematic omissions in the reported data acknowledged by the authors. Epidemiologic data on incidence, sex and age were impossible to assess because the number of captive baboons at any of the reporting institutions was not known, the sex of 37% of the cases was not reported, and the age of many of the wild-caught baboons was either undetermined or estimated.

### Summary

This review assembled and categorized the NHP dermatologic literature in one place for reference. The authors recognize that a more cohesive approach to NHP dermatology – without relying on assumptions that NHP pathology most commonly behaves similarly to other veterinary and

human diseases – is required. Given the paucity of evidence-based information currently available, this approach was not found to be possible with regard to all of the diseases reviewed. A discerning view of the existing scientific work must be followed by an increased willingness by the veterinary community to study and report the dermatologic diseases of NHPs. This review has hopefully provided a platform upon which more specific and organized study of NHP diseases can be based.

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**Résumé** En général, les dermatologues vétérinaires n'ont pas d'expérience importante des dermatoses des primates non humains (NHP). L'analyse de la littérature publiée ne permet pas d'avoir une approche basée sur les preuves des cas de dermatologie des NHP. Le vétérinaire dermatologue doit rechercher l'information à partir des données humaines et vétérinaires, une approche qui peut être problématique car elle oblige le clinicien à faire un diagnostic et choisir un traitement à partir de deux éléments disparates de la littérature. Une approche plus complète de la dermatologie des NHP est requise, nonobstant les affirmations comme quoi la dermatologie des NHP se comporte de façon similaire à celle de l'humain ou d'autres espèces. Cette revue de la dermatologie des NHP inclut une discussion des dermatoses primaires, ainsi que des maladies pour lesquelles les signes cliniques représentent un composant secondaire important. Elle procure un premier pas encourageant la communauté vétérinaire à étudier et reporter les maladies dermatologiques des NHP.

**Resumen** En general los dermatólogos veterinarios no tienen mucha experiencia clínica en las dermatosis de primates no humanos (NHP). La mayor parte de la literatura publicada no aporta un abordaje organizado basado en evidencias en los casos dermatológicos de NHP. El dermatólogo veterinario queda pues limitado a extraer información de la dermatología humana y veterinaria, una estrategia que puede resultar problemática ya que fuerza al clínico a tomar decisiones diagnósticas y de tratamiento basados en dos áreas muy dispares de la literatura. Es pues necesario un abordaje mas coherente en la dermatología en primates no humanos -sin asumir que la patología de primates no humanos se comporta generalmente de forma similar a otras enfermedades humanas y veterinarias. Esta revisión de la dermatología de especies de primates no humanos incluye discusiones de dermatosis primarias de primates, así como enfermedades donde los signos dermatológicos representan un componente secundario de importancia, y aporta un primer paso para animar a la comunidad veterinaria a estudiar y reportar las enfermedades dermatológicas de primates no humanos.

**Zusammenfassung** Im Allgemeinen haben Veterinärdermatologen keine reiche klinische Erfahrung mit nicht-menschlichen Dermatosen von Primaten (NHP). Der Großteil der publizierten Literatur bietet keine organisierte, auf Evidenz basierende Herangehensweise an einen dermatologischen Fall bei einem NHP. Dem Veterinärdermatologen bleibt nichts anderes übrig als Information aus der Human- sowie aus der Veterinärdermatologie zu extrahieren, was eine problematische Herangehensweise darstellen kann, da es den Kliniker dazu zwingt, diagnostische und therapeutische Entscheidungen basierend auf zwei sehr unterschiedlichen Literatursammlungen, zu treffen. Es ist eine mehr zusammenhängende Herangehensweise an die NHP Dermatologie notwendig – ohne sich auf Vermutungen zu berufen, dass die Pathologie der NHP sich normalerweise ähnlich verhält wie andere tierische oder menschliche Erkrankungen. Diese Review der Dermatologie von NHP Spezies beinhaltet Diskussionen über Primärdermatosen, sowie über Krankheiten, bei denen dermatologische Symptome eine wichtige zweite Komponente darstellen. Sie stellt somit einen ersten Schritt dar, die Veterinärgemeinschaft zu ermutigen, dermatologische Krankheiten von nichtmenschlichen Primaten zu erforschen und zu publizieren.