Dermatology in non-human primates: a comprehensive review

Dermatologia em primatas não-humanos: uma revisão abrangente

Dermatología en primates no humanos: una revisión exhaustiva

DOI: 10.55905/revconv.17n.7-329

Originals received: 06/18/2024
Acceptance for publication: 07/08/2024

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ABSTRACT
There have been limited studies conducted on the anatomy, physiology, and histology of the skin of non-human primates (NHPs). The majority of this research was done by William Montagna and his colleagues in the 1960s and 1970s. Understanding the skin characteristics of NHPs is important for comprehending their biology and behavior, as well as for conducting complementary dermatological examinations and various experiments. This knowledge is particularly important in the diagnosis of specific zoonoses. However, veterinary dermatology for NHPs faces a challenge in obtaining information from both human and veterinary dermatology disciplines, which can lead to diagnostic and therapeutic decisions based on two distinct bodies of literature. Therefore, an integrated approach to dermatology in NHPs is critical, without assuming that the pathology in NHPs is identical to that in humans. This review article aims to highlight the key scientific studies related to the skin of NHPs, with the goal of expanding knowledge about their dermatological characteristics. It also seeks to provide valuable insights for researchers in the field, contributing to a better understanding of dermatology in non-human primates.

Keywords: skin, coat, dermatopathies, zoonosis.

RESUMO
Existem poucos estudos que abordam a anátomo-fisiologia e histologia da pele de primatas não-humanos (PNHs), sendo principalmente vinculados ao trabalho pioneiro do autor William Montagna e seus colaboradores nas décadas de 60 e 70. Uma compreensão aprofundada das características da pele desses animais não apenas contribui para o entendimento de sua biologia e comportamento, mas também desempenha um papel crucial na condução de exames dermatológicos complementares e na realização de experimentos diversos. Isso proporciona um conhecimento mais abrangente sobre a apresentação dermatológica de zoonoses específicas. A
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Palavras-chave: pele, pelagem, dermatopatias, zoonoses.

RESUMEN
Existen pocos estudios que abordan la anatomofisiología e histología de la piel de primates no humanos (PNH), principalmente vinculados al trabajo pionero del autor William Montagna y sus colaboradores en las décadas de los 60 y 70. Una comprensión profunda de las características de la piel de estos animales no solo contribuye al entendimiento de su biología y comportamiento, sino que también desempeña un papel crucial en la realización de exámenes dermatológicos complementarios y en la realización de diversos experimentos. Esto proporciona un conocimiento más amplio sobre la presentación dermatológica de zoonosis específicas. La dermatología veterinaria, con énfasis en primates no humanos, enfrenta el desafio de obtener información de ambas disciplinas, dermatología humana y veterinaria. Este enfoque puede ser problemático, ya que obliga al profesional a tomar decisiones diagnósticas y terapéuticas basadas en dos literaturas distintas. Por lo tanto, es esencial adoptar un enfoque más integrado para la dermatología en primates no humanos, sin presumir que la patología en ellos tenga una etiología idéntica a la humana. Este artículo de revisión tiene como objetivo destacar los principales estudios científicos relacionados con la piel de los PNH, con el fin de ampliar el conocimiento sobre sus características dermatológicas. Además, busca proporcionar insumos valiosos para los investigadores en el área, contribuyendo al avance del entendimiento de la dermatología en primates no humanos.

Palabras clave: piel, pelaje, dermatopatías, zoonosis.

1 INTRODUCTION

According to Andrade et al. (2010), non-human primates (NHPs) have been used as experimental models for over 5 thousand years. This highlights their effectiveness in the applicability of techniques in humans. NHPs are widely distributed across the globe, and due to their taxonomic proximity to humans, they are of significant interest for biomedical, behavioral, and biological applications.

Studies on the variation of skin color, hair, attached and pigment glands in non-human...
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primates are scarce (Hirano et al., 2003; Cramer et al., 2013; Snyder, 2020). This is mainly due to the lack of techniques that can elucidate these characteristics, as well as the little knowledge regarding the characteristics of the skin of these animals.

Comparative dermatological literature between NHPs and humans covers various topics, including the healing of skin wounds, early changes in burns, dermatographism, chloracne, geriatric dermatological changes, treatment of facial wounds with Botox, Lyme disease, treatment of pressure ulcers, and male baldness. It is widely accepted that most lesions in NHPs are similar in appearance and clinical progression to those seen in humans and other animals. As such, therapies that work well in these species are generally satisfactory in NHPs (Bernstein, Didier, 2003).

A better understanding of these animals’ skin, in addition to clarifying their biology and behavior, also helps in carrying out complementary dermatological exams. Therefore, this study aims to increase knowledge about these dermatological characteristics and assist researchers in the area by reviewing scientific studies on the skin of NHPs.

2 THEORETICAL FRAMEWORK

A documentary research of a historical and descriptive nature was conducted, aiming to contextualize the dermatological characteristics and assist researchers in the field through a review of scientific studies on the skin of Non-Human Primates (NHPs).

2.1 DERMATOLOGY

The skin is the largest organ in mammals and serves as their primary physical barrier to the outside world (Goldsmith, 1990). While there are few studies on the anatomical, physiological, and histological aspects of the skin in non-human primates (NHPs), author Willian Montagna and his team have published over 50 articles in the American Journal of Physical Anthropology, detailing the skin of NHPs. Their research shows that there are many similarities in the morphology, metabolism, and immunology of the skin between NHPs and humans. Humans differ from all other primates in their primitive hair cover. Although all non-human primates have a dense coat, characterized by certain morphological and physiological
similarities, each species has significant variations, even between closely related species. The epidermis appears uniformly thin, and each primate species bears epidermal and dermal melanocytes that are often distinguishable from each other. Eccrine sweat glands are found on the friction surfaces of all species, but only New World primates with prehensile tails and Old World apes have them on their furry skin. All primates have numerous apocrine glands in their hairy skin (Montagna, 1972).

There are some significant differences between New World and Old World NHPs. In the New World, prehensile tails have evolved, whereas in the Old World, ischial calluses on the buttocks are more common. These are hairless, keratinized areas where they sit. (Fowler and Miller, 2003). Kamberov et al. (2018) found that humans and chimpanzees have indistinguishable hair follicle density, and both have lower hair density compared to monkeys. They also discovered that human skin contains a greater density of eccrine sweat glands in almost all regions of the body than chimpanzees and monkeys. The only exception is the chest, which was not extensively studied in their research. A recent analysis of eccrine gland characteristics in primates indicates that natural selection has played a role in increasing sweating capacity in primates living in hot, arid environments (Best and Kamilar, 2018). They link the evolution of eccrine gland functionality to environmental selective pressures. Within catarrhines, the density of eccrine glands is lowest in Old World monkeys, intermediate in great apes, and reaches its peak in humans (Montagna, 1963, 1972).

In 1871, Charles Darwin discussed the concept of "sexual skin" in Old World monkeys. This refers to the genitals becoming more prominent and reddish or bluish (depending on the species), which may indicate dominance within the group (Dixson, 1998; Andersson, 2000; Gerald, 2001; Cramer, 2013). Some experts believe that the red color is caused by vascularization and that the blue color is due to melanin deposition, both of which represent a sign of intra and inter-specific dominance (Hirano et al., 2003; Cramer et al., 2013).

Some species and subspecies exhibit significant sexual variation in their adult pattern coloration, in addition to their basic skin color. In some primates, the external coloration is not limited to their fur. For instance, the skin on parts of their body such as the face and perineum may be blue, gray and/or red. These colorations are visual signals that are part of a behavioral context of social organization (Tunquist and Hong, 1995).

Animal coloration's main functions are: identification, thermoregulation, communication
and escape from predators, which can act as joint or antagonistic relative forces (Endler, 1978; Brakefield, 1985). Most of the time, the color pattern only has a function when adjusted to a behavioral mechanism.

New World primates have dense, woolly coats that contrast with the sometimes thick and sparse fur of many Old World primates and chimpanzees. The idiosyncrasies and generalities of primate skin are almost limitless; its unique characteristic is the lack of uniformity (Montagna, 1972).

"Grooming", the act of searching for and collecting material from the skin and hair that NHPs constantly perform among themselves, does not mean the collect of ectoparasites in primates. In fact, lice, fleas, ticks and scabies are not frequently observed, with "grooming" having an important meaning of social function, at the same time as ingesting saline skin flaking (Diniz, 1997).

In NHPs, as in all mammals almost without exception, there is an inverse relationship between the thickness of the epidermis and the abundance of hair. On the body, which is usually well protected by hair, the epidermis, particularly the malpighian layer, is relatively thin, with a barely visible granular layer. On the face, however, where hair is sparse or absent, the epidermis is invariably much thicker. In the skin covered with hair, the dermoepidermal junction has a relatively flat underside, some dimples in skin with few hairs, and intricate patterns characteristic of glabrous skin. Hair growth cycles are specific to each species, although most animals shed some hair constantly in a diffuse or mosaic pattern. Studies on non-human primates have shown that only lemurs have as many sebaceous glands as humans (Montagna, 1972).

The dermis shows many differences between families, genders, and even species. The two layers, the pars papillaris on the surface and pars reticularis below, are generally well differentiated in most NHPs. Prosimians have a very thin papillary dermis, while simian primates have a thicker, more vascular dermis. The dermis consists of layers of fibers, which are arranged orthogonally in some prosimians but not in simian primates. As in all other mammals, the thickness of the dermis varies from place to place. Unlike other mammals, including non-human primates, there are few elastic fibers in human skin. This is because the main function of elastic fibers is to anchor the epidermis. The greater the number of hair follicles in an area of the skin, the fewer elastic fibers are present (Montagna and Giacometti, 1969). The arrangement of these fibers in humans is different from that in other mammals, suggesting that human skin has a
greater capacity to stretch and recoil than in other mammals (Starcher et al., 2005).

NHPs have two main types of cutaneous glands: apocrine and eccrine. While not all apocrine glands are associated with hair follicles, most of them are. Eccrine glands are found on the volar surfaces of the hands and feet in all primates. New World primates with prehensile tails have them on the specialized ventral surface of their tails, while gorillas and chimpanzees have them on their finger joints (Montagna, 1971).

In NHPs, the cutaneous circulation is supplied by two types of arteries: musculocutaneous arteries and direct cutaneous arteries. Perforating arteries send several branches to the underlying muscle mass before terminating as musculocutaneous arteries, which irrigate a small area perpendicular to the skin. Direct cutaneous arteries, on the other hand, originate from perforating arteries that send some branches to the underlying muscle mass before ascending to the subdermal plexus. These arteries run parallel to the skin towards the subdermal plexus, but they play a secondary role in the total cutaneous circulation of humans (Feitosa, 2014).

2.2 MAJOR SKIN DISEASES IN NON-HUMAN PRIMATES

Skin diseases are common in non-human primates, and they can be caused by a variety of external factors, such as heat, cold, injuries from fights, and contact with chemicals. Opportunistic infections are the most frequent and usually secondary to these external factors. These conditions in non-human primates are similar to those found in humans, both in appearance and the types of infections (Hubbard, 2001).

It's worth noting that veterinary dermatologists do not have extensive clinical experience in dermatological diseases of NHPs. There is a scarcity of literature on dermatology and primary dermatological diseases in wild or captive NHPs. Most of the published literature does not provide an organized description of dermatopathies (Bernstein, Didier, 2003). The most common dermatological presentation seen by veterinarians is the opportunistic secondary bacterial infection of the skin. This is usually associated with fighting wounds and trauma, but it can also be caused by environmental factors and immunodeficient states. Clinical diseases may result from overgrowth of normal skin flora (such as Staphylococcus and Streptococcus), or the introduction of non-resident pathogens (Bielitzki, 1998). *Pseudomonas aeruginosa* is predominantly a problem in immunocompromised, debilitated, burned, and neutropenic patients.
but other bacterial species have also been reported to cause skin infections (Bernstein, Didier, 2003).

Parasites are a serious public health issue in underdeveloped and developing countries, potentially leading to zoonoses (Pontes, 2006). Flies, lice, fleas, ticks, and mites are the most common parasites. These arthropods parasitize the skin and follicles of several species of platyrrhines. Among mites, *Sarcoptes scabiei* and *Phthirus* are the most common (Catão-Dias, 2001), *Demodex* spp. have been reported in captive-bred squirrel monkeys and marmosets. *Psorergates* mites have been reported to cause pruritic papular dermatitis or non-pruritic alopecic dermatitis with crusts (Ulrich *et al*., 1981; Hubbard, 2001).

Lice are commonly found in weakened caged animals and ticks are mainly important for transmitting other diseases. *Ixodes* is the most identified genus among platyrrhines, but *Amblyomma oblonguttatum* was observed in *Alouatta caraya* (Catão-Dias, 2001). Dermacentor and *Rhipicephalus* have been implicated in the transmission of *Rickettsia rickettsii*, which is the etiological agent of Rocky Mountain spotted fever (Roberts *et al*., 1995).

Pediculosis is a common condition in neotropical primates, mostly caused by lice of the genus *Pediculus* in the order anoplura. This condition affects howler monkeys, spider monkeys, tamarins, and marmosets. Fly larvae from the *Cuterebridae* family, including *Cuterebra*, *Dermatobia*, and *Alouattamyi*, can also cause myiasis, which poses a risk of secondary bacterial infection (CATÃO-DIAS, 2001). Lesions caused by *Tunga penetrans*, also known as chigoe fleas, allow entry of microorganisms from the soil, such as *Paracoccidioides brasiliensis*, which causes deep mycosis, and bacteria like *Clostridium tetani* and *C. perfringens* (Urquhart *et al*., 1987; Georgi, 1985).

Fungal infections are also common in primates, with *Microsporum canis* and *Trichophyton mentagrophytes* being the most frequent causes. *Microsporum canis* are more common, both in Old World and neotropical apes. *Candida albicans*, an opportunistic infection, is found in debilitated and immunocompromised patients. Some dermatophytes have a zoonotic aspect, such as white piedra (*Trichosporon cutaneum*) and black piedra (*Piedra hortai*) (Benirschke, 1994). Generally, the skin and hair of primates are considered reservoirs of pathogenic dermatophytes (Altmann, 1972). Non-dermatophyte mycelial fungi like Candida, Fusarium, *Mallassezia*, *Microsporum*, and *Mucor* are also associated with dermatoses, indicating their role in the development of skin diseases (Costa *et al*., 1995).
Viral diseases are a significant group of diseases that affect the skin of NHPs, both in captivity and in the wild (Hubbard, 2001). Some of these diseases cause dermatological lesions, while others are accompanied by secondary dermatological signs that indicate systemic infection, such as Herpes B (Cercopithecine herpesvirus 1), Herpesvirus papio 2 (Cercopithecine herpesvirus 16, HVP-2), Simian varicella virus (SVV), Herpesvirus tamarinus (Cebid herpesvirus 1), Herpes simplex virus (Herpes hominis), Epstein-Barr virus (EBV), Monkeypox virus, Yaba pox, Benign epidermal Monkey pox (BEMP), Molluscum contagiosum, Human measles virus, Papillomavirus, Hemorrhagic fever viruses and Simian retroviruses (SRV) (Bernstein, Didier, 2003).

Alopecia resulting from a variety of etiologies is also a common dermatological problem and the most common cause of focal alopecia is associated with behavioral stress, excessive grooming or overgrooming which can be self-inflicted or caused by other primates within a social group (allogrooming). Other causes of alopecia include bacterial folliculitis, dermatomycoses, ectoparasitism, burns and wound scars. Zinc and protein deficiencies in captive animals fed an inadequate diet have been associated with hypotrichosis, lichenification, hyperkeratosis and increased hair fragility (Roberts et al., 1995).

Cases of allergy, seborrheic dermatitis and psoriasis have also been described and there are case reports of a variety of malignant and benign neoplastic skin diseases in NHPs (Bernstein, Didier, 2003).

A summary panel about dermatological information of non-human primates adapted from various authors was created to aid comprehension (Figure 1).
Figure 1. Summary panel about dermatological information of non-human primates.

- **ANATOMY, HISTOLOGY, AND HISTOCHEMISTRY.**
  - Hair coverage;
  - Epidermis and dermis;
  - Sweat, sebaceous, and pigmenting glands;
  - Hair follicle complexes.

- **DERMATOPATHIES.**
  - Opportunistic infections (secondary bacterial infection) - *Staphylococcus, Streptococcus, Pseudomonas aeruginosa, Clostridium tetani,* and *C. perfringens* can be significant contributors to the health challenges faced by individuals.

- **ALOPECIA.**
  - Behavioral stress, grooming alterations, bacterial folliculitis, dermatomyoceses, ectoparasitism, burns, and scars from wounds.

- **FUNGI**
  - *Paracoccidioides brasiliensis*
  - *Microsporum canis*
  - *Candida albicans*
  - *Trichosporon cutaneum*
  - *Piedrai hortai*
  - *Trichophyton mentagrophytes*

- **PARASITES THAT OCCUR!**
  - **Mites:** *Sarcoptes scabiei,* *Phthirus, Demodex spp., Psoergerates spp.*
  - **Lice:** *Pediculus spp.*
  - **Ticks:** *Ixodes, Amblyomma oblonguttatum,* *Dermacentor,* and *Rhipicephalus.*
  - **Fleas:** *Tunga penetrans.*
  - **Fly larvae:** *Cuterebra, Dermatobia,* and *Alouattamyi.*

- **Other condition:**
  - Allergy, seborrhoeic dermatitis, and psoriasis, have also been described, and there are reports of cases of various malignant and benign neoplastic skin diseases in NHPs (BERNSTEIN, DIDIER, 2003)

- **VIRUS!**
  - Herpes B (*Cercopithecine herpesvirus 1,* *Herpesvirus papio 2* (*Cercopithecine herpesvirus 16, HVP-2,* *Simian varicella virus* (SVV), *Herpesvirus tamarinus* (*Cebid herpesvirus 1*), *Herpes simplex virus* (herpes hominis), *Epstein-Barr virus* (EBV), *Monkeypox virus,* *Yaba pox, Monxepox* epidérmico benigno (BEMP), *Molluscum contagiosum,* Human measles virus, *Papillomavirus, Hemorrhagic fever viruses,* and *Simian retroviruses* (SRV)).

Source: Designed by the authors (2024).
3 CONCLUSION

It has been shown that there are significant gaps in our knowledge of dermatology in non-human primates (NHPs). A comprehensive literature review has highlighted the lack of practical and up-to-date information, particularly related to primary skin conditions, in both wild and captive NHPs. The limited availability of references beyond case reports highlights the urgent need for more comprehensive and current studies that explore the anatomy, morphophysiology, and histological aspects of the skin across different species of NHPs. It is evident that the field of dermatology in NHPs lacks a solid foundation of knowledge, underscoring the importance of investing in future research. Achieving a deeper and more comprehensive understanding of the dermatological health of these primates is essential not only for effective clinical practice but also for promoting the well-being of these animals in both captive and natural environments, while also highlighting potential risks to human health.
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