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Skin diseases of South American rodents

Dél-Amerikai rágcsálók bőrbetegségei

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Abstract

This thesis presents a comprehensive overview of skin diseases affecting various south American rodents. The primary focus of this work is on wild rodents in their natural habitats and captive rodents kept in zoos or wildlife parks while acknowledging domestic pet rodents such as guinea pigs and chinchillas. Bacterial and viral infections of the skin will be reviewed first. Some poxviruses (cowpox, vaccinia virus, Brazilian porcupinepox virus), papillomavirus and foot and mouth disease will be discussed). Additionally, the thesis explores fungal skin infections (dermatophytosis) and helminths affecting the skin as well. Another focus is on ectoparasites (ticks, mites, lice and fleas) of the different South American rodents. Finally, non-infectious skin diseases that include vitamin C deficiency, cutaneous tumours and cold injuries will be analysed.

Dermatological case studies focusing on the histopathology of dermal lesions of select South American rodents from Budapest Zoo will be overviewed. Since the reports are collected from one zoo, they will include only the following species: capybaras, muenster yellow-toothed cavies and the guinea pig.

Absztrakt

Ez a szakdolgozat átfogó áttekintést nyújt a különböző dél-amerikai rágcsálókat érintő bőrbetegségekről. Elsősorban a természetes élőhelyükön előforduló vadon élő rágcsálókra, valamint az állatkertekben és vadasparkokban fogságban tartott rágcsálókra összpontosít, ugyanakkor a munkában háziállatként tartott rágcsálók, mint például a tengerimalacok és a csincsillák is helyet kapnak. Elsőként a bőr bakteriális és vírusos fertőzéseit tekintjük át. Szó lesz néhány himlővírusról (tehénhimlő, vaccinia vírus, brazil sertéshimlő vírus), valamint a papillomavírusról és a száj- és körömfájásról. Emellett a dolgozat feltárja a bőr gombás fertőzéseit (dermatophytosis) és a bőrt érintő parazitás bántalmakat is. További hangsúlyt kapnak a különböző dél-amerikai rágcsálók ektoparazitái (kullancsok, atkák, tetvek és bolhák). Végül a nem fertőző bőrbetegségeket elemezzük, amelyek közé tartozik a C-vitamin hiány, a bőrdaganatok és a fagyási sérülések.

A dolgozat további résézben a Fővárosi Állat- és Növénykertből származó kiválasztott dél-amerikai rágcsálók bőrelváltozásainak szövettani vizsgálatára összpontosító bőrgyógyászati esettanulmányok kerülnek áttekintésre. Mivel a beszámolók egy állatkertből származnak, ezért ezek a következő fajokra terjed ki: vízidisznó, szirti tengerimalac és tengerimalac.

Contents

1. Introduction

Discussing skin diseases of rodents in general is an important aspect since they are known reservoirs for several diseases that are transferrable to other animals and humans. It is especially important to focus on specifically South American rodents as some infectious diseases that are notifiable in Europe for example, may still be endemic in some South American countries and their native rodents may occasionally play a role in transmitting them. An outbreak of such diseases could lead to devastating results, whether by causing a health risk to the general public or by damaging local economies by affecting livestock output. For example, foot and mouth disease will be reviewed later and whether South American rodents have some role in maintaining the disease. A unique aspect to consider when researching skin diseases of South American rodents is that some rodents are hunted or farmed for their hide and meat. This can predispose people who are in regular contact with them, such as hunters and those involved in processing the carcasses, to any zoonotic diseases. Skin lesions can also reduce the quality and economic value of the harvested hides. Latin American game rodents include but are not limited to guinea pigs and agoutis, which are used for their meat, capybaras and coypus used for both their meat and hide, and chinchillas, for their fur [1]. Both wild chinchilla species, the short-tailed chinchilla (*Chinchilla chinchilla*) and long-tailed chinchilla (*Chinchilla lanigera*) are endangered today due to illegal hunting and habitat loss [2, 3]. Historically, their population declined due to overhunting for their meat and fur in the Incan empire, while in the 1800s, due to commercial hunting in northern Chile for their fur [4], While domestic chinchillas, descendants of *C. lanigera* species, are often kept as pets. Similarly, the common Degu (*Octodon degus*), native to central Chile, has recently started being kept as pets as well [5]. The cavy family (*Caviidae*) are native South American rodents that include species such as the Patagonian mara, rock cavy, yellow toothed cavy and guinea pig species like the wild Brazilian guinea pig (*Cavia aparea*), and domestic guinea pigs (*Cavia porcellus*) [5]. Capybaras (*Hydrochoerus hydrochaeris*) are semi-aquatic giant rodents that can be found close to bodies of water in dense forests. They can be found in most South American countries and are particularly numerous in Brazil [5]. Although they are regularly hunted for their meat, their conservation status is of least concern, and they have stable populations [6]. In addition, maras (*Dolichotis patagonum*), which live in dry areas of Central and Southern Argentina are a near threatened species due to hunting and habitat loss [5, 7]. Coypus (*Myocastor coypus*), another semi-aquatic rodent native to wetlands in South America, was introduced worldwide mainly by fur farmers and is now an invasive species in several countries [5, 8]. They harm native ecosystems and can cause extensive damage to agricultural crops, bodies of water and infrastructure, causing severe economic loss [5, 8]. Azaras grass mouse (*Akodon azarae*), *Oligoryzomys* species, Red hocicudo (*Oxymycterus rufus)*, and the South American water rat (*Nectomys squamipes*) are a few of the many Sigmodontin rodents of the family *Cricetidae* that are found in various habitats in South America [9]. While Agoutis, rodents from the *Dasyprocta* genus that are also hunted for their meat, are known for their significant role in the survival of Brazil nuts through seed dispersal [5]. Finally, Prehensile tailed porcupines (*Coendou* sp.), new world porcupines of the family *Erethizontidae*, are arboreal species that are distributed in Central and South America, with the dwarf porcupine (*Coendou speratus*) classified as endangered [5, 10].

Some important non-infectious diseases that can manifest in rodents' skin includes Vitamin C deficiency in cavies, cutaneous and subcutaneous tumours of capybaras and pet rodents, and cold injuries described in coypus and guinea pigs. Some of these rodents are also vulnerable to pathogens affecting the skin, such as keratinophilic fungi, bacterial infections and viruses such as poxviruses and papillomavirus or act as asymptomatic carriers, potentially infecting other species. Ectoparasites found on South American rodents will also be mentioned, mainly those found in their natural habitats, furthermore the significance of some of them in harbouring and transmitting disease will also be discussed. Since some of these rodents are often found in zoos like the capybara, additional dermatological issues that affect them in captivity will be acknowledged and compared to their occurrence in existing literature. This will be done by looking at histopathological reports of skin lesions collected from the affected South American rodents in Budapest Zoo & Botanical Garden (Budapest Zoo).

2. Literature review

2.1. Bacterial infection

Onset of dermatitis can be attributed to environmental factors involving skin irritation and damage, often from rough or sharp objects. In a specific incident, it was observed that Achene awns, characterised by their barbed thorn-like appearance, acted as the primary cause for skin lesions in some wild coypus [11]. This led to the concomitant development of secondary bacterial and fungal infections. As a result, the affected regions developed thickened skin accompanied by inflammatory cell infiltration and the presence of necrotic debris [11]. Bacterial infiltration in deeper wounds caused by bite wounds or trauma, for instance, may result in a subcutaneous abscess, which is somewhat common in guinea pigs [13]. Staphylococcus species are often the main culprit in them, while other species such as Streptococcus spp., Actinomyces spp. and Fusobacterium spp. may also be involved [12,13]

Pododermatitis is another common infection occurring on the footpads of guinea pigs due to inappropriate keeping hygiene, obesity, abrasive flooring or vitamin C deficiency [14]. Milder lesions are characterised by erythema, swelling and ulceration on the bottom of the feet, which may develop abscesses or progress to osteomyelitis in severe cases due to secondary bacterial infection [14]. Osteomyelitis is usually irreversible, and relapse is common after treatment. *Staphylococcus aureus* is often the main causative agent, and other species, including *Corynebacterium pyogenes*, *E.coli*, *Proteus* spp., *Streptococcus* spp., and *Pseudomonas* sp. may also be present [15].

2.2. Poxviruses

Poxviruses are large DNA viruses affecting both vertebrates (*Chordopoxvirinae*) and invertebrates (*Entomopoxvirinae*). *Chordopoxvirinae* subfamily contains several genera, three of which comprise viruses with zoonotic potential: *Orthopoxvirus*, *Parapoxvirus* and *Yatapox* genera [16]. Poxviruses are epitheliotrophs, primarily replicating on epithelium of broken skin and mucosal surfaces [16]. Symptoms of an infection varies from mild local skin lesions to generalised infections. Pox lesions progress from erythema to papules to vesicles and pustules before drying off and shedding the crust and healing. Animals can be infected through direct contact or indirectly from the environment or even by arthropod vectors for specific viruses [16].

2.2.1 Cowpox

Cowpox is a zoonotic orthopoxvirus with a broad host range and occurs mostly in Europe [17]. The disease was first detected in cows, hence its name, however, wild rodents are the main reservoirs of the virus, while humans, cats, cows and exotic animals are incidental hosts. Cowpox typically has low pathogenicity in infected rodent reservoirs, either causing mild skin lesions or no obvious clinical disease [17, 18].

The first reported case of cowpox in maras occurred in 5 maras kept in an educational park in the Netherlands, where one died, and the other four were euthanised [19]. Conjunctivitis and anorexia were the first visible clinical signs. Post-mortem examination exhibited ulceration of the oral cavity, the skin of the nose and genitals and other pathological changes of the internal organs. The intracytoplasmic eosinophilic inclusion bodies in the epithelium, and other histologic alterations, were in line with the characteristics of a poxvirus infection [19]. PCR was done to confirm the cowpox virus infection. Since the virus had a high pathogenicity in the maras, they are not considered as a reservoir and were likely infected by rats within the park [19].

2.2.2. Vaccinia virus

Vaccinia virus (VACV), also called Bovine vaccinia (BV) in Brazil, is also a member of the *Orthopoxvirus* genus, typically affecting cattle and humans [20]. In some cases, it can cause vesicular and pustular lesions on the teats and udder of cattle and mastitis, leading to a decrease in milk production, which can harm local economies in rural Brazil. It is also a zoonotic disease mainly causing Nodular and ulcerative lesions on milkers' hands. Several outbreaks in rural Brazil have occurred since 1999 associated with Bovine Vaccinia [20]. Although the disease doesn't seem to affect wild rodents, it is noteworthy to mention it due to their potential role in the natural transmission cycle of the vaccinia virus. Capybaras are especially important to mention as potential reservoirs due to the proximity of their habitats to cattle farms in Brazil. The presence of neutralising antibodies against orthopoxvirus in captive and wild capybaras from different regions in Brazil [21], as well as in *Trinomys setosus* (hairy Atlantic spiny rat), *Nectomys squamipes* (South American water rat), and Oligoryzomys species, provides evidence that they might play a part in circulating the virus [22]. More research should be done to understand the role of rodents in maintaining VACV in nature to manage outbreaks and protect public health.

2.2.3. Brazilian porcupine poxvirus

In recent years, a novel poxvirus was investigated following the detection of pox-like lesions in some Brazilian porcupines. It is proposed to name it Brazilian porcupine pox virus (BPoPV), categorised under *Chondropoxvirinae* subfamily, *Poxviridae* family [23]. Its lethality to porcupine populations, host spectrum and zoonotic potential are yet to be investigated.

BPoPV infection was reported in the following species: Hairy dwarf porcupine (*Coendou spinosus*), Brazilian porcupine (*Coendou prehensilis*) and *Coendou longicaudatus boliviensis* [23, 24, 25] The virus manifests as thickened and wrinkled erythematous skin, primarily affecting the eyelids, muzzle, limb extremities, tail and perigenital region. The skin lesions include erosions, ulceration, oedema, crusts, exudation, and purulent nasal and ocular discharge [23]. Furthermore, the virus can lead to the formation of papule clusters with coalescing plaques on the face and around the genitals, which can obstruct vision when occurring on the eyelids [24]. Microscopic examination of a skin section revealed proliferative dermatitis, keratinocyte degeneration in addition to intercellular oedema, ulceration and multifocal necrosis in the epidermis. Dermal lesions include inflammatory cell infiltration, oedema and necrosis [23]. Supportive treatment can be given, considering it is a self-limiting disease [25]. In the case of one hairy dwarf porcupine, treatment included Enrofloxacin, metamizole and peptidic bovine thymus extract with periodic chemical restraint for wound debridement and cleaning. After treatment, the porcupine's body condition improved, and the skin lesions healed without scarring [25]. However, the other cases had fatal outcomes despite treatment. Wildlife veterinarians observed similar clinical manifestations in wild porcupines in Brazil and documented high mortality rates [24].

2.3. Papillomavirus

Papillomaviruses are a family of DNA viruses that infects primarily the skin and mucous membrane of several animal species. They are highly host-specific and are responsible for producing benign tumours called warts or papillomas that are self-limiting while some specific types of the virus can cause proliferations of a high risk of malignancy [26]. Virus transmission occurs from the surface of papillomatous lesions, harbouring large amounts of virions [26]. Papillomavirus was documented in coypus with different sized lesions in the oral and nasal cavities and on the skin of the tail and limbs. Affected adult females transmitted the disease to their offspring and spread it to other young by contact. Spontaneous healing occurred about 3 months later [27].

2.4. Foot and Mouth disease

Foot and mouth disease (FMD) is caused by a highly contagious virus belonging to the *Picornaviridae* family, *Apthovirus* genus [28]. It affects even-toed ungulates like cows, pigs and sheep, causing significant economic loss due to the reduced meat and milk production and trade restrictions imposed [28]. FMD can be spread by animals carrying the disease by direct contact, through their excretions or even through their milk and semen. It produces vesicles on the muzzle, in the oral cavity, and often on the udder, teats and feet [28].

It is important to explore the role of capybaras in transmitting the virus due to the abundance of capybaras in FMD endemic regions in some South American countries. The susceptibility of capybaras to the disease was demonstrated by Rosenberg FJ and Gomes I by inoculating the virus in some capybaras [29]. Vesicles were detected in all their feet after 72-96 hours post-infection. The virus titres were obtained from the majority of organ extracts, antibodies developed against the virus and shedding of the virus in the faeces lasted at least until 10 days post-infection [29]. It was also demonstrated that experimentally infected capybaras can transmit the disease by contact with other healthy capybaras and cattle, which resulted in generalised clinical signs in all the infected species. However, the experiment concluded that capybaras are unlikely reservoirs for FMD in nature [30]. Coypus and agoutis are also susceptible to the disease through experimental infection and through contact with other infected animals [31, 32].

2.5. Dermatophytosis

Dermatophytosis or ringworm is a contagious infection caused by a special group of fungi called dermatophytes. These fungi require keratin to grow, so they can superficially invade skin, hair and nails [33]. Several dermatophytes are zoonotic, the most common being *Microsporum canis*, and *Trichophyton mentagrophytes* [33]. Pets and stray animals are common sources of these dermatophytes in humans. Typical skin lesions are circular alopecic areas surrounded by an erythematous border. Seemingly healthy animals can be asymptomatic carriers of dermatophytes, potentially infecting humans or other animals coming in close contact [33].

Woods lamp is a common tool used for examining dermatophytosis. It emits UV light to detect fluorescence on the hair and skin, characteristic to some dermatophytes, including *Microsporum canis*, *Nannizzia gypsea*, and a few others [33]. A negative exam result does not exclude an infection as not all dermatophytes fluorescens. False positive results can also occur in the case of some bacterial and yeast infections [33]. Microscopic examination of hair and skin scrapes is very useful in determining the presence of fungi, however, determining the specific species and viability of the fungi is not possible using this method. KOH or lactophenol blue stain can be applied to the scrapes to enhance fungal elements [33]. Histopathology is also useful for deep dermatophyte infections that invade deeper tissue. The gold standard for identifying dermatophyte species is through fungal cultures, despite it being a poorly sensitive and time-consuming method. Dermatophytes test medium agar (DTM) is a common selective medium used in these cultures [33]. PCR tests are highly sensitive and can distinguish the species, although not the viability, while the Elisa test, a highly specific method, can also be utilised but may give out false positive results due to past infections [33].

Several fungal species were found on the coats of wild coypus in Italy. The positive rodents were asymptomatically infected; thus, no skin lesions were observed [34]. The mycoflora of the positive coypus included *Microsporum gypseum* (now called *Nannizzia gypsea*), *Trichophyton terrestre*, *Alternaria* sp. and a few others. Since they may act as reservoirs of several dermatophytes and saprophytes, they may pose a zoonotic risk to humans at risk of coming in close contact [34].

Trichophyton mentagrophytes most often cause dermatophytosis in guinea pigs and chinchillas. *Microsporum canis*, and *Microsporum gypseum* have also been less frequently reported in both species as well as *Microsporum audouinii* in guinea pigs [13]. Skin lesions commonly include diffuse scaling and alopecia often on the nose, ears, face and feet. However, it can also manifest as inflammatory pruritic pustules or ringworm with folliculitis [13]. Fungal spores can be transmitted directly between animals or by exposure to contaminated hay, bedding or fomites. Common stressors such as overcrowding and husbandry inadequacies can increase their predisposition to the infection [35].

2.6. Helminths

Although helminthiasis involving the skin is not a common in rodents, it is worth noting that some juvenile forms and adults of certain helminths can sometimes be detected in the skin [36, 37, 38]. Microfilaria were found during the histological examination of some select capybaras' upper and middle dermal layers [36]. They were identified as belonging to the *Mansonella* species, specifically *M. longicapita, M. rotundicapita*. Some adults were also found in the dermis, which is not uncommon for those in the subspecies Esslingeria [36]. Another filarial nematode, *Yatesia Hydrochoerus* was previously documented in capybaras skeletal muscle fascia, with its microfilaria detected within the skin as well [37]. In guinea pigs' case, the *Pelodera strongyloides* larvae, a saprophytic nematode, can occasionally invade their skin, resulting in clinical symptoms such as inflammation, pruritus, alopecia, crusting, and papules [13, 38]. However, these larvae don't undergo development into adults within the host. Instead, adult worms can be found in the surrounding environment and bedding, while the larva can be detected in skin scraping or biopsies [13, 38].

2.7. Ectoparasites

Ectoparasites play an important role in disease transmission dynamics, particularly in vector-borne diseases as they act as carriers for several pathogens, including bacteria, protozoa and viruses. Studying the prevalence and life stages of different parasite species in rodents is critical in understanding their role in spreading disease to both animals and humans.

2.7.1 Ticks

Brazilian spotted fever (BSF) is a zoonotic disease caused by *Rickettsia rickettsia* bacteria that is transmitted by ticks. It causes high mortality in humans, with most cases occurring in southeast Brazil [39]. Amblyomma tick species, specifically *Amblyomma cajennense* species complex that includes *A. cajennense* and *A.sculptum* ticks, are some of the vectors for this disease [40,41]. The rise in human BSF cases has been linked to the growing population of capybaras in the area, which contribute to the epidemiology of the disease by maintaining these Amblyomma ticks and by amplifying *R. rickettsia* [40]. This is a crucial aspect in maintaining the bacteria in nature, given the ticks' inability to maintain them through transovarial transmission. Capybaras are responsible for spreading the disease by transporting the tick from BSF endemic regions to other locations or by directly carrying the bacteria to other ticks [40].

A parasitic fauna research done on 23 free ranging capybaras in two different Brazilian biomes reported that all were parasitised by ticks. These included larvae and nymphs of *Amblyomma* species, including adults of *A.sculptum* and *A.dubiatum* ticks [42]. In addition, another research showed the abundance of *A. sculptum* ticks on capybaras and in the environment and its prevalence over *A.dubiatum* was much higher in BSF endemic areas compared to non-endemic areas [43].

Nevertheless, Amblyomma tick infestations in capybaras do not always imply rickettsial infection [44]. In a health survey of free-ranging capybaras in a state park in Brazil, a total of 218 ticks were recovered from 31 capybaras that included: *Amblyomma* sp. larvae and nymph, *A. dubitatum* and *A. cajennense* adults. Despite these large numbers of ticks, serological tests did not reveal their exposure to *R. rickettsii* [44].

Tick bite lesions caused by *Amblyomma dubitatum* and *Amblyomma cajennense* tick infestations were collected and investigated from captive capybaras from different locations and origins in Brazil [45]. The tick bite macroscopically appears erythematous and swollen.

Microscopic exam reveals an eosinophilic homogenous mass extending from the penetrated epidermis site and deep into the dermis. Necrosis was visible at the deep end of the dermis. Oedema, hyperplasia and keratinocyte necrosis were visible at the damaged epidermis, possibly due to tissue damage done by the tick or the hosts inflammatory response [45].

Amblyomma maculatum, *Amblyomma triste*, and *Amblyomma tigrinum* are three separate species comprising the *Amblyomma maculatum* group which were once considered a single species. They serve as the primary carriers of *Rickettsia parkeri*, which belongs to the spotted fever rickettsia group as well. [46]. Immature stages of *Amblyomma triste*, tick namely the larva and nymph can be found on some rodents of *Sigmodontinae* submfamily in Argentina, including *Akodon azarae*, some *Oligoryzomys* species and *Oxymycterus rufus* [47]. The presence of these stages was also documented in the Brazilian guinea pig (*Cavia aparea*), while the adult stages of *A. triste* in Argentina rather tend to parasitise a variety of larger mammals including the capybara [47].

In northwest Argentina, *Caviidae*, specifically the common yellow toothed cavy (*Galea musteloides*) in this case, is important in maintaining *Ambylomma tigrinum*. They are host to this tick's larval and nymph stages, with nymph infestations being significantly more common [48]. In contrast, *Cricetidae* represented by *Akodon dolores*, *Graomys* species and *Calomys* species in the same region, are host to primarily the larva of *A. tigrinum* [48]. Despite the presence of these ticks in different rodent species, the role of these rodents in maintaining the disease has not been well researched yet.

Ixodes species, another member of Ixodidae family (hard ticks) were sourced from different South American rodents. *Ixodes lasallei* was sourced from black agoutis and red-rumped agoutis in Colombia, Peru and Venezuela. While a recently described species- *I.bocatorensis* was collected from red-rumped agouti and Central American agouti in Venezuela, Panama and Colombia [49]. Subadults of *Ixodes loricatus* can be found on some rodents of *Sigmodontinae* subfamily in Argentina, notably on *Akodon azarae*, *Oxymycterus rufus* and *Oligoryzomys flavescens* [47].

Rhipiciephalus sanguineus ticks, also belonging to the hard tick family (*Ixodidae*), were collected from wild coypus in Buenos Aires. However, they were detected in minimal numbers in only 1 of the coypus studied, and they are suspected to be an accidental host [50].

In northern Chile, *Ornithodoros octodontus*, an Argasid tick (soft tick), was retrieved from degus (*Octodon degus*) [51]. In the Brazilian savannah, Brazilian guinea pigs (*Cavia aperea*) and *Thrichomys* species were host to the recently described *Ornithodoros cerradoensis* n. sp., belonging to the *O. talaje* group [52]. Meanwhile, *Ornithodoros rietcorreai* was discovered in rock cavy (*Kerodon rupestris*) burrows in northeastern Brazil. *Amblyomma parvum* and potentially *Ornithodoros talaje* are 2 other ticks that could be found on rock cavies as well [53]. In Argentina's Cordoba province, *Ornithodoros quilinensis* was characterised in association with the central leaf-eared mouse (formerly *Graomys centralis*, now called *Graomys chacoensis*) by identification based on their larval specimen [54]. Additionally, *Ornithodoros xerophylus* was later documented infesting the same host species within the same region [55].

2.7.2. Mites

Scabies is a highly contagious parasitic skin infection caused by the *Sarcoptes scabiei* mite that affects a range of mammals, including humans. The female mite lays eggs as it burrows into the most superficial skin layer, known as the stratum corneum, leading to the development of larvae, nymph and adults [56]. Typical skin symptoms include intense pruritus, scaling, hyperkeratosis and hair/fur loss. The symptoms are attributed to hypersensitivity to the mite and its secretions. [56]. The significance of this skin condition lies in its rapid and easy transmission through close skin contact and with the potential to spread to humans [56]. Most common examination method is by direct microscopy of skin scrapings. Treating the skin scrapings in saline for an hour before mounting them on a slide can make the mites move out of the skin, making it easier to visualise [57]. However, this examination method is generally not very sensitive and often yields false negative results due to the low number of mites even in intense pruritus. Therefore, skin scrapes should be collected from a large skin surface area to improve the chances of finding the mites. Histopathology of a skin biopsy can also be done from the affected region, often revealing hyperkeratosis, parakeratosis and tunnels with mite sections in the epidermis, but is time-consuming [58]. In humans, dermoscopy is often used as a non-invasive technique to visualise the mite and its burrows on the skin. Although dermoscopy is often used in companion animals to examine dermatopathies rather than visualising parasites, it can potentially be utilised to examine a possible *S. scabiei* infection because it is a quick and sensitive method of visualising the mites without additional equipment or the need for a laboratory, however, it is not very specific [59]. Serological tests such as ELISA can potentially be useful in diagnosing scabies in animals, with high sensitivity and specificity, as demonstrated in dogs [60].

A case study demonstrated evidence of *S. scabiei* transmission occurring naturally between a captive capybara and southern tamandua housed in the same room with no direct contact. The mites recovered from each were genetically identical [61]. The tamandua initially developed skin lesions and died despite treatment, due to unknown causes. The capybara was examined a few weeks later and revealed generalised erythema and multifocal crusts along with hyperkeratosis patches present ventrally and erosions on the flank and face [61]. Skin scrapings were collected from the affected regions and were processed to isolate the mite, thus confirming *S. scabiei* by microscopic examination. After 2 topical treatments of selamectin, pruritus and the skin lesions resolved [61].

Sarcoptic mange was also detected in a dead Andean porcupine (*Coendou quichua*) found in a natural park in Colombia. It suffered severe skin lesions described as hyperkeratosis and alopecia starting on the chest area and extending to the inguinal region and the tail base. The mandible, forelimb and hindlimb were also among the regions affected [62]. Skin scrapings were done, and skin samples were collected from lesions on the abdominal and inguinal areas. Microscopic examination of the scrapes revealed mites consistent with *S. scabiei* morphology [62]. Histopathology revealed epidermal necrosis, acanthosis, pustules, mite structures and intraepidermal tunnels. Molecular identification also confirmed the presence of *S. scabiei* [62]

Trixicarus caviae, a sarcoptic mange mite is a very common ectoparasite of guinea pigs [12]. The most prominent clinical sign is severe pruritus, causing self-trauma and erythema, along with alopecia and hyperkeratosis. Seizures can be triggered in some cases when handling the animal and are resolved by treating the infestation [12]. Asymptomatically carrying the mite has also been reported, only developing clinical symptoms under stressful conditions [63].

Chirodiscoides caviae, a common guinea pig fur mite that attaches to their hair shaft, are often asymptomatically present for an elongated time. Clinical signs, if any, tend to be mild and not life-threatening. In heavy infestations, they may exhibit signs of pruritus, scaling, alopecia and excessive grooming with a possibility of ulcerative dermatitis [13]. The lumbosacral region seems to be the most commonly affected area [64].

Among the mites and ectoparasites harvested from Azaras grass mouse in Buenos Aires, Argentina, *Androlaelaps azarae* was the prevalent species. *A. fahrenholzi* represented the second most abundant mite on them, while *Ornithonyssus bacoti* mites were the least common among the mites collected [65].

2.7.3. Lice

Chewing lice of the genus *Eutrichophilus* have been described in several new world porcupines (*Erethizontidae*), including *coendou* species and the bristle spined rat (*Chaetomys subspinosus*) [66,67]. 18 *Eutrichophilus* species were characterised by Tim and Price in 1994 and were described to be very host specific [66], in addition to *Eutrichophilus koopmani* described in the Brazilian black dwarf porcupine a few years later [67]. Presence of lice in porcupines tends to be in high numbers, seemingly due to the nature of their quills that makes grooming more difficult, however they don't seem to cause skin symptoms despite their numbers [66].

From the Ectoparasites collected from free-ranging coypus in Buenos Aires, Argentina, *Pitrufquenia coypus* (a chewing lice), which is an obligate parasite of the coypus was the most abundant on several coypus [50]. Other than the cutaneous miasis by *Dermatobia hominis* fly larva observed in one of the *P.coypus* infested coypus, no skin lesions associated with the lice were reported in the rest of the examined coypus [50]. While on *Akodon azarae,* also in Buenos Aires Argentina, *Haplopleura atikeni* was the predominant lice species collected and the second most abundant ectoparasites found on them [65].

Lice infestation, particularly by *Gliricola porcelli* is a prevalent issue in pet guinea pigs. Other species of chewing lice, including *Gyropus ovalis* and *Trimenopon hispidum,* have been reported as well, but with less frequency [13]. Clinical signs may include pruritus, scaling, erythema and papules on the skin, however, not all instances of lice infestation are associated with pruritus. Furthermore, lice can sometimes be found on guinea pigs with a healthy hair coat as well [12].

2.7.4. Fleas

Echidnophaga fleas were documented in captive agoutis (*Dasyprocta mexicana*) within a safari park as well as in maras (*Dolichotis patagonum*) kept in a shared enclosure. Heavily infested agoutis developed flea-induced anaemia and were fatal in some cases [68]. Other agoutis developed alopecia, hyperkeratosis and crust formation along the dorsal region. Two agoutis presented penetrating wounds on the flank, and one of them developed cellulitis and myositis and consequently died due to bacterial infection of the wound [68]. The cause of the wound was suspected to be due to flea bite hypersensitivity, provoking pruritus and selfmutilation. The Maras inhabiting the same enclosure exhibited similar symptoms but with less severity [68].

Polygenis spp. are a commonly found flea species on *Akodon azarae*, in Argentina, compared to *Craneopsylla minera minera*, found less frequently on them [65]. *Nosopsyllus fasciatus* (flea species) was documented in two coypus in Argentina during a coypus ectoparasite study, with no flea-associated skin lesions observed during collection [50].

2.8. Vitamin C deficiency

Members of the *Caviidae* family, including capybaras, guinea pigs and maras, share a genetic mutation that renders them incapable of synthesising ascorbic acid (vitamin C). This results in their livers being unable to produce L-gulonolactone oxidase enzyme that is essential for converting glucose to ascorbic acid [69]. Vitamin C is a crucial component of collagen synthesis, essential for maintaining skin, joint and bone health. In their natural habitats, *Caviidae* are surrounded by an abundance of fresh vegetation that readily fulfils their vitamin C requirements. In contrast, in captivity, the availability of vitamin C should be ensured by their caretakers through providing enough fresh produce and adjusting the amount needed accordingly to maintain normal physiology and promote the health of their coats. For instance, capybaras residing in Seoul Zoo exhibited symptoms such as weight loss, general dermatitis, skin pigmentation, alopecia and dull hair- common indicators of hypovitaminosis C [70]. The overall condition of their coat significantly improved by enhancing their diets with vitamin C-rich fruits, vegetables and leafy greens [70]. Conversely, in maras kept in the same exhibit, dermatopathies were not observed, but bone fractures were more common, which still supports the hypothesis of their vitamin C deficiency [70]. In another group of captive capybaras in Argentina, vitamin C deprivation resulted in general signs of scurvy, such as gum bleeding, weak joints, reduced growth and reproductive issues, although no skin symptoms were observed [71]. Similarly, in guinea pigs, hypovitaminosis C can predispose them to dental disease, swollen joints, alopecia, skin sores, and a roughened haircoat. It is particularly prevalent in guinea pigs fed seed-based diets or diets mainly consisting of inadequately supplemented pellets, lacking sufficient vitamin C [72].

2.9. Tumours

There are limited reports of skin tumours in capybaras. In one case, a dermal plaque was reported on the flank of a capybara. It was characterised as an unencapsulated and well-demarcated mass with a thickened overlying epidermis. Upon further investigation, it was identified as a histiocytoma, the first of such a case reported in capybaras [73]. In another study done on 341 older guinea pigs, out of the 223 tumours found in different organ systems, none were histiocytomas, so it seems to be a rare tumour in these rodents [74]. Furthermore, another histiocytic disorder was documented in a captive capybara. The subcutaneous multinodular mass resided between two digits of the hindlimb and invaded the dermis. The diagnosis of histiocytic sarcoma was determined through histopathology and immunohistochemistry [75].

Squamous cell carcinoma (SCC) was also reported in two captive capybaras in a Japanese aquarium, which was the first documentation of such a case in capybaras [76]. The skin lesions started as keratinous hyperplasia with scaling and crusting on the buttocks, with a generalised secondary alopecia. Initially, it was suspected to be bacterial dermatitis and it responded to antibiotics but recurred intermittently despite repeated treatments [76]. A 3 cm haemorrhagic and encrusted mass appeared on the buttocks about six weeks after the last remission. Six months later, with further growth and infiltration of the mass, it appeared ulcerated and alopecic. SCC was confirmed upon further C.T and histological examination. The intermittent chronic abnormal keratinisation may have been related to the development of the neoplasm [76]. Squamous cell carcinoma has also been documented in guinea pigs but is very infrequent in them as well. In a study of skin tumours in small mammals, out of 103 guinea pigs, only 1 was presented with SCC [77].

Most of the skin tumours diagnosed in guinea pigs tend to be benign [77]. Trichofolliculomas are frequently reported as the most common cutaneous tumour, however, Otrocka Domagala et al found lipomas (presenting as single or multiple tumours) to be more frequent in their study done on 103 guinea pigs [77]. Malignant skin tumours occur less frequently in guinea pigs, with a predominance of soft tissue sarcomas, specifically fibrosarcoma and liposarcomas [77].

The incidence of tumours is generally low in degus [78]. Soft tissue sarcoma seems to be the prevalent tumour occurring in them. Research on pet degus reported cutaneous fibrosarcoma as the most frequent tumour present among the 16 degus studied with localisation mainly on the hindlimb and the tail, back, and auricular region [78]. Another study also mentions the uncommon occurrence of malignant histiocytoma and subcuticular myxosarcoma in degus

[79]. Fibrosarcoma cases were also reported in chinchillas, although they have limited reports on cutaneous tumours. [77].

2.10. Cold injuries

Frostbite results from the injury to blood vessels in freezing weather conditions, leading to reduced blood supply, oxygen deprivation and tissue freezing in the affected area [80]. This is frequently observed in the extremities such as digits, ears and tails. Animals that lack adaptations for freezing weather, as in the case of invasive species like coypus, are at an increased risk of developing local cold injuries. Additionally, animal keepers may encounter this problem while housing non-native animals in outdoor enclosures that lack adequate protection against dropping temperatures [80].

Gethöffer F et al. observed abnormal behaviour and skin lesions in coypus after a two-week cold period in lower Saxony, Germany [81]. Post-mortem examinations conducted on 10 adult coypus revealed severe skin lesions on all their tails and varying degrees of lesion on the limbs in seven coypus. The skin lesions included superficial erosion and ulceration that can extend to subcutaneous tissue, or even progressing to bone involvement, disrupting joint capsules, as well as lesions with necrosis and bone resorption [81]. Although it cannot be confirmed, the localisation of lesions corresponds to the typical pattern of frostbite injuries commonly observed in animals so frostbite should also be considered when it comes to long term death of coypus in extreme cold periods [81].

Another possible cold injury was reported in a captive capybara left outdoors in freezing temperature. It exhibited ulceration and blisters on the dorsal aspect of the forefoot and dry gangrene ventrally on the digits, distinctly demarcated from the adjacent healthy tissue [80].

3. Method

Existing literature was compiled to have an overview of skin diseases affecting South American rodents in one paper, while histological reports of skin problems occurring in some South American rodents in Budapest Zoo in 2021-2023 were collected as well for additional resources. Two capybaras, three muenster yellow toothed cavies and one guinea pig were among the affected species in the zoo. All the specimens were presented with non-specific skin lesions such alopecia and erythema. Skin biopsies were collected from all the cases and sent to the lab for further histopathological processing. Haematoxylin and Eosin stain were used on all skin samples and perpendicular full cross-sectional planes of the samples were examined.

4. **Results**

Capybara 1

The first sample presented mild parakeratotic hyperkeratosis in the epidermis with uneven hyperplasia and hyperpigmentation. No pathogens were identified on the epidermis, while the dermal epidermal junction was intact. The superficial dermis exhibited a mild perivascular infiltration of mixed inflammatory cells that included Lymphocytes, plasma cells, and eosinophilic and heterophilic granulocytes [figure 1]. The hair follicles in the telogen phase had a hyperplastic epithelium and some abnormal signs of trichilemmal keratinisation [figure 2]. Some cocci bacteria colonies were also seen in some hair follicles in the keratinous material. Sebaceous glands were absent in the planes examined.

The second sample collected from a different skin lesion had a mild orthokeratotic hyperkeratosis of the epidermis with uneven acantomatous hyperplasia and hyperpigmentation as well, and no pathogens detected on the surface [figure 3]. All dermis layers had a similar inflammatory cell infiltration as the first sample but more pronounced. The follicles were also similar to the other sample: in the telogen phase, hyperplastic, hyperpigmented, with some bacterial colonies and abnormal trichilemmal keratinisation [figure 4]. The sebaceous glands found were slightly atrophic.

Based on these histological findings, the capybara was diagnosed with chronic allergic dermatitis with signs of secondary chronic bacterial folliculitis. Further microbiology testing is recommended in the follicle samples and the investigation and exclusion of possible allergic backgrounds.

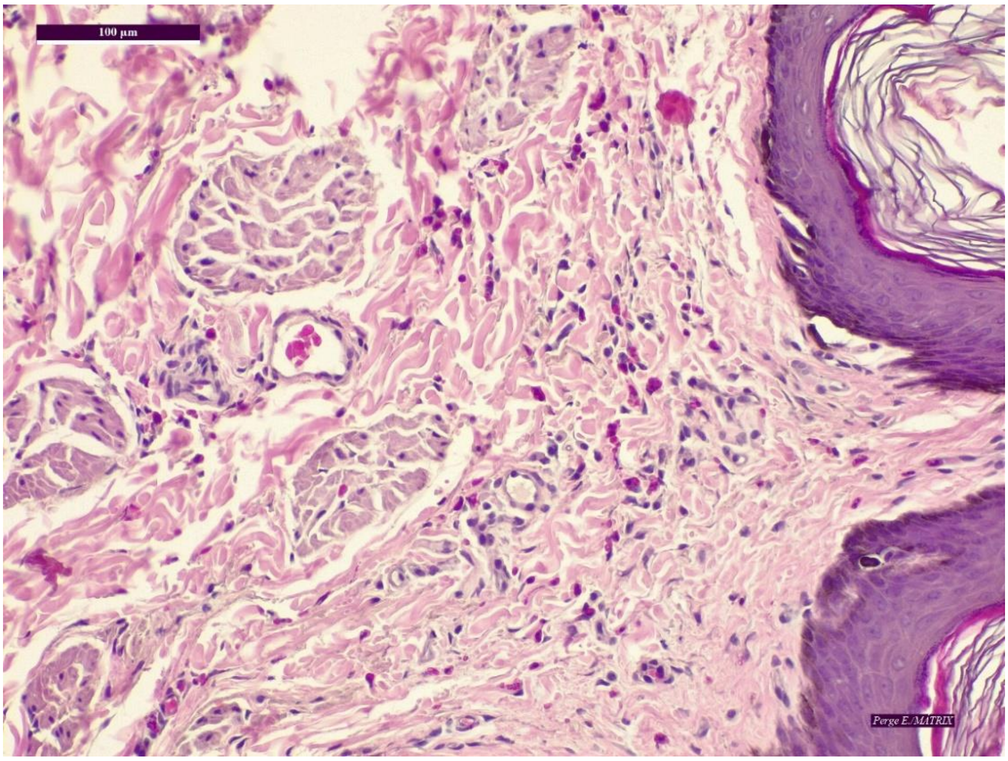

Figure 1. mild perivascular infiltration of mixed inflammatory cells in the dermis.

From Dr. Perge E, Matrix lab

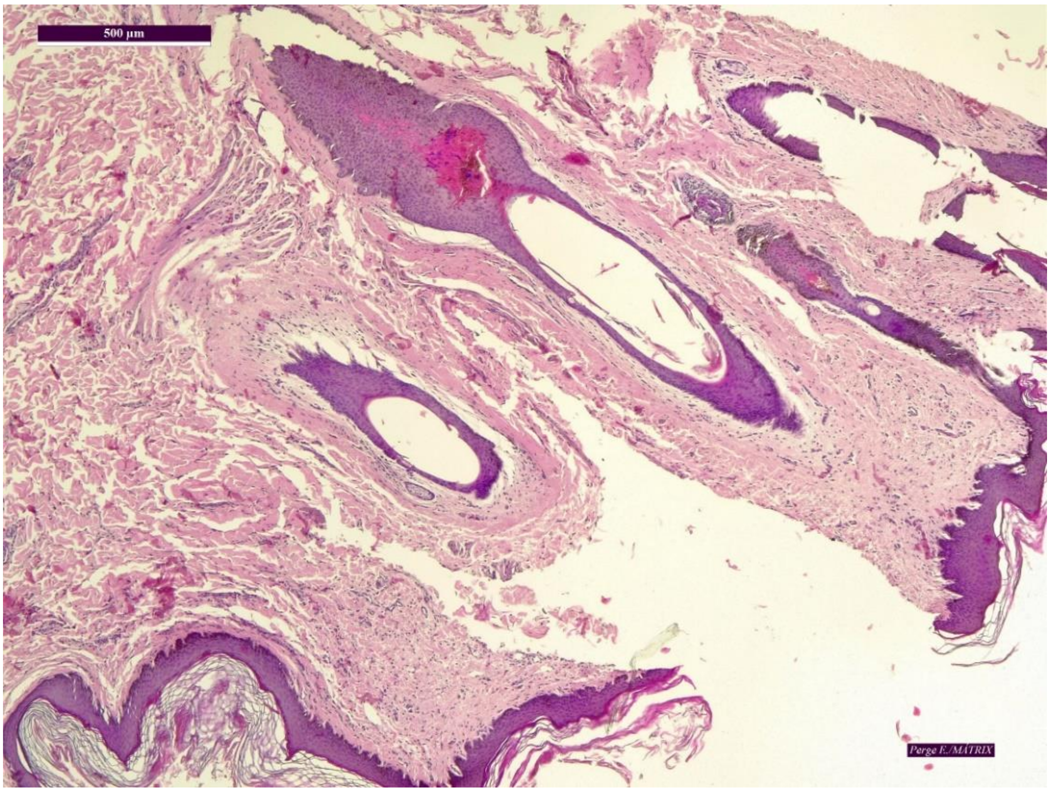

Figure 2. abnormal trichilemmal keratinization in hair follicle**.** From Dr. Perge E, Matrix lab

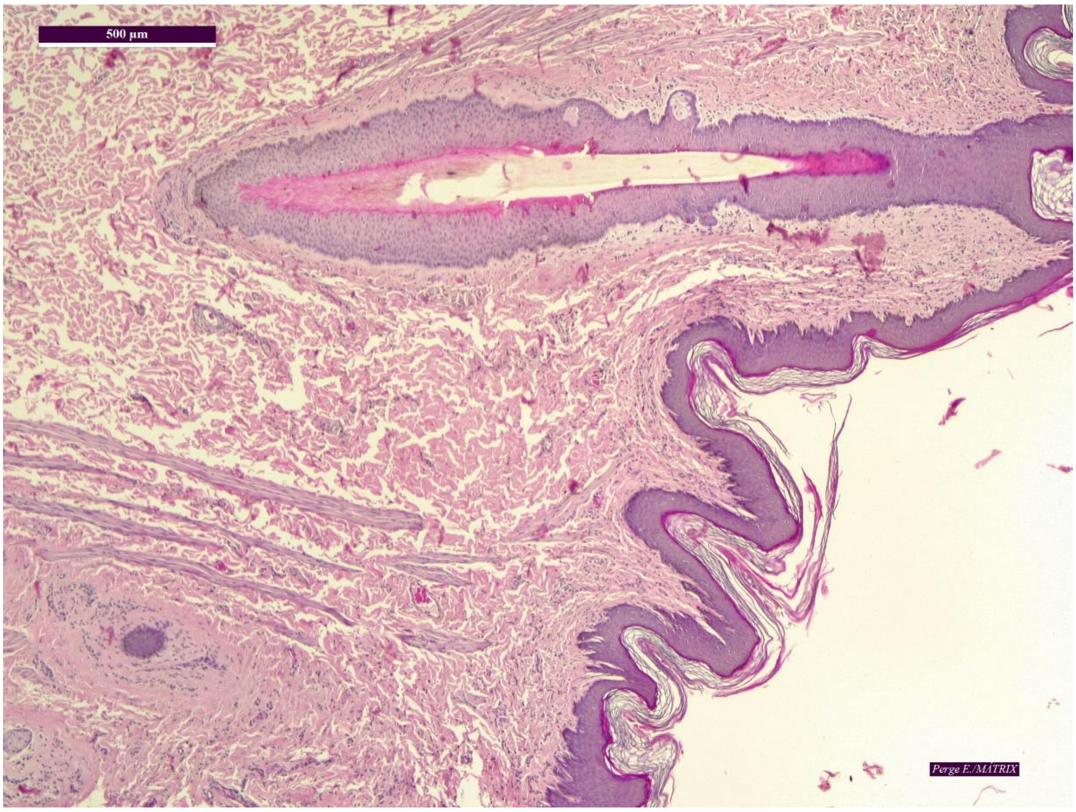

Figure 3. hyperkeratosis, hyperplasia and hyperpigmentation of the epidermis and abnormal trichilemmal keratinization of the hair follicle. From Dr. Perge E, Matrix lab

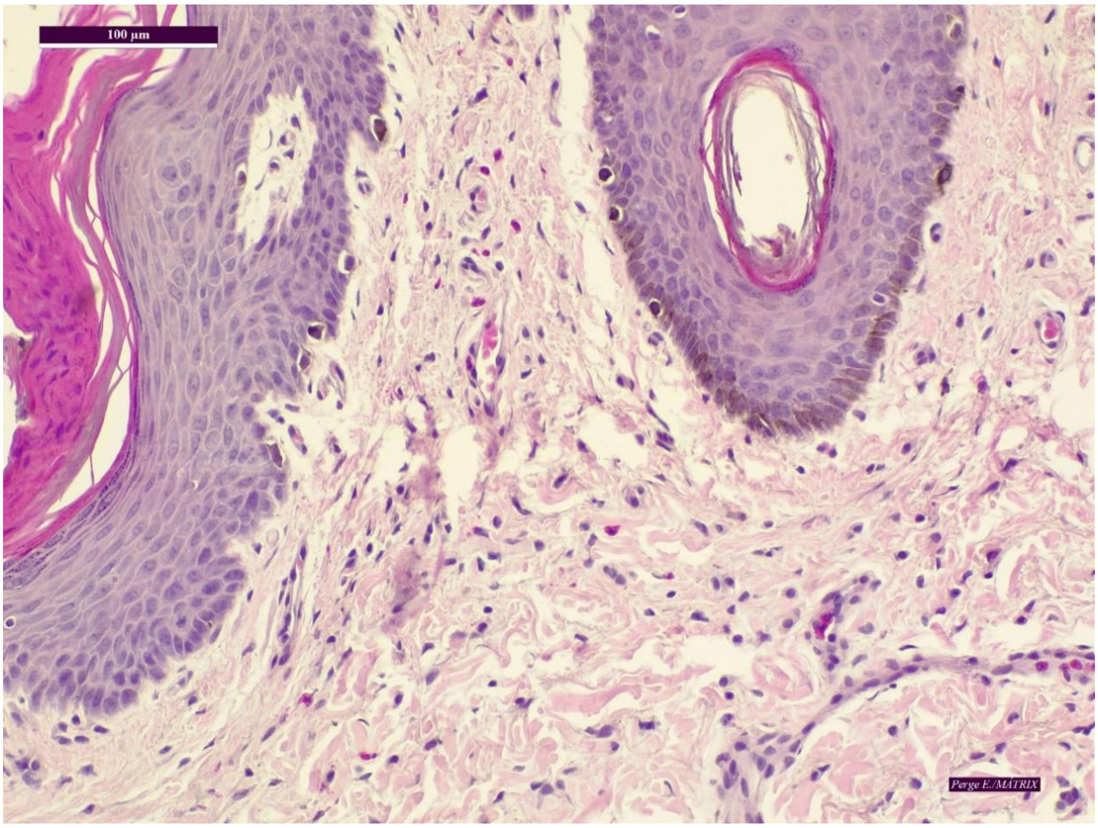

Figure 4. abnormal trichilemmal keratinization of the hair follicle. From Dr. Perge E, Matrix lab

Capybara 2

Some areas in the epidermis had mild parakeratotic hyperkeratosis, along with uneven hyperplasia and hyperpigmentation while pathogens were not detected on the surface [figure 5]. Mild to moderate mixed inflammatory cellular perivascular infiltration, with a large number of heterophil granulocytes, Lymphocytes, plasma cells and mast cells were visible in the dermis. Hair follicles were in the telogen phase, with hyperplastic and hyperpigmented epithelium. Abnormal tricholemmal keratinisation was seen in a few follicles, while mild fibrosis is detectable perifollicularly [figure 6]. Sebaceous glands are atrophic. Pathogens are not found in the dermis or follicles either.

It was diagnosed with chronic nonspecific hyperplastic dermatitis and chronic perifolliculitis and mild nonspecific atrophic dermatosis. Based on the histology and clinical data, stress dermatosis was highly suspected.

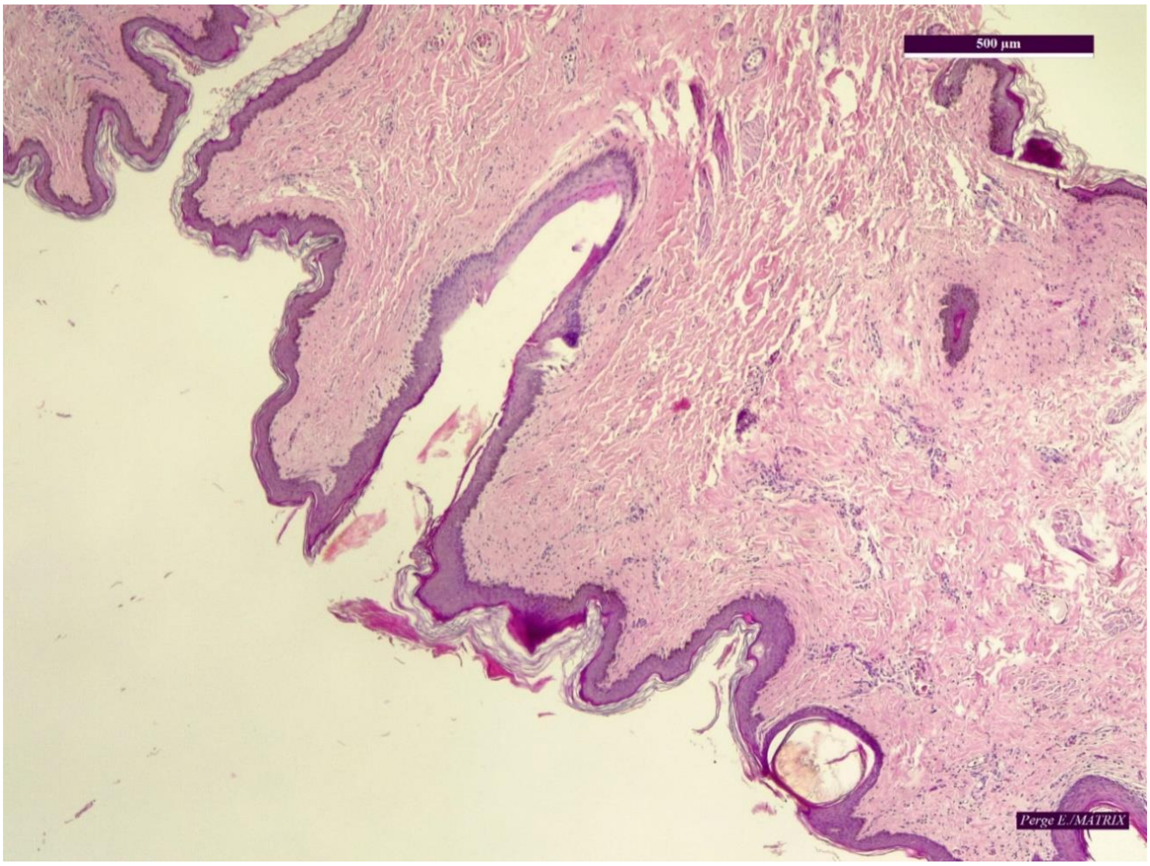

Figure 5. parakeratotic hyperkeratosis and hyperplasia in the epidermis. From Dr. Perge E, Matrix lab

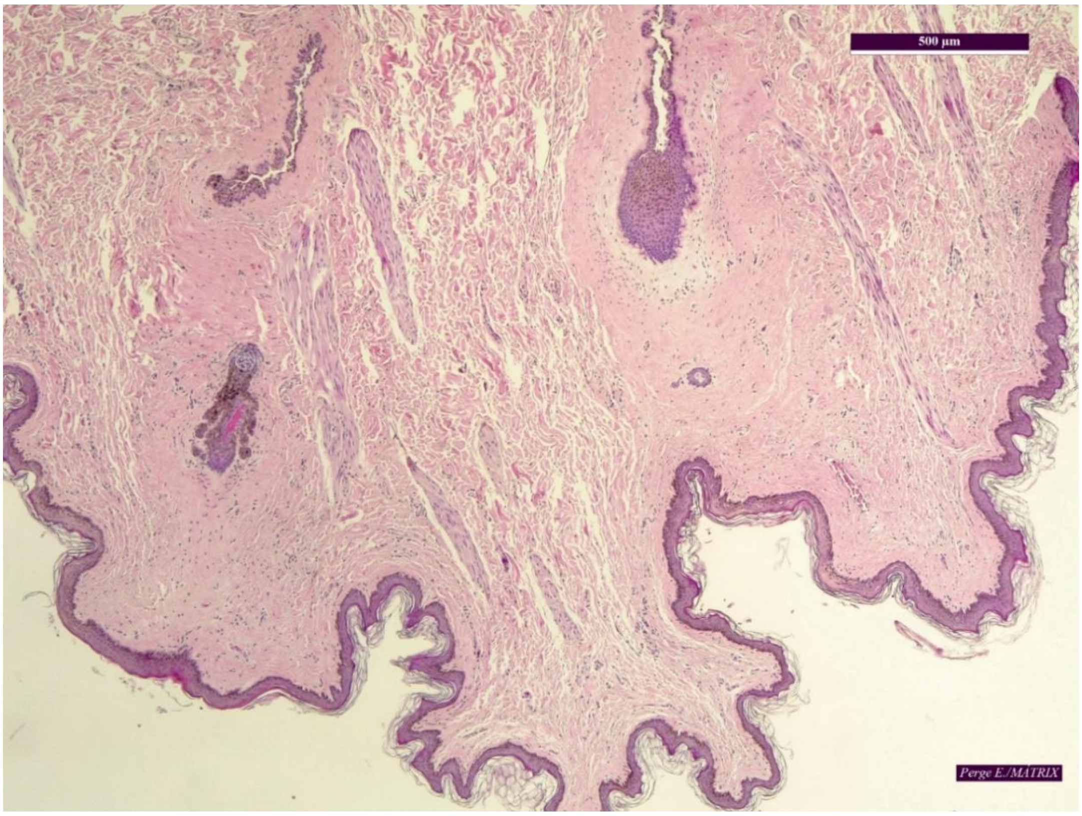

Figure 6. hair follicle with hyperpigmented and hyperplastic epithelium, mild fibrosis in the dermis.

From Dr. Perge E, Matrix lab

Muenster yellow-toothed cavy 1

Severe uneven hyperplasia with ulceration in small areas was visible in the epidermis, along with mild orthokeratotic hyperkeratosis and no pathogens were identified on the epithelial surface. Spongiosis was visible in the deeper part of the epidermis. At one edge of the sample, the proliferating superficial epithelium deeply extended towards the dermis but does not penetrate the basement membrane. A mitotic figure was detected in the cells of the basal layer (stratum basale). The nuclei were large, heterochromatic, and contain larger prominent nucleoli. One area also displays subepidermal vesicle formation. Apoptotic figures were also be seen in the basal layer. The dermis exhibited fibrosis along with diffuse interstitial infiltration of mixed inflammatory cells, including heterophil granulocytes, some mastocytes, lymphocytes and plasma cells. The follicles were in telogen phase and reveal hyperplastic epithelium and minimal hyperpigmentation.

The diagnosed chronic interface dermatitis with subepidermal vesicle formation suggested a suspected autoimmune dermatopathy (such as paraneoplastic pemphigus).

Muenster yellow-toothed cavy 2

In one skin area, severe purulent necrotic superficial dermatitis and folliculitis was circumscribed. Orthokeratotic hyperkeratosis, epidermal hyperplasia of variable severity, and a mild degree of eosinophilic cellular perivascular infiltration in the superficial dermis was also present. Mild multifocal superficial purulent dermatitis with scab formation and coccoid bacterial forms were in the other skin region. These findings suggest purulent necrotising dermatitis.

Muenster yellow-toothed cavy 3

Massive uneven hyperplasia, and uneven orthokeratotic hyperkeratosis were found in the epidermis. Few Acanthocytes may be seen in the middle layers. Slight spongiosis was evident in the basal layer (Stratum basale). Slight lymphocytic infiltration and signs of subepidermal vesicle formation were observed at the epidermal dermal boundary. The dermis was fibrotic in most of the sample, with mixed inflammatory cellular interstitial infiltration with large numbers of heterophilic and eosinophilic granulocytes. The few follicles seen were in catagen and telogen phases. The epithelium of the follicles was hyperplastic in the proximal part and slightly hyperpigmented. Substantial inflammatory infiltration was not seen at the follicular epithelial-dermis border, while the sebaceous glands were slightly atrophic.

Severe chronic allergic dermatitis was suggested with marked epidermal hyperplasia and dermal fibrosis. Since no pathogens are evident, the lesions found could be due to atopy, food allergy, or contact dermatitis.

Guinea pig

Lung and skin tissue samples were submitted. The tissue structure of the lung was preserved, in addition to the hyperaemia visible, atelectasis was seen in some smaller areas. Heterophilic granulocyte infiltration can be seen in widened alveolar septa along with some lymphocytes and macrophages. Smaller foci showed signs of anthracosis.

The skin epidermis had a slight uneven hyperplasia and larger areas of necrolysis and signs of parakeratosis. In one region of the dermis and subcutis, there was connective tissue proliferation under the intact epidermis, and scar tissue formation. A slit-like cavity is found at the base of the excision with the inner surface lacking epithelium, and colonies of coccus-shaped bacteria were found in the walls. Coccus bacterial colonies were also found in many places in the superficial dermis and in the follicles, without any inflammatory cellular reaction. In the subcutaneous connective tissue, the above-mentioned fissure-like cavity, segmental necrosis and mild mixed cell infiltration were present, including macrophages, lymphocytes and plasma cells. In the subcutaneous connective tissue veins, there was heterophilic granulocyte colonisation in some areas, and heterophilic cellular vasculitis was also observed.

Severe epidermal necrolysis, segmental necrotising panniculitis, and acute granulocytic vasculitis was diagnosed. Severe, mostly unreactive bacterial infection was seen. Acute interstitial pneumonia was also be observed. The skin lesions were suspected to be due to the so-called toxic epidermal necrolysis, possibly hepatocutaneous syndrome.

5. Discussion

Some of the skin problems detected in the zoo are not commonly found in literature of South American rodents. This could be due to the different set of challenges faced in varying environments in the wild or in captivity. Since some of the skin problems detected in the zoo is of environmental or food origin, keeping conditions are an important factor in the manifestation of skin diseases.

For instance, in the case of suspected stress dermatoses, after eliminating the possibility of infectious diseases as an etiological factor, we should perform further diagnostics. Measuring faecal cortisol metabolites or blood cortisol levels or using the novel leukocyte coping capacity (LCC) method [82] can be used to measure stress levels in specific rodents to further understand the relationship between stress and dermatological symptoms. The subsequent aim would be to reduce stress by implementing measures such as preventing overcrowding of animals in an exhibit and providing environmental enrichment to allow the animals to exhibit natural behaviour [83].

In case of the capybara with chronic allergic dermatitis, it would be difficult to determine and eliminate the specific environmental allergens that trigger the onset of dermatitis in individual animals. Inflammation and itching of the skin are common in this case which can decrease the integrity of their skin barrier, making them more susceptible to bacterial or fungal infections [84]. It is important in this case to eliminate other possible underlying causes of the mentioned clinical symptoms. Another cause of allergic dermatitis is food allergies. In companion animals, elimination diet is often used to help determine the food allergen [85]. However, it would be difficult to completely control the food intake for several weeks in an individual capybara, kept in a group setting in the zoo. In addition, there is no specific reliable test that confirms food allergies currently [85]. Glucocorticoids are often used to relieve the symptoms of allergic dermatitis in other animals; however, they have proven to cause adverse effects in long-term treatment, thus alternative anti-inflammatory and antipruritic therapies should be explored [86].

There are limited reports on autoimmune skin diseases in guinea pigs. Reports are mostly available on cats and dogs. Some examples include pemphigus complex, systemic lupus erythematosus, and bullous pemphigoid [87]. Controlling autoimmune disease requires immunosuppressive therapy like corticosteroids or cyclosporin. Secondary bacterial infections could be expected and should be treated accordingly [87].

Presence of bacteria in histological skin samples, especially those presenting purulent lesions warrants further microbiological testing to determine the bacterial species. Appropriate antibiotics should be administered to prevent further penetration of bacteria in the skin which can lead to abscesses and cellulitis in deeper wounds which is not uncommon in guinea pigs [13].

Hepatocutaneous syndrome is a rare chronic and often lethal disease in animals, mostly described in dogs. The skin symptoms are believed to be the result of metabolic disturbances caused by chronic liver disfunction [88]. The provided histological report gives evidence to the possible occurrence of this disorder in guinea pigs as well. Performing a liver biopsy could help determine the presence of the disease [88].

Generally, it is more difficult to control infectious disease spread between free-ranging wild animals as it requires large-scale planning and surveillance while considering several factors including geographical and ecological aspects [89]. Further attention should be directed towards devastating diseases that could potentially be carried by wild rodents such as the capybaras and coypus that live in close proximity to residential areas or farms. In the case of a serious disease outbreak in humans living in rural areas in Latin America, it is worth investigating the potential role of local wildlife in maintaining or transmitting diseases.

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