

# Ferret Dermatology



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## KEYWORDS

- Parasites • Neoplasia • Endocrine disease • Skin • Integument • Pruritus
- Alopecia • *Mustela putorius furo*

## KEY POINTS

- Alopecia in ferrets is common and frequently results from adrenal gland disease, hyperestrogenism, seasonal alopecia, fleas, and neoplastic conditions.
- Pruritus in ferrets does not only occur with infectious diseases but also can be associated with endocrine and neoplastic conditions, including hyperadrenocorticism, lymphoma, and mast cell tumors.
- Blue ferret syndrome is a condition in which the skin obtains a bluish tinge after clipping of the fur; it resolves within a few weeks without treatment.
- Zoonotic skin diseases in ferrets include sarcoptic mange (*Sarcoptes scabiei*), leishmaniasis, and dermatophytosis, whereas inhalation of blastomycotic spores is also possible during culturing.

## INTRODUCTION

Ferrets can present with a multitude of dermatologic conditions, which can either be the result of a primary skin disease or involve a secondary manifestation of a systemic disease. This review provides an overview of dermatologic conditions that can be seen in ferrets, including their diagnosis and management.

Among the dermatologic diseases most commonly seen in ferrets are ectoparasites, cutaneous tumors, and endocrine diseases. Owing to the possibility for underlying systemic diseases, the clinical workup of a ferret with dermatologic signs should consider the ferret's signalment (eg, age, gender, and reproductive status) and consist of a detailed history (regarding the skin condition, general health, lifestyle, preventive treatments, and health of other pets and members of the household) and a thorough physical and dermatologic examination. Specific tests can subsequently be used to diagnose or rule out primary skin disease. These tests may include bacterial and/or

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fungal cultures, skin scrapings, cytologic evaluation of fine-needle aspirates, and histopathology of skin biopsies. In addition, a complete blood cell count, serum biochemistry, hormonal panels, and imaging should be considered if an underlying systemic disease is suspected.

## FERRET SKIN AND COAT: ANATOMIC AND PHYSIOLOGIC CONSIDERATIONS

The body of the domestic ferret (*Mustela putorius furo*) is covered with thick dermis, especially on the neck and upper back because this is the area where bites are administered during play-fighting or mating.<sup>1,2</sup> Numerous sebaceous glands, which are under androgenic control and therefore most active during the breeding season (March to August in the northern hemisphere), give the ferret its characteristic musky odor, oily fur, and yellowish to reddish undercoat that is most noticeable in light-coated ferrets.<sup>1,3</sup> Furthermore, ferrets have 2 prominent scent glands located lateral to the anus, which produce a secretion when the ferret is frightened, excited, or in estrus. Because the odor will be unaffected by removal of these glands, routine anal saccullectomy (albeit performed by some breeding farms) is not recommended. Because ferrets only have eccrine sweat glands on the footpads, they are at increased risk for developing hyperthermia when exposed to high environmental temperatures.

Ferrets have long and coarse guard hairs in a variety of colors and patterns, from albino to black, depending on type.<sup>4</sup> A heavy shed in the spring reveals the shorter and darker summer coat.<sup>5</sup>

A bilaterally symmetrical, patchy, seasonal alopecia involving the tail and perineal area may be seen during the breeding season, particularly in intact females (jills).<sup>6</sup> Neutered individuals of both sexes display less dramatic molts.<sup>7</sup> Proper husbandry, including a high-quality diet of 30% to 35% animal protein and 15% to 20% fat, and avoiding excessive bathing, is important to prevent a dull, dry haircoat.<sup>8–10</sup>

Intact females are known to pull hair to use as bedding material, which may inadvertently be misdiagnosed as pruritic skin disease. Similarly, the typical bluish discoloration of the skin that can be seen during initial hair regrowth (eg, following hair clipping for surgery or treatment of hyperadrenocorticism) should not be mistaken for bruising or cyanosis (see section Blue Ferret Syndrome).

## PARASITIC DISEASES

### Fleas

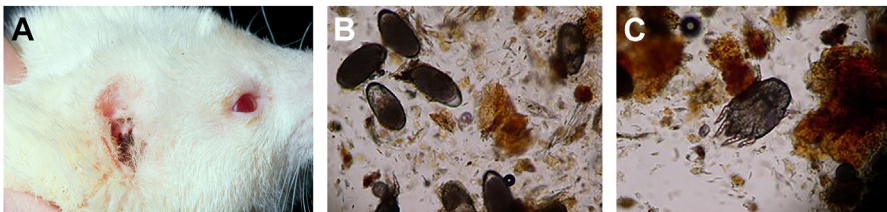
Flea infestation with *Ctenocephalides felis* or *Ctenocephalides canis* is a common problem in ferrets that are housed together with cats or dogs.<sup>11–13</sup> Infestations with other species, including *Pulex irritans*, *Paracaros meli*, *Ceratophyllus sciurorum*, and *Ceratophyllus vison*, in contrast, are rare.<sup>10,11</sup> Although asymptomatic infections occur, most ferrets show mild to moderate pruritus, resulting in self-induced alopecia and trauma with a papulocrustous dermatitis on the tail base, ventral abdomen, and inner thighs.<sup>1,11,13</sup> Flea-bite hypersensitivity has been reported in ferrets.<sup>14</sup> The diagnosis is based on history and clinical signs. In case no fleas or flea excrements are found on dermatologic examination, the diagnosis is usually made based on response to treatment.<sup>10</sup> Effective treatments include monthly treatments with selamectin spot-on treatment (6–18 mg/kg, or 15 mg/ferret), fipronil spray (0.2–0.4 mL of a 9.7% solution), or imidacloprid (10 mg/kg or 0.4 mL/ferret), alone or in combination with 1% moxidectin.<sup>11,15–17</sup> Environmental eradication of fleas and treatment of other susceptible animals in the household is important to prevent reinfection.<sup>18</sup>

### Ear mites: *Otodectes cynotis*

Ear mite (*Otodectes cynotis*) infections are common in ferrets. Transmission occurs via contaminated ear debris or direct contact with infected ferrets, dogs, or cats.<sup>19,20</sup> Otocariasis often leads to excess production of brown cerumen (Fig. 1A), which can be differentiated from normal ear wax by direct visualization of mites or eggs on otoscopy or microscopy (Fig. 1B,C).<sup>10,14,21</sup> Animals are mostly asymptomatic,<sup>21,22</sup> but may show head shaking, pruritus, self-induced alopecia, periaural crusting, excoriations, and aural hematomas as a result of scratching.<sup>23,24</sup> With heavy infestations, secondary bacterial or yeast infections may occur, and neurological deficits can develop in sequela to otitis media or interna.<sup>25,26</sup> Rarely, mites are found in alternative locations, for example, the perineum, in which case the diagnosis is made by microscopic examination via a skin scrape.<sup>14</sup> Treatment comprises flushing and cleaning of the ear canal followed by topical treatment using selamectin (15–45 mg/ferret every 28 days) or imidacloprid 10%/moxidectin 1.0% 2 to 3 times every 14 days.<sup>21,24,27,28</sup> Subcutaneous ivermectin (0.4 mg/kg every 14 days) can also be used, but it is less effective than intrauricular ivermectin (0.4 mg/kg, diluted 1:10 in propylene glycol every 14 days), which can be used provided that the tympanic membrane is intact. Ivermectin should be avoided in pregnant jills due to its teratogenicity.<sup>23,24</sup> As an alternative, 1 drop of fipronil can be administered in each ear canal.<sup>24,29</sup> Secondary infections may warrant additional use of antifungals and/or antibiotics. Treatment of in-contact ferrets, dogs, and cats, and the environment, is important to avoid reinfection.<sup>14,23</sup>

### *Sarcoptes mange*

*Sarcoptes scabiei* is a burrowing mite that infects dogs, cats, and ferrets by direct or indirect contact.<sup>26,30–32</sup> Outdoor ferrets are at higher risk for infection with *S. scabiei* because wild members of the canine family are potential sources of infection.<sup>33</sup> Two clinical forms exist in ferrets, that is, the pedal and generalized forms (Fig. 2).<sup>31</sup> The pedal form is characterized by alopecic and swollen feet, formation of dark brown scabs, and eventually sloughing of the claws,<sup>33,34</sup> and may progress into the generalized form characterized by intense pruritus and alopecia of the face, pinnae, and ventrum.<sup>33</sup> Severely affected ferrets can become lethargic and eventually die.<sup>34</sup> Because the number of mites present is relatively small, the diagnosis can be difficult, with a high risk of false-negative results.<sup>26,31</sup> Multiple superficial skin scrapes are indicated to increase the chance of detecting the mites, larvae, ova, and nymphs, although mites will occasionally be found upon examination of scabs that are broken into smaller pieces and treated with 10% potassium hydroxide.<sup>14,33</sup> Ivermectin (0.2 to 0.4 mg/kg subcutaneously every 7 to 14 days) use combined with treatment of in-contact animals, and environmental cleaning every 3 to 4 days, until eradication of the mites, is



**Fig. 1.** (A) In ferrets with an *O cynotis* infection excessive brown/black debris may be seen in the ear canal. (B, C) *O cynotis* eggs (B) and an adult mite (C) from a ferret. (Reprinted from: Powers, L. V. (2009). Bacterial and parasitic diseases of ferrets. *Veterinary Clinics: Exotic Animal Practice*, 12(3), 531-561. With permission.)



**Fig. 2.** *S. scabiei* infection in a ferret, pedal form. (Reprinted from: Chapter 10 - Parasitic diseases of ferrets, Editor(s): John H. Lewington, Ferret Husbandry, Medicine and Surgery (Second Edition), W.B. Saunders, 2007, Pages 224-257, ISBN 9780702028274, <https://doi.org/10.1016/B978-0-7020-2827-4.50016-4>.)

recommended.<sup>14,26,31</sup> Ferrets with the pedal form may benefit from warm-water soaks and trimming of affected claws, alongside treatment of secondary bacterial infections.<sup>26,31</sup> To prevent reinfection, materials that cannot be thoroughly disinfected (eg, wooden toys, sleeping huts) should be removed and discarded.<sup>34</sup> Because *S. scabiei* has zoonotic potential, in-contact humans should wear gloves and be carefully monitored.<sup>14,31,35</sup>

### **Demodicosis**

Clinical demodicosis is uncommon in ferrets, and mostly limited to immunocompromised individuals.<sup>14,23,36–40</sup> Infections with both the larger, slender-bodied *Demodex canis* and shorter *Demodex criceti* have been reported.<sup>38,41,42</sup> Symptomatic ferrets may display no to mild pruritus, alopecia, erythematous and thickened skin, small follicular papules, and yellow-brown seborrhea with seborrheic scales (Fig. 3).<sup>23,38,39</sup> Some animals may have brown debris in the external ear canal, similar to the exudate seen in ear mite infestations.<sup>39</sup> Diagnosis is made by identification of the mites on skin scrape from affected areas or analysis of aural exudate.<sup>23,39,40</sup> Treatment options include ivermectin (0.05–0.3 mg/kg every 24 hours orally), imidacloprid 10%/moxidectin 1% spot-on treatment once monthly, and amitraz 0.0125% once weekly.<sup>26,38,40</sup> Because demodicosis can be hard to treat, with relapses frequently occurring, treatment is continued for weeks after negative skin scrapes are found.

### **Fur mites**

Ulcerative facial lesions caused by the fur mite *Lynxacarus mustelae* have been reported in kits<sup>40</sup> (Fig. 4A,B). Topical treatment with permethrin powder and cleaning of the environment successfully resolved the facial lesions that were noted in these animals.<sup>14</sup>



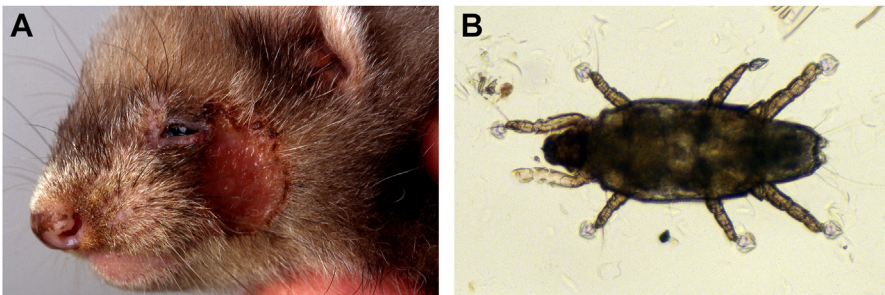
**Fig. 3.** Peribuccal and periocular alopecia, erythema, and skin thickening in a ferret. *Demodex* sp were found in skin scrapings from these areas. (Reprint from: Beaufre, H., Neta, M., Smith, D. A., & Taylor, W. M. (2009). Demodectic mange associated with lymphoma in a ferret. *Journal of exotic pet medicine*, 18(1), 57-61. With permission.)

### Ticks

Tick infestation is primarily a concern in ferrets exposed to outdoor environments. Generally, it results in erythema and inflammation of the site of the bite, but heavy infestations can lead to anemia.<sup>26,31,43</sup> Most infestations involve *Ixodes ricinus* (the castor bean tick); however, other tick species have been described in ferrets depending on geographic location.<sup>14,31</sup> Transmission of pathogens has not yet been documented in ferrets, but ticks can serve as vectors for *Babesia* spp, *Leishmania* spp, and other pathogens, hence posing a risk to both the ferret and in-contact humans.<sup>14,31,34,44</sup> Upon identifying a tick during the clinical examination, the tick should be manually removed, including head and mouth parts.<sup>31</sup> In addition, treatment with a tick preventative such as selamectin, fipronil, and ivermectin should be initiated.<sup>18,26,31</sup> Anemia, if present, will resolve with the removal of ticks.<sup>43</sup>

### Cutaneous myiasis

Cutaneous myiasis is uncommon in ferrets and occurs mostly in ferrets exposed to flies and bot flies under warm and humid conditions.<sup>10,26</sup> Cutaneous myiasis can present as migratory, furuncular, or wound myiasis, depending on the infesting fly species.<sup>14,43</sup> *Hypoderma bovis* causes migratory myiasis, which may be associated with intense pruritus.



**Fig. 4.** (A) In this ferret kit and its 4 siblings ulcerative lesions were seen on the left cheeks. The jill had licked these cheeks excessively. Skin scrapings revealed that the primary cause of these lesions was the fur mite *Lynxacarus mustelae*. (B) *L mustelae*.



Typically, the infestation leads to granulomatous masses and sinuses in the cervical region, which results from the larvae burrowing through the skin into the lower layers of the dermis.<sup>26</sup>

Furuncular myiasis is the most commonly reported type of myiasis, caused by the bot fly (*Cuterebra* spp) larvae. After the egg is laid on the skin, the developing larva buries into the skin, while leaving a hole for respiration.<sup>43</sup> Typically, the larvae pupate in the ventral cervical, axillary, and inguinal regions or over the back.<sup>10,26</sup> On clinical examination, one or multiple 1- to 3-mm-diameter localized swellings can be found.<sup>10,26,43</sup> Upon inspecting the respiration hole, the larva can be visualized.

Wound-related myiasis, or fly strike, is caused by flesh fly larvae of *Wohlfahrtia vigil*, and primarily is a risk in young kits housed outdoor in warm and humid weather.<sup>26</sup> Following deposition of the eggs in an open wound, the larvae feed on the surrounding tissue, which—depending on the duration and severity—can lead to massive tissue destruction, secondary infections, and death.<sup>43</sup>

Following diagnosis, larvae need to be manually or surgically removed in toto. Extraction should be done gently, because remaining pieces of larvae might result in anaphylaxis.<sup>10,34</sup> Analgesia and sedation can be provided as needed. In addition, debridement of necrotic tissue should take place, followed by flushing of the wound or cavity with diluted chlorhexidine. In case of furuncular or migratory myiasis, the cavity can either be closed with tissue glue or left open to heal by secondary intention, while continuing daily wound care.<sup>43</sup> Antibiotics can be used, if indicated.<sup>10</sup>

Regardless of the type of myiasis, owners should be counseled on fly control and preventative measures to decrease the risk of reoccurrence.<sup>43</sup>

### ***Leishmaniasis***

Leishmaniasis is a potentially zoonotic, vector-borne disease caused by the protozoan organism *Leishmania infantum*, which is transferred through infected female phlebotomine sandflies (*Phlebotomus perniciosus* and *Phlebotomus ariasi*).<sup>45,46</sup> This disease is primarily found in Southern Europe, and mostly infects domestic dogs, although it has been described in cats, rabbits, and ferrets as well, particularly in individuals that are immunosuppressed or housed outdoors.<sup>46–48</sup> Cutaneous leishmaniasis in ferrets manifests as inflammatory, erythematous, papular, nonpruritic lesions, with potential local lymph node enlargement and splenomegaly.<sup>46,47</sup> Leishmaniasis can be diagnosed through identification of amastigotes in infected macrophages and multinucleate giant cells on cytologic, histopathologic, or immunohistochemical examination of samples collected from the dermal lesions.<sup>46,49</sup> Polymerase chain reaction (PCR), western blot, or enzyme-linked immunosorbent assay for specific serum IgG antibodies can also be used for confirmation of the diagnosis.<sup>46,47</sup> Treatment has largely been extrapolated from dogs and cats and includes the use of miltefosine and meglumine antimoniate in combination with allopurinol, which has led to good long-term results, as indicated by resolution of clinical signs and decreased antibody titers.<sup>47,49</sup> Monitoring for xanthinuria is recommended upon initiating treatment with allopurinol.<sup>49</sup> Preventive measures consist of the (off-label) use of repellents with activity against sand flies (because the use of sand fly repellents in ferrets is off-label, close monitoring for side effects is warranted), and keeping the ferret inside at times when sand flies are active.<sup>48</sup>

### **VIRAL DISEASES (CANINE DISTEMPER VIRUS)**

Canine distemper virus (CDV) typically infects members of the canine family and causes fatal disease within 5 to 35 days following development of clinical signs, regardless of strain.<sup>48</sup> Ferrets can be infected through aerosols, fomites, or direct

contact with infected animals.<sup>31,50,51</sup> After viral exposure, the infection is spread hematogenously, with clinical signs developing after 7 to 10 days, although incubation periods of up to 56 days have been reported.<sup>52,53</sup> Initial signs include lethargy, photophobia, and hyporexia. In addition, brown facial crusts due to accumulation of nasal and ocular secretions (Fig. 5A,B) and secondary bacterial pneumonia leading to dyspnea can be seen upon infection of the upper and lower respiratory tract.<sup>54</sup> Dermatologic changes characteristic for CDV infections include pruritic rashes on the chin and inguinal region, and swelling and hyperkeratosis of the footpads.<sup>31,50,54</sup> In rare cases, superficial pyoderma can progress into generalized desquamation.<sup>54</sup> Neurologic signs commonly develop in the terminal stages of the disease. Antemortem diagnosis of CDV in ferrets involves antigen detection in samples from conjunctival, tonsillar, or respiratory secretions using fluorescent antibody labeling or PCR. In addition, CDV antigens or inclusion bodies can be identified on postmortem immunohistochemistry or histopathology of affected tissues, including the tonsils, lymph nodes, urinary bladder, lung tissue, stomach, and spleen.<sup>52,54,55</sup> Humane euthanasia is usually recommended, although successful treatment has been reported in rare cases that were infected with a low-virulent strain and that were treated promptly using intense supportive care, vitamin A, and hyperimmune serum.<sup>52,54,56</sup> In case of an outbreak of CDV, healthy ferrets should be isolated and vaccinated, and the environment thoroughly disinfected.<sup>52</sup> Availability of CDV vaccines licensed for ferrets vary from country to country, and for some countries, a canine vaccine might be the only available option.<sup>53</sup> If using vaccines intended for dogs, advice from the manufacturer should be sought on the use in ferrets, because myofasciitis is a reported risk following vaccination.<sup>57</sup>

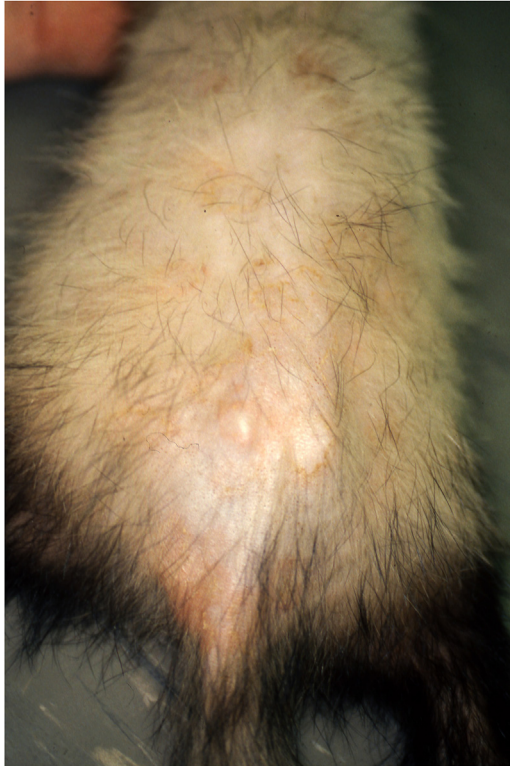
## FUNGAL DISEASE

### *Dermatophytosis (Ringworm)*

Dermatophytosis in ferrets is caused by *Trichophyton mentagrophytes* or *Microsporum canis*, and—in rare cases—*Microsporum nanum*.<sup>1,10,23</sup> Although often mentioned in books and reviews, dermatophytosis is relatively uncommon in healthy ferrets, and occurs most often in young or immunosuppressed individuals exposed to infected cats.<sup>10,35,58,59</sup> Upon infection of the hair shafts and stratum corneum, an annular nonpruritic alopecia develops that spreads peripherally<sup>23,31,35</sup> (Fig. 6). With severe infections, a generalized alopecia with diffuse scaling, erythema, and crusting



**Fig. 5.** Canine distemper virus infection in a ferret with hyperkeratosis and crusting of foot pads (A) and severe crusting dermatitis on the face (B). (Photograph courtesy Dr. David Perpiñán.)



**Fig. 6.** This 9-month-old male ferret displays annular alopecic lesions that proved to be due to a *M canis* infection upon culture.

can develop.<sup>23</sup> Rarely, dermatophytosis spreads into the dermis and subcutaneous adipose tissue creating nodules with potential ulceration and granular discharge, referred to as dermatophytic pseudomycetomas (**Fig. 7**).<sup>60</sup> Dermatophytosis should be considered in the differential diagnosis for any animal housed with other animals



**Fig. 7.** Dermatophytic pseudomycetoma in a ferret. On rare occasions, these ulcerated, granular discharge-producing nodules can develop following spread of the fungal infection into the dermis and subcutaneous adipose tissue. (Photo courtesy of Seth Oster and Amelia White.)



or humans in the household that have similar annular skin lesions. Although being potentially zoonotic, spread from ferrets to humans has thus far not been documented.<sup>10,59,61</sup> Diagnosis is usually made by culture. On dermatophyte test media, fungal growth will appear approximately 2 to 4 weeks after culture of hair or skin scrapes from the periphery of the lesions.<sup>62</sup> If positive, identifying the fungus involved is recommended. Other options to diagnose dermatophytosis include identification of fungal hyphae or arthrospores on microscopy of hair or scales prepared in 10% potassium hydroxide,<sup>26</sup> and PCR of skin or hair samples. Similar to other animals, use of a Wood's lamp carries a high risk of false-positive and false-negative results depending on the dermatophyte species.<sup>23</sup> However, up to 100% of *M canis* demonstrates fluorescence.<sup>63</sup> Treatment includes clipping of the affected hair, using broad margins around all lesions, and the use of keratolytic shampoo.<sup>18</sup> Topical antifungals usually suffice and include enilconazole, clotrimazole, or miconazole cream every 12 hours, or weekly lime sulfur dips.<sup>10,23</sup> As systemic treatment, griseofulvin (25 mg/kg by mouth every 24 hours), itraconazole (5–10 mg/kg every 24 hours by mouth), or fluconazole (10 mg/kg every 12 hours by mouth) can be used.<sup>31,61,63</sup> Treatment should be continued for 2 to 4 weeks after resolution of dermal signs, or, preferably, until 2 consecutive fungal cultures with a negative outcome. Treatment of infected in-contact animals and environmental disinfection should also be initiated to minimize the risk of reoccurrence.<sup>10,23,26,63</sup> In addition, monitoring for signs of liver damage and bone marrow suppression is advised for animals treated with griseofulvin or itraconazole. Although most dermatophytosis cases respond favorably to treatment, dermatophytic pseudomycetomas can be difficult to treat, and carry a high risk of progressive disease leading to euthanasia or death.<sup>61</sup>

### **Fungal ear infections**

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Fungal otitis externa caused by malasseziosis (*Malassezia* spp) or mucormycosis (*Absidia corymbifera*) has been documented secondary to *O cynotis* in ferrets, most often transmitted from in-contact cats.<sup>26,63</sup> Although ear mite infections in ferrets are usually nonpruritic, concurrent fungal infections can result in intense pruritus. Malasseziosis commonly leads to generalized multifocal pustular dermatitis with hyperkeratosis and alopecia, although mucormycosis potentially spreads from the external ear canal, through the middle ear, to the inner ear, where it causes granulomatous meningoencephalitis and associated central nervous signs.<sup>64,65</sup> Fungal hyphae are identifiable on cytology of ear samples or skin histopathology.<sup>65</sup> Treatment consists of antifungal therapy combined with eradication of ear mites.<sup>23,26,64</sup>

### **Cryptococcosis**

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Systemic mycosis caused by *Cryptococcus* organisms (*Cryptococcus bacillisporus*, previously *Cryptococcus neoformans* varians *gattii*, or *Cryptococcus neoformans* varians *grubii*) are rare in mammals, including ferrets.<sup>66–70</sup> Ferrets are infected through inhalation of spores from contaminated environments. Plants like *Eucalyptus* spp are associated with an increased risk of spore formation.<sup>66,71–73</sup> Spore inhalation causes rhinitis and pneumonia, followed by lymphatic and hematogenous spread leading to meningoencephalitis, abscessation of the draining lymph nodes, and fungal nodules on internal organs.<sup>66,67</sup> Dermal presentation of cryptococcosis might be more common in ferrets than in other species, and presents as an erythematous, scaly, pruritic rash of the nasal bridge and cutaneous masses.<sup>66,74</sup> Identification of fungal hyphae on impression smears of cutaneous lesions, or fungal growth of aspirates from masses and abscessed lymph nodes, can be used to confirm the diagnosis.<sup>66,73</sup> Other diagnostic options include histopathology with immunohistochemistry or

serology.<sup>66–69,75</sup> Surgical excision of localized masses combined with systemic antifungal therapy (itraconazole or fluconazole) carries a good prognosis.<sup>66</sup> However, in late stages of systemic fungal disease or meningitis, prognosis is generally poor.<sup>63</sup>

### **Blastomycosis**

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Blastomycosis can occur in immunosuppressed ferrets and is caused by inhalation of *Blastomyces dermatitidis* spores from sandy, acidic soil near water, especially in Eastern North America.<sup>63</sup> Interindividual transmission has not been reported, and there are no published reports documenting direct transmission from ferrets to humans.<sup>73</sup> Blastomycosis can present as systemic neurologic and pulmonary disease, or as ulcerative, nonhealing lesions on the skin and footpads.<sup>76,77</sup> Agar gel immunodiffusion assay, cytology, or histopathology can be used for diagnostic purposes.<sup>76,77</sup> Cultures should only take place in a professional laboratory to eliminate the zoonotic risk of infective blastomycosis spores.<sup>63</sup> Prognosis depends on the extent of infection at the time of diagnosis.<sup>77</sup> Amphotericin B (0.7–25 mg/kg intravenously, administered in smaller doses) can be used in cases nonresponsive to itraconazole,<sup>63,73</sup> whereas fluconazole or voriconazole can be effective in case of neurologic spread.<sup>76</sup> Although glucocorticosteroids can be used for anti-inflammatory purposes, mixed results and potential for further immunosuppression render their use controversial.<sup>76</sup>

### **Histoplasmosis**

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Histoplasmosis (*Histoplasma capsulatum*) is a rare cause of systemic mycosis in ferrets, with one case reporting formation of subcutaneous nodules.<sup>73,78</sup>

### **Systemic candidiasis**

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Systemic candidiasis caused by *Candida parapsilosis* has been diagnosed postmortem in a ferret with necrotizing encephalitis, lymphadenitis, and ulcerative and perivascular dermatitis.<sup>79</sup>

## **BACTERIAL INFECTIONS**

Pyoderma and deeper skin infections in ferrets can be caused by a wide range of bacteria, most frequently *Staphylococcus aureus* or *Streptococcus* spp.<sup>31,43,80</sup> Dermal wounds created during mating or pruritus-related, self-inflicted trauma can cause bacteria to penetrate into the skin, creating abscesses.<sup>43,81</sup> Cervical abscesses, known as lumpy jaw, are commonly associated with *Actinomyces* spp. Diagnosis and treatment of abscesses are similar to other species, with penicillin or tetracycline being the treatment of choice for *Actinomyces* organisms.<sup>23,81</sup> Nontuberculous mycobacteria, notably *Mycobacterium avium* subspecies *avium*, have been cultured from a ferret with alopecia, bruises, scabs, and numerous skin nodules<sup>82</sup> (Fig. 8).

## **TUMORS AFFECTING THE INTEGUMENT**

Neoplasia are commonly diagnosed in older ferrets, and approximately 20% of these affect the skin and/or subcutaneous tissue.<sup>83–85</sup> Most cutaneous tumors in ferrets are benign, with mast cell tumors and sebaceous tumors being the most frequent tumor types, each accounting for a third of the integumentary neoplasms encountered in ferrets.<sup>86–93</sup> Multiple tumor types can be found simultaneously in the same individual.<sup>84,94,95</sup> Diagnosis is made by cytology of fine-needle aspirates, or histopathology and immunohistochemistry of skin biopsies or surgically excised tumors. Staging should be performed as in other species, and treatment fine-tuned based on tumor



**Fig. 8.** Edema of the eyelids and nictitating membrane in a ferret with mycobacteriosis. (Reprinted from: Mentré, V., & Bulliot, C. (2015). A retrospective study of 17 cases of mycobacteriosis in domestic ferrets (*Mustela putorius furo*) between 2005 and 2013. *Journal of exotic pet medicine*, 24(3), 340-349. With permission.)

type (epithelial, mesenchymal, or round cell) and stage.<sup>26,31</sup> **Table 1** provides an overview of the type of integumentary tumors reported in ferrets.

## ENDOCRINE DISEASES

### **Adrenal Gland Disease (Hyperadrenocorticism)**

Steroid-producing tumors of the adrenal cortex occur in up to 70% of neutered middle-aged ferrets, most often at 3.5 years after neutering.<sup>106,107</sup> Prolonged exposure to daylight, as well as chronic stimulation of the adrenal gland cortex by the pituitary gland after neutering are suggested as predisposing factors.<sup>108</sup> Nodular hyperplasia, adenomas, and adenocarcinomas account for 56%, 16%, and 26% of adrenocortical tumors in ferrets, respectively.<sup>106,108</sup> Tumors are unilateral in 84% of cases, with the left adrenal gland most commonly affected.<sup>109</sup> In half of the patients with bilateral hyperadrenocorticism 2 tumor types are present.<sup>109</sup> Clinical signs result from hyperandrogenism, and include bilateral, symmetric alopecia (**Fig. 15**), thinning of the skin, vulvar enlargement, return of hormonal behavior, and urethral obstruction due to prostatic cysts or prostatitis in male ferrets.<sup>108–110</sup> Tumors are best visualized using abdominal ultrasonography, in which one or both adrenals can appear enlarged, rounded, heterogeneous, or hyperechoic.<sup>110,111</sup> Alternatively, contrast-enhanced computed tomography can be used. Blood panels may reveal elevated levels of sex steroids, for example, estradiol and androstenedione.<sup>112,113</sup> However, panels are not reliable for differentiating between hyperandrogenism, intact animals, and those with remnant ovarian tissue or granulosa cell tumors, and are mostly recommended for monitoring of response to treatment and signs of relapse.<sup>111</sup> Medical treatment is preferred to surgical treatment because it results in a longer disease-free period (16.5 months vs 13.6 months) and lower complication rate and is less invasive.<sup>111,114</sup> Long-acting, deslorelin acetate-containing implants usually result in resolution of dermatologic and behavioral changes within 2 weeks, and hair regrowth appears within 6 weeks postimplantation. Alternatively, leuprolide acetate depot injections (100 µg/kg subcutaneously) can be given every 3 to 4 weeks, and have been proved to be effective for 3 to 4 months.<sup>115,116</sup> Adrenalectomy, although leading to complete remission of clinical signs and identification of the tumor type involved through histopathology, is markedly more invasive, especially in case of right-sided

**Table 1**  
Overview of integumentary tumors reported in ferrets

Tumor Type	Origin	Prevalence	Location	Morphologic Appearance	Malignancy Grade	Treatment	Prognosis
Sebaceous or basal cell tumor <b>Fig. 9</b>	Epithelial	Common; one-third of integumentary neoplasia. Average age 5.2 years; no known sex predilection	Head and neck region, although tumors may also occur on flanks, limbs, or tail	Large, warty, exophytic to pedunculated masses; ulceration can occur due to self-inflicted trauma <sup>92,96</sup>	Benign and slow-growing, despite grossly and histologically aggressive appearance <sup>97,96,97</sup>	Surgical excision	Good, although can develop into squamous cell carcinoma (rare) <sup>96</sup>
Apocrine scent gland (cyst) (adeno) carcinoma <b>Fig. 10</b>	Epithelial	Common; approximately 75% of apocrine scent gland tumors are malignant; adenomas can also occur but less frequently	Head, neck, genital areas (vulva, prepuce)	Large, firm mass, sometimes fluid-filled; should be differentiated from benign apocrine cysts <sup>93</sup>	Malignant with aggressive infiltration of adjacent tissues and high metastatic potential to regional lymph nodes and lungs <sup>96,98</sup>	Surgical excision with wide margins of at least 1 cm, which often necessitates partial to complete preputial and/or penile amputation, and use of flaps or Y-plasty to close or reconstruct the prepuce; additional radiation therapy and chemotherapy should be considered to reduce risk of metastases and eliminate local residual malignant cells	Often poor due to local infiltration; prognosis may improve upon use of radiation therapy and chemotherapy <sup>96,97</sup>
Mammary tumor (adenoma/adenocarcinoma)	Epithelial	Uncommon; seen in older males (6–7 years) and younger females (2–5 years)	Mammary gland	Smaller or larger nodule in the mammary tissue, which can become ulcerated	Usually benign (30% of mammary tumors are malignant)	Surgical excision	Generally good prognosis, with surgery being curative; adenocarcinomas have potential for recurrence, especially if surgical margins are insufficient
Squamous cell carcinoma	Epithelial	Rare	Often arise from the lining of the anal sac, but can also be seen on lip, gingiva, or feet	Firm, ulcerated mass, <sup>18</sup> or multiple pigmented, proliferative skin lesions (papillomavirus associated) <sup>96,99</sup>	Malignant	Surgical excision; chemotherapy usually not effective	Guarded; local recurrence is common <sup>18</sup>

<p><b>Mast cell tumor</b> <b>Fig. 11</b></p>	<p>Round cell tumor</p>	<p>Common in older (4.5–5 years) male ferrets; account for one-third of integumentary neoplasia<sup>92,97</sup></p>	<p>Face, ear, tail, limb, flank; in 30% of animals, multiple tumors are present</p>	<p>Discrete, flat, round, plaque-like, crusted, and often pruritic<sup>94</sup></p>	<p>Benign; easily recognized on cytology (non-Wright stain) by their characteristic granules<sup>94</sup></p> <p>Surgical excision</p> <p>Good due to low metastatic potential<sup>92,94</sup></p>
<p><b>Lymphoma</b> <b>Fig. 12</b></p>	<p>Round cell tumor</p>	<p>Cutaneous form is less common than other (multicentric, gastrointestinal, mediastinal, extranodal) types<sup>105</sup>; appears more common in middle-aged ferrets with possible female predilection</p>	<p>Often involving the feet but also reported to involve inguinal, anal, and/or periorcular tissues</p>	<p>Focal dermal or subcutaneous masses, or more generalized, chronic dermatitis with rashlike or ulcerated appearance, alopecia, and pruritus with self-trauma (epitheliotropic lymphoma)</p>	<p>Highly malignant, usually T-cell type on immunohistochemistry</p> <p>Chemotherapy as for other lymphomas. Palliative treatment with steroids may slow the course of disease.</p> <p>Epitheliotropic lymphoma (1% of lymphomas) responds poorly to corticosteroids, but may benefit from isotretinoin</p> <p>Often poor prognosis due to late diagnosis, even with chemotherapy<sup>96,106</sup>; may develop into multicentric lymphoma, leading to clinical deterioration and euthanasia<sup>102</sup></p>
<p><b>Hemangioma/hemangiosarcoma</b> <b>Fig. 13</b></p>	<p>Mesenchymal</p>	<p>Relatively uncommon</p>	<p>Often on head, neck, limb, and feet<sup>97</sup></p>	<p>Small, round, red or black masses that are well vascularized and bleed easily, if traumatized<sup>97</sup></p>	<p>Usually benign</p> <p>Surgical excision</p> <p>Good for hemangioma, but hemangiosarcomas are highly aggressive and have a high recurrence rate<sup>97</sup></p>
<p><b>Leiomyoma/leiomyosarcoma</b></p>	<p>Mesenchymal, arising from smooth muscles (arrector pili muscle)</p>	<p>Uncommon; malignant form most common in male, middle-aged ferrets<sup>97</sup></p>	<p>Head and back (dorsal midline)<sup>91,102</sup></p>	<p>Raised, pink, ulcerated nodules or painful, multiple, raised, parallel, cordlike structures in the skin<sup>97,102</sup></p>	<p>Both benign and malignant forms can occur</p> <p>Surgical excision</p> <p>Malignant form carries high risk for recurrence after surgical removal<sup>101,103</sup></p>
<p><b>Fibroma/fibrosarcoma</b></p>	<p>Mesenchymal</p>	<p>Uncommon; associated with vaccinations<sup>104</sup></p>	<p>Dorsum and flanks (injection sites)</p>	<p>Subcutaneous, round mass</p>	<p>Generally benign, low-grade malignancies with a slow growth rate and low metastatic potential (unlike cats)</p> <p>Surgical excision with wide margins<sup>8,6,104</sup></p> <p>Usually favorable</p>
<p><b>Chordoma</b> <b>Fig. 14</b></p>	<p>Mesenchymal, skeletal tissue</p>	<p>Uncommon</p>	<p>Usually on the tail (tip), but may develop in a vertebrae in any region of the spinal column</p>	<p>Irregular gray, firm, whitish gray, firm, clublike swelling</p>	<p>Tail tip chordomas are often easily cured by tail amputation</p> <p>Generally good for tumors on the tail tip, but poor when other parts of spinal column are involved due to the infiltrative nature of the tumor</p>





**Fig. 9.** In this 5-year-old female ferret with alopecia due to an adrenal tumor, multiple wartlike lesions were seen. Histology revealed these tumors to be sebaceous epithelioma. Although they appear aggressive, and thereby malignant, these tumors are considered to be benign.

hyperadrenocorticism.<sup>106,110,111</sup> For bilateral tumors, adrenalectomy of the largest gland combined with subtotal adrenalectomy of the contralateral gland is recommended to avoid induction of Addisonian disease (and associated treatment) postoperatively.<sup>109</sup>

### **Hyperestrogenism**

Hyperestrogenism can be seen in up to 50% of ovulating unmated jills as a result of persistent estrus, but is occasionally seen in ferrets with ovarian remnants, cystic ovarian disease, ovarian neoplasia (granulosa cell tumors or thecomas), or hyperadrenocorticism.<sup>111,117,118</sup> In the long term, hyperestrogenism causes bone marrow suppression, pancytopenia, and nonregenerative anemia.<sup>115</sup> Jills with hyperestrogenism present with alopecia over the tail base, vulvar swelling, and symptoms related to pancytopenia, including pale mucous membranes, petechia and/or ecchymoses, infections, weakness, systolic murmurs, and posterior paresis.<sup>115,119</sup> Diagnosis is based on history, clinical signs, identification of adrenal or ovarian changes on ultrasonography, and response to treatment. Elevated serum estradiol and progesterone are not helpful in differentiating between the various diseases.<sup>120</sup> Acute stabilization and possible blood transfusion are often needed in critical patients, alongside hormonal treatment with human chorionic gonadotropin, or gonadotropin-releasing hormones



**Fig. 10.** A soft swelling at the entrance of the prepuce in a 6-year-old neutered male ferret was diagnosed as a basal cell carcinoma. Radical resection is an important step in the treatment of these highly malignant tumors.



**Fig. 11.** An irregular mass on the head of a 4-year-old neutered female ferret was diagnosed as a mast cell tumor. Although this type of tumor is considered malignant in most companion species, in ferrets these tumors are benign.

(eg, deslorelin) to end estrous. Upon stabilization, surgical or chemical neutering should be performed.<sup>115,121</sup> Hyperestrogenism is best prevented by gonadectomy or subcutaneous implantation of long-acting deslorelin-containing implants, which needs to be repeated every one to two years,<sup>122</sup> with implants being the preferred option to avoid induction of adrenal gland disease.<sup>106,123</sup>

### ***Testicular Tumors***

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Testicular leiomyosarcoma has been reported to cause nonpruritic alopecia of the back, neck, tail, and abdomen, which resolved after surgical castration.<sup>124</sup>

### ***Hypothyroidism***

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Hypothyroidism is rare in ferrets and usually not associated with dermatologic changes noted in other mammals.<sup>106</sup>

## **ALLERGIC SKIN DISEASE**

Allergic skin diseases are uncommon in ferrets, and most often involves contact dermatitis associated with frequent exposure to shampoos or insecticide spray, or



**Fig. 12.** Lymphomas are considered one of the most common tumors diagnosed in ferrets. This swollen tissue in the interdigital space of a 5-year-old neutered male ferret was diagnosed as cutaneous lymphoma.



**Fig. 13.** Hemangiosarcoma on ferret pinna. (Courtesy of Peter G. Fisher, DVM, Virginia Beach, VA.)

reactions to environmental allergens.<sup>43,125</sup> Atopy manifests as generalized symmetric dermatitis and pruritus of the trunk, rump, and skin folds, leading to self-induced alopecia.<sup>35,43</sup> Despite a single case report on food hypersensitivity in a ferret, this should be ruled out as a differential.<sup>31,35</sup> Atopy can generally be diagnosed using histopathology of skin biopsies, intradermal allergy testing, and resolution of clinical signs following elimination of environmental allergens.<sup>31,43</sup> Hyposensitization with triggering allergens can be attempted, in addition to the use of antihistamines, corticosteroids, and omega-3 and -6 fatty acid supplementation to alleviate the clinical signs.<sup>43</sup>

## MISCELLANEOUS SKIN DISEASES

### *Erythema Multiforme*

Erythema multiforme is a rare autoimmune disease, which has currently only been reported in ferrets with concurrent adrenal disease.<sup>43,126</sup> Exposure to drugs, infections, or neoplasia can alter epidermal keratinocytes, making them a target for the host's



**Fig. 14.** A nonpruritic swelling at the tip of the tail of a 6-year-old neutered male ferret represents the typical presentation of a chordoma. When located at this region, this commonly benign tumor can easily be resected by partial amputation of the tail.



**Fig. 15.** Severe alopecia, as seen in the 7.5-year-old neutered female ferret, is commonly seen in ferrets with hyperandrogenism, also commonly known as hyperadrenocorticism. Severe pruritis may be seen among ferrets with this disease.

T cells, which induces keratinocyte apoptosis. Clinical signs include nonpruritic erythema, papules, and crusts, which appear 7 to 18 days postantigen exposure (**Fig. 16A, B**). The erythema starts in the inguinal region, and then spreads cranially to the axillary regions, face, ears, and foot pads. On tape cytology cornified epithelial cells



**Fig. 16.** Clinical signs reported in ferrets with erythema multiforme include erythematous macules and papules in the inguinal and the axillary area (**A, B**) and hyperkeratosis and erythema of the foot pads (**C**), and ear pinna (**D**). (Reprinted from: Fisher, P. G. (2013). Erythema multiforme in a ferret (*Mustela putorius furo*). *Veterinary Clinics: Exotic Animal Practice*, 16(3), 599-609. With permission.)

are found, whereas histopathological analysis shows mild to moderate hyperkeratosis, epidermal keratinocyte necrosis, and bulla formation. The symptoms can be periodically relieved with immunosuppressive doses of prednisolone, azathioprine, and cyclosporine until ineffective, after which euthanasia is warranted.<sup>126</sup>

### ***Pemphigus Foliaceus-Like***

*Pemphigus foliaceus* is an autoimmune disease attacking the desmosomes of the epidermal keratinocytes, resulting in fluid accumulation between the keratinocytes. The fluid accumulates into pustules, and gives rise to bilaterally symmetrical, yellow-brownish skin crusts on the mucogingival areas of the head (mouth, nose, chin, eyes) and prepuce; and the foot pads.<sup>127</sup> Mild pruritus, weight loss, and decreased activity levels were also noted.<sup>127</sup> The diagnosis is made on histopathology of skin biopsies showing epidermal hyperplasia, acantholysis and intra-/subcorneal pustulae, as well as a clinical response to immunosuppressive doses of prednisolone.<sup>127</sup>

### ***Blue Ferret Syndrome***

Blue ferret syndrome is caused when the fur on the ventral abdomen is clipped during the catagen phase of the hair growth cycle; this can cause the hair follicles to produce melanin, which gives the skin a bluish discoloration. The ferret is asymptomatic, and the discoloration resolves within a few weeks when the hair starts to regrow.<sup>1,43</sup>

### **CLINICS CARE POINTS**

- Mast cell tumors in ferrets are, in contrast to those in dogs and cats, nonmalignant
- Hyperestrogenism should be suspected in the intact female ferret with nonregenerative anemia.
- Ferrets infected with ear mites (*O cynotis*) are often asymptomatic, but should be suspected with the clinical finding of brown cerumen.

### **DISCLOSURE**

The authors have no known competing financial or personal interests affecting the work reported in this article.

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