

# UNIVERSITY OF CALGARY FACULTY OF VETERINARY MEDICINE

This review accompanies the relevant episode of the Cutting Edge veterinary podcast. In each episode of this podcast, 3rd year students in the University of Calgary's veterinary medicine program fill you in on the most up-to-date literature and evidence-based practices on topics that matter to you, the practicing veterinarian.

# A Small Animal General Practitioner's Guide to the Identification, Diagnosis, and Treatment of Dermatologic Conditions in Reptiles and Amphibians

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# Introduction

There has been a steady increase in the number of non-traditional or 'exotic' species, such as reptiles and amphibians, being kept as companion animals since the mid-20th century (1). Today, many exotic pet owners have more than one species under their care, including the more traditional companion animals such as cats and dogs. Conveniently, many owners opt to have a single veterinarian for all their animals, which promotes many exotic pets being seen in small animal general practice (1). Although exotic species have become more common, many general veterinary practitioners may still feel uneasy or less confident in treating exotics compared to the more traditional species (1). Reptiles and amphibians commonly present in general practice with conditions that are dermatologic in nature. Dermatologic diseases can be a challenging issue to tackle as they are commonly multifactorial and often related to husbandry or environmental issues (2). This review aims to guide the average small animal general practitioner through the identification, diagnosis, and treatment of common dermatologic conditions in reptiles and amphibian species.

# **Basics of Handling and Restraint**

There are many options for the handling of reptiles and amphibians. The proper technique used is dependent on the species, the size of the animal, how potentially dangerous the species can be, and the comfort and skills of the handler. Handling and restraint of reptiles and amphibians should only be conducted, when necessary, as it is ideal to use visual assessment whenever possible to limit stress on the animal and promote the safety of all parties involved. Free handling, without the use of tools, can be done when the animal is an appropriate size, non-venomous, and is deemed reasonable with the disease condition at hand (3). It is important when handling amphibians to wear powder-free nitrile or vinyl gloves to prevent epithelial damage to the amphibian and prevent the transdermal absorption of compounds that may be present on the handler's hands (e.g. lotions), and to protect the handler against toxic excretions (4). Restraint devices may also be used to aid in handling. Examples include snake hooks, pinning tools, snake tubes, and a variety of other instruments (3). Please note that venomous animals should only be handled by those who are properly trained, and referral to specialized clinics may be more appropriate for these pets. Chemical restraint is another option and can be accomplished via inhalation, injection, or immersion in an anesthetic solution following proper, species-specific

procedures. Consultation with experienced colleagues is best before undertaking these procedures when possible.

## **Critical Care Upon Arrival**

Transportation of reptiles and amphibians to clinics often requires them to be taken out of their controlled environments. It is crucial to try to maintain the proper conditions for the animal during transport and while in the clinic. This can include, but is not limited to, the use of heat sources (e.g. heat packs/warm water bottles, lamps, ceramic heat emitters) and ensuring a wet environment to maintain moisture for amphibian skin (3). After a visual assessment, perform the physical exam in an efficient manner with proper personal protective equipment, and collect appropriate samples simultaneously to minimize the duration of handling (4).

## **Overview of Reptile and Amphibian Skin**

A key difference in the approach to diagnosis and treatment of dermatological disease in reptiles and amphibians compared to traditional companion animals is the structure and function of the skin. The epidermis and dermis of reptile skin have evolved into scales and there is much variation between reptile species (2). For example, in turtle species, the epidermal scutes of the carapace and plastron of the shell are derived from the stratum corneum layer of the epidermis (2). In addition, reptiles will shed their skin (ecdysis) at regular intervals, with the pattern and timing of these sheds varying between species. For example, snakes shed as a singular large fragment when healthy, while lizards and chelonians shed in multiple, smaller segments (2). Crocodilians and chelonians are noted to shed their epidermis continuously throughout the year, whereas lizards and snakes shed periodically throughout the year (2).

Amphibian skin is thin and delicate as it is principal for the function and survival of the animal, having an important role in water absorption, osmoregulation, and respiration of the individual (5). Many genera of amphibians have specific adaptions of their skin, varying from the development of dermal scales in caecilians to the creation of "drinking patches" in anurans (5,6). Amphibians, like reptiles, will shed their skin; however, the stratum corneum is normally shed as one piece at specific times of the year and then consumed by the animal. This process is called dermatophagy and when not completed, this can be an indication of illness (2,6). It is crucial to keep the skin of amphibians moist and take great care to minimize any disruption to the mucus layer during clinical evaluation (2,4).

# **Common Diagnostic Tests for Dermatologic Disease**

Many of the diagnostic tests for dermatologic disease in reptiles and amphibians are similar to those used in companion animals. The collection of these samples can then be sent for cytological evaluation, culture, PCR, or histopathology, after evaluation in the clinic (1). These include but are not limited to:

- Skin scraping using a clean blunted scalpel blade and glass slide (2).
- Direct impressions and swab smears (2).
- Tape impressions (2) only to be used for reptiles.
- Biopsy (2).

# Reptiles

### Bacterial

In reptiles, superficial or deep invasion of the skin or shell with a wide variety of bacteria can result in bacterial dermatitis. Interruption of the skin barrier due to traumatic events leading to injuries such as abrasions and lacerations, or thermal burns allows bacteria to invade, causing localized or extensive infection with associated clinical signs. Different reptilian species have varying susceptibility to distinct organisms, resulting in numerous clinical manifestations of dermatologic bacterial infections (7). Despite differing bacterial sources, the etiology, treatment, and prognosis of all bacterial dermatitis in reptiles remain relatively similar. Environments that promote the proliferation of bacteria such as suboptimal temperatures, high humidity, and moist bedding increase the risk of infection, thus, addressing these husbandry issues is necessary for its prevention (8). Treatment of all reptilian bacterial dermatitis will be carried out similarly despite the inciting bacteria. The first step will be to identify and treat the cause of the infection, which will coincide with further prevention attempts. Reptiles should be placed on systemic antibiotics for 3-4 weeks, or one week past clinical resolution, based on culture and sensitivity (8). Owners should also be taught to treat superficial causes with 2% chlorhexidine or povidone-iodine every 12 hours until resolution (8). In the clinic, lesions should be cleaned and debrided before discharging the patient (8). Here, the most common, species-specific forms of bacterial dermatitis will be discussed.

### Ulcerative Dermatitis of Chelonians (Shell Rot)

Ulcerative dermatitis ('shell rot') is a commonly seen form of dermatitis in chelonians caused by environmental gram-negative bacteria, but also can have fungal or algal etiologies. *Benechia chitinovora* is the most frequently isolated bacterial etiological agent, however, *Citrobacter spp*. and *Aeromonas spp*. have also been associated with the disease (2, 8). Infection may result in ulceration of the shell surrounded by areas of erythema, hyper-pigmentation, and loosening and avulsion of scutes (8).

## Septic Cutaneous Ulcerative Disease (SCUD) of Chelonians

Septic Cutaneous Ulcerative Disease (SCUD) affects both aquatic and semi-aquatic chelonians, especially soft-shelled turtles (7). This form of shell rot occurs when bacteria, most often gram negative in nature, spread into the bloodstream and internal organs, resulting in systemic signs of disease. Chelonians will present with anorexia, lethargy, petechiae and ecchymoses alongside the previously indicated shell rot-associated lesions (7). While diagnosis will be similar to other dermatologic conditions, blood culture should be done if there is suspected septicemia and radiographs can be performed to assess the depth of lesions and assess for boney involvement (7).

### Necro-Ulcerative Dermatitis (Scale Rot)

Scale Rot is a broad form of ulcerative or necrotic bacterial dermatitis affecting a wide variety of reptilian species, each species affected by differing bacterial pathogens. Scale rot in lizards can be caused by *Actinobacillus* spp, *Arizona* spp, *Pseudomonas* spp, *Corynebacterium* spp, *Dermatophilus* spp, *Edwardsiella* spp, *Enterobacter* spp, *Flavobacterium* spp, *Flavomonas* spp, *Morganella* spp, *Serratia* spp, *Staphylococcus* spp, *Mycobacterium* spp., and *Salmonella* spp. (9). Skin infection with these agents may cause various dermatologic signs including blisters, crusts, ulcerations and exudative lesions of the ventrum (2). Chronically, these can progress to abscesses or granulomas (8). *Devriesa agamarum* is regularly isolated from scale rot in spiny-tailed lizards (Agamidae and Iguanidae), giving rise to crusty and exudative dermatitis and cheilitis (10). In tortoises, aquatic turtles, lizards, and snakes, *Austwickia chelonae* is a frequently inciting agent of scale rot (11). Both *Devriesa agamarum* and *Austwickia chelonae* propagate into deeper tissues and can result in the development of granulomas (11).

### **Blister disease**

Blister disease is a form of early ulcerative or necrotic bacterial dermatitis arising from opportunistic infection by *Aeromonas sp.* and *Pseudomonas sp.* often associated with wetter environments than is ideal for the species (2). If treatment is performed early enough, the progression of blisters and pustules to ulcerative lesions can be prevented (12).

### Cutaneous Abscesses

Cutaneous abscessation arises from focal bacterial infection of the skin and can affect all orders of reptiles. Bite wounds, inadequate husbandry, and trauma allow a spectrum of bacteria to invade, consequently forming capsulated, soft to firm, non-painful to painful swellings filled with caseous exudate (2). Common bacteria isolated from abscesses include *Pseudomonas* spp, *Proteus* spp, *Aeromonas* spp, *Serratia* spp, *Providencia* spp, *E coli, Citrobacter, Proteus, Salmonella, Streptococcus, Corynebacterium pyogenes*, and *Neisseria* (2). Less commonly, *Serratia, Erysipelothrix, Morganella, Staphylococcus, Klebsiella, Dermatophilus* and *anaerobic Peptostreptococcus* can be associated (12). When abscesses are smaller and more localized, they can be excised completely, while larger abscesses may require more aggressive treatment. This may include marsupialization, local wound treatment, and antiseptic lavage (2).

## Viral

## Invertebrate Iridovirus

Invertebrate iridovirus can infect snakes and lizards via oral insect transmission or transfer through wounds and skin imperfections (13, 14). This viral infection of the skin causes a range of clinical signs with different reptilian species, manifesting distinct demonstrations of the disease. In a broad sense, iridovirus can cause no clinical signs to rhinitis, stomatitis, conjunctivitis, tracheitis, edema, and cutaneous abscesses (13). Both green iguanas and spiny-tailed lizards will often display hyperkeratosis as their prominent expression of the disease. Bearded dragons may also exhibit hyperkeratosis, as well as pox-like lesions, cheilitis, and dropping of scales (14).

## <u>Ranavirus</u>

Ranavirus is a severe to fatal viral infection of chelonians, lizards, and snakes causing head and neck edema, dermatitis, and abscess formation of the skin (11). Due to the systemic effects of the infection, multiple organs may be concurrently involved, especially the liver and spleen. This results in a wide variety of clinical signs associated with many body systems (15). Unfortunately, antivirals have been ineffective in the treatment of iridovirus. Studies have noted that increasing the ambient temperature of enclosures to the high end of the preferred optimal temperature zone (POTZ) may increase ranavirus antibody production by ectotherms, improve humoral immunity, and aid in disease treatment. Otherwise, infected reptiles should be treated with supportive care (15).

# **Boid Inclusion Body Disease**

Boid inclusion body disease\_is a reptarenavirus affecting members of the Boidae and Pythonidae family. Although the most common presentation involves abnormalities of the central nervous system, skin lesions are often concurrently observed in boas, ranging from irregular shedding to severe dermatitis associated with opportunistic bacterial or fungal infections secondary to immunosuppression caused by the virus (11). Inclusion body disease can be histologically diagnosed on antemortem, similar to some other viral diseases by demonstrating eosinophilic to amphophilic intracytoplasmic inclusions of H&E stained biopsy specimens (16). It also can be diagnosed via PCR. Unfortunately, there is no effective treatment against inclusion body disease or vaccine, therefore, snakes testing positive should be isolated from other snakes to avoid transmission, and their enclosures disinfected with suitable disinfectants such as sodium hypochlorite (bleach) or phenolic compounds (16).

# **Papillomaviruses**

Papillomaviruses, similar to those of mammalian species, cause skin lesions, papillomas, and squamous epithelial carcinoma in chelonians, snakes, and lizards (11). In the European green lizard, infected individuals may develop single or multiple papillomas that require resection. Bolivian side-neck

turtles, however, develop white, oval skin lesions on the head, requiring supportive care. All infected reptiles should be isolated to prevent the spread to other individuals in close contact (14).

## **Reoviruses**

Reovirus infections are a relatively common viral infection in lizards, snakes, and sometimes turtles and tortoises. Dermatologic presentation of reovirus manifests with papillomatous growths and necrotizing and ulcerative dermatitis (11). This viral infection can cause a variety of clinical signs, the most common being pneumonic respiratory diseases (17). There is no specific treatment for reoviruses, thus, provide supportive care and isolate individuals.

# Parasitic

## Mites

Similar to mammalian species, reptiles can be infected with a variety of mites. From the family Macronyssidae, *Ophionyssus natricis* and *Ophionyssus acertinus* feed on the blood of snakes and lizards, respectively (2). Because of their mechanism of parasitism, anemia may indicate a severe infestation. These mites are commonly found under scales, around the eyes, nose and within the gular fold of snakes. Therefore, diagnosis can be achieved through direct or microscopic observation (2). Mite infestation can cause dermatologic irritation, pruritus, and can interfere with normal cycles of shedding (2). Chiggers, caused by *Hirstiella trombidiformis*, is also a common cause of irritation and pruritus in lizards. These organisms will ingest lymph and host tissue and will require similar treatment to *Ophionyssus* mites (2). Elimination and treatment can be achieved by adding 0.5 ml of 10mg/kg ivermectin to 1 L of water and spraying snake and snake enclosure three times at two-week intervals. This can also be achieved as a subcutaneous injection of ivermectin at 200 ug/kg, use of moxidectin or selamectin (18). Fipronil sprays or vapona strips can also be used for environmental elimination of the mites.

# Fungal

# Fungal Dermatitis

Fungal dermatitis can affect all reptilian species secondary to poor husbandry and environmental conditions, skin trauma (especially thermal burns), and immunosuppression (9). Similar lesions can be caused by several opportunistic pathogens including *Aspergillus, Basidobolus, Geotrichium, Mucor, Saprolegnia and Candida, Fusarium, Trichosporon, Trichoderma, Penicillium, Paecilomyces, Oospora,* and *Trichophyton* (2). These infections can be both superficial or deep, differing in appearance depending on the stage of infection. Superficial infections commonly arise as ulcerations and blisters with moist exudate, crusts and hyperkeratosis. Deeper infections, however, may present with systemic signs alongside nodulations and inflammation (2). All dermatologic fungal infections can be treated first by debridement of dead, fungal-contaminated skin. Afterwards, administration of systemic antifungals such as voriconazole, amphotericin B, terbinafine or itraconazole should be provided based on fungal identification (19).

# Yellow Fungus Disease

*Chyrsosoporium* anamorph of *Nannizziopsis vriesii* and several other *Nannizziopsis* species have been frequently associated with fungal skin disease in lizard species and crocodiles. In the bearded dragon, infection with *Nannizziopsis guarroi* is associated with the development of yellow fungus disease. Invasion of the skin initially causes white, raised bumps that progress to yellow to brown, hyperkeratotic, discoloured scales. Swelling and necrosis can occur at the site of infection, and in many cases, will lead to an eventual fatality (2, 20). It is important to note that this granulomatous dermatomycosis is contagious

and therefore, affected reptiles should be isolated. Any other reptiles that share housing or equipment should be concurrently monitored and treated if need be (2). While diagnosis is similar to other dermatologic fungal infections, specific histopathologic features include necrosis within the dermis and epidermis, as well as granulomatous dermatitis and intralesional hyphae (20).

## Snake Fungal Disease

Snake fungal disease, or ophiodiomycosis, is caused by *Ophiodiomyces ophiodiicola*. Normally, the cutaneous flora of snakes prevents the growth of this fungus. However, activities such as antibiotic use may cause dysbiosis and predispose snakes to a fungal proliferation of the skin (13). In mild to moderate cases, the fungus invades the epidermis and results in epidermal necrosis and hypertrophy with yellow-brown crusting around the head or tail (13, 21). In more severe cases, the dermis and subcutis may become infected, producing granulomas, and invading deeper skeletal muscle (21). The use of antifungals to treat ophiodiomycosis has had unclear results, with terbinafine showing promise, however, supportive care alone may facilitate recovery in mild cases (21).

## **Non-Infectious**

## Nutritional Deficiencies

Nutritional deficiencies can result in dermatologic issues in reptile species, most notably hypovitaminosis A and secondary nutritional hyperparathyroidism. Hypovitaminosis A can arise in aquatic turtles, tortoises and some lizards when being fed commercial food that has an improper or complete deficiency of supplementation (22). The lack of vitamin A can manifest as blepharodema of the eyes and aural abscesses (22). Acceptable treatment of hypovitaminosis A includes injectable or oral vitamin A, as well as ongoing care with a new, properly balanced diet (22).

Secondary nutritional hyperparathyroidism, also referred to as metabolic bone disease, can be seen in lizards and chelonians given insufficient levels of calcium, high levels of phosphorus, inadequate UVB light exposure to synthesize Vitamin D3, or low quantities of vitamin D3 in their diet (22). When calcium intake is insufficient, or cannot be absorbed from the intestinal tract, the release of parathyroid hormone maintains blood calcium levels by mobilizing calcium stores from the bone. Animals affected by this condition can be seen with fractured limbs, hind limb paresis with the appearance of swollen extremities, and a "rubber" mandible (22). Turtles have been noted to have deformed or asymmetrical shells when affected (22). Diagnosis of secondary nutritional hyperparathyroidism can be done by investigating the animal's husbandry, management, clinical signs, and the presence of generalized osteopenia on radiographs (22). Gentle handling is required due to the fragility of the bones (4). When diagnosed, oral or parenteral calcium should be administered and a discussion revolving around proper husbandry (e.g. adequate UVB light exposure) and nutrition (cholecalciferol supplementation) is necessary (22).

### Dysecdysis

One of the most common dermatological diseases seen in reptiles, specifically snakes is dysecdysis, which is the abnormal or poor shedding of skin (23). As mentioned previously, the pattern and timing of ecdysis depends on the reptile species. Dysecdysis can be caused by improper husbandry or systemic illness that impacts the hormonal mediation of normal ecdysis (24). Husbandry related issues include inappropriate temperature, humidity, or the absence of materials, such as rocks, to ease shedding (24). Common presentation of dysecdysis in snakes is retained epithelium over the eyes – commonly referred to as a spectacle (8). The spectacle, when retained, will be appear wrinkled and cloudy or even opaque, instead of the normal smooth and clear spectacle expected in normal shedding. Treatment includes removal of the retained spectacles to prevent corneal damage or the formation of subspectacular

abscesses. Blunt removal of the retained skin is not recommended as it can often lead to ulceration, loss of fluids, or even permanent damage to the cornea if the new epithelial layers are developed. For small sections of retained epithelium, lightly spray the animal with water or increase the humidity of the enclosure to aid in the shed (25). To remove larger sections, soak the animal in warm water for a short period of time (25). After the removal of the retained shed it is prudent to have a complete understanding of the enclosure and husbandry practices to treat the underlying cause of the dysecdysis.

#### <u>Trauma</u>

Trauma in captive reptiles can be caused by various factors, often relating to issues with management and husbandry. Most commonly, individuals demonstrate assorted types of burns, bite wounds from prey, and in chelonians, shell fractures.

#### Burns

Thermal burns, characterized as first-, second-, or third-degree, are injuries associated with misuse of heat lamps and heated rocks with high wattage incandescent bulbs (26). First degree burns in reptiles affect the epidermis, presenting as erythematosus and moist dermatitis. Management of these wounds requires appropriate analgesics, cool compresses, and saline irrigation (26). Second degree burns generally affect the epidermis and dermis with associated blister formation, while third degree burns are full thickness with necrosis of integument and muscles. Like first degree burns, both second- and third-degree thermal burns should be treated with analgesics, irrigation, as well as broad spectrum antimicrobials such as fluroquinolone or cephalosporins prior to culture and sensitivity (26). Third degree burns may require topical antiseptics, sterile dressings, and resection of the area as necessary (26).

Electrical burns, while rare, are often the result of reptiles biting cords within their enclosure and can result in muscle and skin necrosis. Management of these wounds depends on severity but should be treated similarly to previously mentioned thermal burns (26).

Chemical burns can occur when the integument encounters irritating compounds such as household cleansers. Reptiles present with signs like thermal burns, however, the first step to management involves identifying the cause (26). If an anecdote is available, this should be given immediately and then focus should be shifted to maintaining tissue viability. The burn should be irrigated with warmed saline to remove the chemical and the individual should be given fluid therapy and supplemental heat when there is a wide area of skin damage (26). Tissue necrosis may not present for 24-72 hours. In this case, a delayed response is necessary and post irrigation antiseptic creams and sterile bandages should be administered to prevent opportunistic infections (26).

### Shell fractures

Shell fractures in turtles can be seen in trauma cases. Human-induced trauma, such as a car collision, is a primary presentation for many shell fractures (27). In most cases, damage to the shell is severe and not compatible with life, and the animal should be euthanized, but there are both medical and surgical treatments available for select less severe cases (28). Surgical repair is suitable for open or displaced shell fractures and includes the use of plates, screws, and wires to provide stability for the fracture to heal. Less invasive management for fracture fixation include bone cement, inert epoxy and other resins to fill in the cracks, and can be used with cable ties or metal bridges to provide stability when funds are limited (28).

### Prey Bite Wounds

Bite wounds from prey can cause traumatic injury in captive reptiles. The most common of these occur in snakes that are fed live rodents, however, even insects such a crickets can induce significant dermal wounds in smaller reptiles (26). The bite wounds can be superficial to full thickness with

penetration into the coelomic cavity. Prey bite wounds should be considered contaminated and proper wound management with flushing and debridement is necessary; common practice can include the use of a wet to dry bandage (26). It is essential to educate the owners on the risks of feeding live prey to their reptiles and promote owners to feed pre-killed prey (26).

## Amphibians

## Bacterial

## Bacterial Dermatosepticemia ("Red Leg")

Also referred to as 'Red Leg Disease', bacterial dermatosepticemia can be observed in any amphibian, however, is most frequently identified in immunocompromised individuals who are subjected to poor husbandry conditions. The disease is the result of a generalized skin infection by opportunistic bacteria and fungi, including gram-negative bacteria such as *Aeromonas hydrophilia*, *Citrobacter sp., Pseudomonas sp.* and *Enterobacteria sp.* (29). Patients will present with dermal petechiation, ventral erythema of the legs, epidermal erosion, anasarca, bloat, and sudden death (30). These dermatological signs are suggestive of several differential diagnoses including ranavirus, chlamydiosis, chytridiomycosis, and neoplasia. Due to the broad spectrum of etiologies, bacterial culture and sensitivity should be considered when offering additional diagnostic testing to clients (30). Treatment comprises of parenteral broad-spectrum antimicrobials (fluoroquinolones, amikacin with metronidazole), supportive therapy (preferred optimum temperature zone, fluids, nutrition) and husbandry changes. Despite treatment, the prognosis for this condition is poor and has an expected mortality rate of 81-100% (30).

## **Bacteria Abscesses**

A common presenting complaint of amphibian is the presence of cutaneous abscesses. This condition has no species or sex predilection and is often associated with poor husbandry and stress allowing for the dermal invasion of opportunistic bacteria such as *Pseudomonas sp, Salmonella sp* and *Mycobacterium* sp (31). This leads to the development of firm masses, accompanied by local inflammation and dermal necrosis with chronicity. These presentations may look similar to other cutaneous diseases such as bacterial dermatosepticemia and neoplasia. Due to this resemblance, culture and cytology can offer valuable information for treating bacterial abscesses specific to the etiological agent. A three-point treatment plan is indicated for these presenting patients. First, husbandry evaluation should immediately be discussed and corrected. Next, abscesses should be surgically incised, debrided, and flushed to promote healing (31). Lastly, an appropriate antimicrobial course (e.g. enrofloxicin, ceftazidime, amikacin,) based on culture and sensitivity should be implemented. Depending on the location and etiology of the abscess, the prognosis ranges from poor to good (31).

# **Chlamydiosis**

Chlamydiosis is a multi-systemic disease affecting amphibians such as toads, frogs, and newts, with a heightened incidence in captive colonies living in suboptimal husbandry conditions (29). The primary etiological agents causing this condition are *Chlamydia pneumonia*, as well as *Chlamydia psittaci* affecting African clawed frog species. Additionally, there have been reports of *Chlamydia abortus* and *Chlamydia suis* causing chlamydiosis in amphibians. Due to the potential for zoonotic transmission of this infection, clients and staff must exercise appropriate caution including appropriate personal protective equipment and proper animal handling. The most notable dermatologic signs and presentation are sloughing, depigmentation, and petechiation of the skin, generalized edema and anasarca, along with lethargy, anorexia and sudden death (29). Attributable to the broad nature of these clinical signs, bacterial dermatosepticemia, mycobacteriosis, chytridiomycosis, ranavirus, and neoplasia all serve as possible

differential diagnoses of this condition. Additional diagnostic measures such as bacterial culture and sensitivity and necropsy should be considered owing to the high mortality rate of chlamydiosis (30). Currently, there are no identified effective treatments, thus, supportive therapy including fluids, proper nutrition, and thermoregulation may be attempted. The prognosis for chlamydiosis is grave, therefore, euthanasia is often indicated (30).

## **Mycobacteriosis**

Mycobacteriosis is one the oldest known infectious diseases of amphibians that results from the ingestion or entrance of bacteria through broken skin barriers, leading to chronic infection. A high incidence rate is noted in fully aquatic species and immunosuppressed individuals, presenting with similar occurrence in both juvenile and adult life stages (29). Identified etiologies in amphibians are atypical environmental Mycobacterium species - Mycobacterium avium, Mycobacterium fortuitum, Mycobacterium marinum, and Mycobacterium xenopi. These agents have the potential for zoonotic infection; Therefore, it is crucial for clients and staff to exercise appropriate caution while caring for suspected or confirmed cases. Mycobacteriosis presents with broad clinical signs and presentations, most notably, skin lesions. These include hyperemia, petechiae, ulceration, dermatitis, pigmentation change and non-draining abscess. Additionally, a variety of non-specific symptoms such as lethargy, anorexia, bloat, and immune suppression have been reported. Because of these ill-defined signs, dermatological differentials consist of bacterial dermatosepticemia, chytridiomycosis, ranavirus, and neoplasia. Fortunately, coelomic ultrasound or transillumination for nodules within the coelom and cytology of skin lesions with acid-fast stain can be used to characterize present bacteria and serve as an easily accessible form of diagnostic testing. Concurrent definitive tests that include bacterial culture isolation, PCR, and necropsy with histology. The current comprehensive treatment recommendations are to begin antimicrobials based on culture and sensitivity, resection or amputation of discrete nodules, and supportive therapy. Frequently, these therapies prove to be ineffective, leading to the recommendation of euthanasia (32). While considering a treatment plan for your patient, it is important to avoid the empirical use of antimicrobials due to the zoonotic nature and risk of antimicrobial resistance in humans (29).

# Viral

# <u>Ranavirus</u>

Ranavirus has rapidly emerged as one of the most common viral dermatological diseases of amphibians since the 1960s and is classified as an OIE notifiable disease. Although all species of amphibians are vulnerable to infection, larval stages and adults maintained in poor husbandry conditions demonstrate increased susceptibility (29). There are three major viral strains affecting amphibians including frog virus-3 (affecting frogs), tadpole edema virus (affecting frogs) and Ambystoma tigrinum virus (affecting tiger salamanders). The most notable presentations of patients with ranavirus will be skin ulceration, mild to severe erythema, and edema. Additionally, individuals may be weak, swim erratically, have buoyancy difficulties, central nervous system abnormalities, gasp for air and present with acute mortality. These presentations and the appearance of skin lesions may look like chytridiomycosis, bacterial dermatosepticemia and chlamydiosis. If ranavirus is suspected, clinicians should contact the OIE for proper reporting and further steps as there is no current gold standard for its diagnosis (33). Due to the virality of this disease, affected individuals or those in contact should immediately be guarantined with sufficient biosecurity protocols, review of husbandry and disinfection of habitats and equipment with 1% Virkon. There is no standard treatment protocol developed for Ranavirus, however, a combination of thermal treatment (>26°C) and supportive therapy (thermoregulation, fluids, nutrition) has reportedly lowered mortality rates. The prognosis of this disease is grave (29).

## Fungal

## Cutaneous Chytridiomycosis

As an emerging, highly lethal and highly contagious fungal disease, cutaneous chytridiomycosis has threatened numerous populations of amphibians. Historically, the disease primarily affected wild populations; however, recent outbreaks have been reported amongst captive-bred individuals (29). The two recognized etiologies of this fungal disease are Batrachochytrium dendrobatidis and Batrachochytrium salamandrivorans. Although most often presenting as acute mortality, dermatological signs may be noted early in the disease course. These include hyperplastic skin seen as excessive shedding, erythema of the ventrum and feet, and skin ulceration. Additional non-specific clinical signs are anorexia, central nervous system signs, and seeking water immersion. These dermatological indications may look similar to ranavirus and chlamydiosis, however, clinical signs are often enough for a presumptive diagnosis and no further testing is required. As this fungus is highly infectious, clients should be advised to treat those in contact with the patient and implement quarantine and biosecurity protocols, in addition to a thorough review of husbandry (34). Amphibians affected by cutaneous chytridiomycosis can be treated with Itraconazole (0.01% for 5–15min, q24h for 7-11 days) or Terbinafine (0.01% for 5min, q24h for 5 days) soaks, thermal treatment dependent on the likely etiology (B. dendrobatidis >32ºC, B. salmandrivorans >22°C) and supportive therapy (thermoregulation, fluids, nutrition). Despite intensive therapy, the prognosis of clinically ill patients remains poor (29).

## Parasitic

## Ixodidae (Ticks)

While generally rare, ectopic parasites can be of great concern to owners due to their gross visibility. Cases are typically sparse but captive populations have been affected due to the introduction of wild-caught individuals or importation from less than reputable sellers. Rarely are the parasites themselves of immediate concern, however, disease transmission such as bacterial, viral, and fungal should be taken into consideration during your exam. The most common ectopic parasite affecting amphibians is ticks from the family Ixodidae (29). Dermatological clinical signs include the presence of the tick attached to the skin, erythema, edema, and secondary bacterial infection. The affected individuals will also frequently seek water immersion in an attempt to remove the parasite. While the presence of the parasite is often diagnostic, smaller mites may be confused and microscopic visualization is recommended. Without secondary infection, the prognosis for tick infestation is excellent once treated with physical removal, PO or topical avermectins (e.g ivermectin, moxidectin, milbemycin, selamectin), and supplementary supportive care (POTZ, fluids, nutrition), dependent on the patient's condition (29).

### **Non-Infectious**

# Squamous Cell Carcinoma

Squamous cell carcinomas are the most common neoplastic disease of the amphibian skin but remain a rare presentation. This neoplasia is locally invasive and malignant, and there are currently no literature reports of its metastatic behaviour in amphibians. As a result of this low occurrence and/or under-reporting, little is known regarding the specific signalment or history that may predispose an individual. Dermatological signs consist of erythema, hemorrhage, ulceration, and discrete raised lesions (29). Because of this, differential diagnoses include bacterial abscesses and mycobacterial/ fungal granulomas. Histopathology serves as the gold standard for diagnosis; however, fine-needle aspiration (FNA) with cytology may also be sufficient. Common therapy for squamous cell carcinoma in amphibians

involves surgical excision or cryotherapy with analgesics to promote comfort. Depending on the histological margins, prognosis can range from good to guarded (29).

#### Hypervitaminosis A

Hypervitaminosis A is a prominent consequence of over-supplementation in amphibians. Frequently, this condition is the result of nutritional over-supplementation by owners, parental overdoses by attending veterinarians, or high animal-based diets. Young individuals, those with liver disease, actively breeding females, or amphibians with first-time owners, face the highest risk. These individuals present with epidermal flakiness, sloughing and ulceration of the dermis, and dysecdysis. Additionally, anorexia, dehydration, lethargy, ulcerative stomatitis, and secondary infections may be noted. While a definitive diagnosis requires a liver biopsy with vitamin A testing, often presenting clinical signs are sufficient for a presumptive diagnosis (35). Similarly presenting differentials are infection, water-based toxins, poor husbandry, UVB/thermal burns and hypovitaminosis A. Once identified, excessive supplementation should be discontinued, op-site bandage spray and topical triple antibiotic ointment should be applied to skin ulceration is suspected as the cause, a detailed review of nutrition and supplementation is required to prevent repeated offences. The prognosis for hypervitaminosis A is poor to fair, often with recovery extending over months and permanent deficits (35).

#### Hypovitaminosis A

Hypovitaminosis A, similar to hypervitaminosis A, is often the result of improper nutrition, particularly in amphibians fed captive raised invertebrates (29). This is because the majority of dietary vitamin A is in the form of beta carotene, while amphibians require all-trans-vitamin A isomers for physiologic use (29). Due to the lack of useable vitamin A, amphibians dermatologically present with dull colouration and squamous metaplasia (most often lingual). Lingual squamous metaplasia, also known as short tongue syndrome, results in an inability to capture prey, leading to lethargy and weight loss. Affected individuals may also have periorbital edema and increased ecdysis (29). Diagnosis can be confirmed using liver biopsies for histopathology exemplifying squamous metaplasia and testing vitamin A levels, however, this disease is commonly diagnosed by a thorough history (29). Once a presumptive diagnosis is made, parenteral vitamin A (500-5000 iu/kg) IM q7-14 d for four treatments can be administered. Care should be taken not to over supplement as this can have negative effects on other fat soluble vitamins (D, E and K). Following initial treatment, a discussion of future nutritional support should be entertained with the owner. For example, suggesting to gut load invertebrates or dust with vitamin powder immediately before feeding will help to ensure that appropriate forms and sufficient amounts of vitamin A are delivered (29).

#### Renal Disease

Due to their aquatic and terrestrial nature, renal and integumentary systems of amphibians are closely balanced to maintain fluid and electrolyte homeostasis (36). Because of this relationship, dermatological conditions are often the first sign noticed by owners when renal disease occurs. Affected individuals most commonly present with edema in the coelomic cavity and/or subcutaneous space due to decreased plasma oncotic pressure from protein loss and/or decreased electrolyte reabsorption in the tubules (36). Other signs include uremic ulcers, dehydration, changes in skin colour, and anorexia (37). While various infectious agents can contribute to renal disease, noninfectious causes are frequently observed in captive species due to husbandry issues (36). For example, oxalate crystal deposition in waxy monkey frogs due to oxalate rich plant ingestion or cystic calculi deposition due to uricotelism, high protein diets, dehydration and temperature fluctuations. Nephrotoxic contaminants such as heavy metals and volatile compounds in glue may also contribute to renal failure (36). Kidney function can be evaluated

based on blood sampling, with impairment suggested by increased levels of urea, Ca:P ratios <1, and hypoproteinemia. Urinalysis may also be performed for bacteria, fungi, cellular content, and renal casts to indicate renal disease (36). When edema is noted, injectable Furosemide (50 mg/kg) may be administered to help decrease fluid accumulation. Supportive care including celiocentesis, soaking in hypertonic solutions, and maintaining food intake and nutrition are also paramount to treatment (36).

# <u>Trauma</u>

Due to their thin, delicate skin, amphibians are highly prone to trauma by improper handling, abrasion on terrarium materials or decoration, and entrapment. Owners regularly bring in amphibians with injuries such as lacerations and degloving events. Fortunately, most individuals exhibit excellent innate healing abilities for skin wounds, often recovering without the need for medical intervention provided they are given optimal husbandry conditions (31). If a wound is suspected to be infected due to purulent discharge or necrosis, they should be debrided, topical antimicrobials (eg. Gentamicin or triple antibiotic ointment) should be applied, and analgesia administered (31). In cases of extensive or non-healing lesions of a limb, amputation can be considered with success (31).

# <u>Toxicosis</u>

Common toxicants for amphibians, such as ammonia and chloride, can be found in water sources. To avoid increases in nitrites, nitrates, and chlorine, enclosures must provide filtered water to amphibians, particularly frogs, who are extremely sensitive to even slight changes in these levels (2). Overexposure can lead to skin irritation and inflammation, predisposing the animal to infectious disease (2). If nitrite, nitrate and chlorine levels are high enough in the water, death is a possible outcome of prolonged exposure (2). Because of this, when presented an amphibian with signs of skin irritation, it is essential to discuss the available water source, and filtration system used. The treatment for toxicoses is supportive and involves filtration of water sources for future prevention (38).

# **Dehydration in Amphibians and Reptiles**

Dehydration is a common issue in both reptiles and amphibians. Dehydration can be either primary, due to the lack of a water source or "drying out" or secondary to other disease states and trauma. Dehydrated reptile skin may appear dull and wrinkled, with prolonged tenting, sunken eyes, and dry oral mucosa, depending on the severity of dehydration (39). Amphibians are at a higher risk for dehydration due to their permeable skin (40). Affected amphibian skin may appear tacky and dry, accompanied by dry oral mucosa and sunken eyes (39). Providing a new water source or placing the animal in a shallow level of water that is equal to their thermoneutral zone can be used to attend to reptiles and amphibians in a dehydrated state. When severely dehydrated, intravenous or intraosseous routes can be used, with the recommended fluid type varying by species (39). Compared to mammals, the plasma osmolarity of reptiles and amphibians is significantly lower. Therefore, when choosing fluids, it is important to calculate osmolarity prior to fluid therapy. Good choices for rehydration include amphibian ringers or diluted isotonic crystalloids (4).

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