Frostbite in Birds: Pathophysiology and Treatment

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ABSTRACT: Frostbite is a common problem in birds in colder climates and may also be seen with cold weather in southern climates. The pathophysiology involves both the initial freezing injury and secondary vascular impairment. Inflammatory mediators released by damaged tissue cause thrombosis. Pharmaceutical therapy should be directed toward maintaining optimal blood supply to damaged tissue, avoiding secondary infection, and providing analgesia. The line of demarcation of necrosis may take several weeks to become evident.

Frostbite is a localized tissue injury sustained as a result of cooling and thawing of tissues. Although much of the work done on frostbite has been with mammals, birds are susceptible, and it is not an uncommon injury in birds in colder climates. Risk factors in birds include unseasonable weather, use of anesthetics, use of wire caging, metal leg bands, missed migrations, and previous injury or overaggressive bandaging resulting in impaired blood supply. Nonnative species placed in colder habitats are especially at risk, and peafowl (Pavo cristatus; Figure 1) and European starlings (Sturnus vulgaris) are two of the more common species seen with frostbite in upper midwestern North America. Although the majority of frostbite cases involve the feet, a syndrome of distal wing necrosis in falcons may be due to cold injury.

PATHOPHYSIOLOGY

Numerous methods of adapting to colder environments, including arteriovenous countercurrent heat exchange and shunting via arteriovenous anastomoses, have evolved in birds. As the environment cools beyond a bird’s ability to maintain homeothermy, heat is conserved in vital organs. Initially, vasoconstriction of vessels of the extremities is seen, with regular, intermittent vasodilation to preserve tissue viability. This vasodilation is known as the hunting reflex and has been demonstrated in the feet of pigeons, ducks, chickens, and fulmars. As cooling continues, vasodilation ceases. Tissue damage occurs as a result of both direct freezing injury and ischemia resulting from impaired vascular supply (Figure 2). Initially, freezing of tissue leads to extracellular ice crystal formation. As extracellular water freezes, the osmotic gradient is altered, resulting in intracellular dehydration. As crystals become larger, direct mechanical damage to cells also occurs.

Initial freezing is typically less significant than resultant ischemic injury. Skin
transplants from frostbitten areas to undamaged areas survive, whereas healthy skin transplanted to frostbitten areas does not. Tissue ischemia occurs because of several reasons. Initially, vasoconstriction and sludging of blood results in inadequate blood supply. In a mouse model, a return of blood flow to apparent normal pre-freeze rates, followed by the onset of a gradual sludging of blood 15 to 20 minutes postthaw, was seen. Freezing, osmotic, and hypoxic damage to cells results in release of inflammatory mediators, especially by the vascular endothelium. Frostbite blisters in humans and experimentally frostbitten rabbit tissue have been shown to have markedly elevated levels of prostaglandin E2 and thromboxane B2 (a metabolite of thromboxane A2). Increased numbers of mast cells and polymorphonuclear leukocytes (PMN) are seen in frostbitten rabbit ears, and degranulation of these cells may also be a source of inflammatory mediators. Frostbitten rabbits treated at the time of rewarming, with antibodies blocking PMN adhesion, had significantly less tissue loss.

Inflammatory mediators trigger further vasoconstriction, platelet aggregation, and thrombosis, leading to a cycle of further microvascular damage, hypoxia, tissue damage, and inflammatory mediator release. Vascular inflammation and thrombosis may not be limited to the damaged extremity. Cardiac lesions have been associated with frostbite in birds. In a study of 26 birds that died because of cold injury, six (23%) had aseptic vegetative valvular endocarditis. In another study, seven of 10 birds (70%) with frostbite had myocardial, valvular, or vascular lesions. Sterile vegetative valvular lesions have also been documented in mammals subjected to cold stress.

There are significant differences between avian and mammalian coagulation. Activated partial thromboplastin times in birds are much longer than those in mammals, indicating that the intrinsic coagulation pathway in birds is much less significant than in mammals. The extrinsic coagulation pathway, which depends on tissue factor, is of primary importance in birds. Tissue factor expressed by damaged vascular endothelium may result in more significant coagulation abnormalities in birds. Alternatively, it is possible that bacterial infection secondary to frostbite leads to endocarditis. However, in one of the studies, only one of seven birds with vegetative valvular endocarditis had septic lesions.

**CLINICAL MANIFESTATION**

The most important part of frostbite diagnosis is the history. It is essential that treatment be initiated as soon as possible, before necrosis is evident. An early sign may be proprioceptive deficit of the affected extremity resulting from nerve injury (Figure 3). Pain may also be present, resulting in self-mutilation. Although cold-stressed birds have been shown to have increased levels of serum lactate dehydrogenase, uric acid, and triglycerides and frostbitten birds typically have elevated levels of aspartate transferase and creatine kinase, biochemistries are less useful for diagnosing frostbite.

In mammals, blister formation occurs during the first 24 hours. This is not typically evident in bird legs, possibly because of the anatomy of the scaled skin on the avian leg. As the injury progresses, edema may be seen within the first 24 hours. Demarcation of viable and nonviable tissue typically occurs slowly. Early detection
Figure 3—Frostbite in a hatch-year great blue heron (Ardea herodias) that has just been found recumbent in a stream during winter in Ontario, Canada. This heron had missed migration.

The line of demarcation in human frostbite may be seen with bone scanning at 7 to 10 days, whereas thermographic imaging in a rabbit ear model did not clearly delineate viable tissue until 3 weeks. According to the author’s observations, visual assessment of the line of demarcation in birds may take 3 to 6 weeks. As the line of demarcation forms, mummified tissue is evident (Figure 4).

Long-term effects in surviving tissue in mammals may include increased susceptibility to cold reinjury, sensory loss, and osteoarthritis (all of which the author has seen in birds).
Figure 4—Mummified toes on a red-tailed hawk (Buteo jamaicensis). The arrowheads indicate the line of demarcation.

TREATMENT

If tissue is still frozen at presentation, rapid rewarming in a warm (body temperature) water bath is indicated. Although past recommendations for birds have suggested more gradual rewarming, rapid rewarming has been shown to be more efficacious in mammals, and no experimental data are available for birds. Because massage is likely to cause mechanical trauma, it is contraindicated, although it has been recommended for birds in the past. Pharmaceutical therapy should be directed toward maintaining optimal blood supply to damaged tissue, avoiding secondary infection, and providing analgesia. This therapy must be initiated before microthrombi form and irreversible tissue ischemia occurs.

Administration of NSAIDs serves to block inflammatory products of cyclooxygenases, such as prostaglandin F₂α and thromboxane A₄, preventing platelet aggregation and thrombosis. Intramuscular flunixin or ketoprofen at 5 mg/kg has been shown to significantly decrease thromboxane B₂ in ducks, although flunixin resulted in significant muscle necrosis. Pharmacokinetic data suggested that administration every 12 hours might be appropriate. Negative fecal occult blood tests suggested that administration of this single dose did not produce significant gastrointestinal bleeding. Ketoprofen has also been shown to have analgesic effects in ducks at a dose of 5 mg/kg IM. In humans, treatment with ibuprofen in combination with aloe vera and penicillin resulted in less tissue loss, a lower amputation rate, and shorter hospital stays than other treatment regimens. Use of cyclooxygenase-2–specific NSAIDs is not likely to be useful; platelet thromboxane A₂ is produced primarily through the action of cyclooxygenase-1, and antithrombotic prostacyclin is primarily a product of cyclooxyge-

nase-2. Therefore, the net effect of cyclooxygenase-2–specific drugs may be prothrombotic and is not likely to have an antithrombotic effect. Further study is needed to establish the safety of multiple-dose administration of ketoprofen and the safety, efficacy, and pharmacokinetics of other NSAIDs in birds.

Pentoxifylline is a methylxanthine derivative that is commonly indicated in treating peripheral vascular disease. There are multiple mechanisms of action. Pentoxifylline increases red cell flexibility, enabling passage through damaged capillaries. Pentoxifylline also decreases reperfusion-associated membrane injury and leukocyte adhesion to ischemic tissue. Additionally, pentoxifylline may inhibit PMN-oxidative bursts in ischemic tissue, although the oxidative response of the avian heterophil is significantly less than that of the mammalian neutrophil.

In experimental frostbite using a rabbit ear model, pentoxifylline has been shown to significantly improve tissue survival, both alone and in combination with aloe vera cream. In another study using a rat foot model of frostbite, pentoxifylline in combination with aspirin significantly improved tissue survival. Extrapolating from pharmacokinetic data in dogs, pentoxifylline has been used for frostbite in birds at a dosage of 15 mg/kg PO q8–12h for 2 to 6 weeks without detection of adverse effects (author’s observations). Further study is needed to establish safety, efficacy, and pharmacokinetics of pentoxifylline therapy in birds.

Aloe vera has a long history of use in thermal burns. Topical aloe vera has been shown to significantly improve tissue survival in a rabbit frostbite model, both alone and in combination with oral pentoxifylline. Specific mechanisms of action must still be elucidated, and studies on safety, efficacy, and pharmacokinetics of specific constituents remain to be done in birds.

Because frostbite is an extremely painful condition, analgesia is essential in patients. In addition to NSAID therapy, opioids may be used. Butorphanol at 1 mg/kg IM has been shown to be efficacious for analgesia in African grey parrots.

Antibiotic therapy should be directed against common skin flora and clostridial infection; pharmacokinetic data have shown that oral clavulanic acid–amoxicillin at a dosage of 125 mg/kg q8h is appropriate in Amazon parrots. In passerine birds, clavulanic acid–amoxicillin at a dosage of 200 mg/kg q8h has been used without the detection of adverse effects (author’s observations).

Early surgical debridement is contraindicated unless uncontrolled infection is present. The line of demarcation of viable tissue may take weeks to develop. An old adage from human medicine is, “frostbite in January,
amputate in July," and current recommendations in humans are to debride mummified tissue at 4 to 6 weeks or longer.41

REFERENCES

5. ________ is an early sign of frostbite that may be seen in birds.
   a. Blistering   c. Purulent discharge
   b. Mummification d. Proprioceptive deficit

6. Proposed mechanisms of action of pentoxifylline do not include
   a. increasing red cell flexibility.
   b. decreasing ice crystal formation.
   c. decreasing leukocyte adhesion.
   d. decreasing PMN oxidative bursts.

7. Antibiotic therapy should primarily be directed against
   a. skin flora and clostridial infection.
   b. coliform bacteria.
   c. Mycobacterial infection.
   d. Mycoplasma infection.

8. Surgical amputation should
   a. occur as soon as it has been determined that frostbite injury has occurred.
   b. never occur.
   c. occur after mummification.
   d. occur after 1 to 2 weeks.

9. Frostbite diagnosis is typically based on
   a. physical examination.    c. radiographic changes.
   b. biochemical changes.    d. patient history.

10. A lesion that has been associated with frostbite in birds is
    a. proliferative ileitis.
    b. aseptic vegetative valvular endocarditis.
    c. encephalomalacia.
    d. chemodectoma.