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CRYOSURGERY IN VETERINARY DERMATOLOGY

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INTRODUCTION

Cryosurgery is growing in popularity in veterinary dermatology. This treatment modality has been around for a long time, and as equipment becomes more accessible, the popularity of this technique continues to grow. Additionally, clients are beginning to ask directly for treatments that go beyond sterile surgical steel. Learning this technique is relatively straight-forward and provides good surgical outcomes. However, it is not without potential harm to the patient and surgical team if proper techniques and standard safety protocols are not followed.

HOW IT WORKS

Cryosurgery requires application of a very cold substance (cryogen) to living tissues to induce physiological stress and destroy the tissue.[1] This ablation technique involves applying two to three rounds, or cycles, of this cryogen to the tissue to create a rapid "freeze" followed by a slow "thaw" repeatedly. Typically, the thawing portion of the freeze-thaw cycles should last about twice as long as the freezing. Keep in mind that tissue destruction occurs which will eliminate the possibility of a histopathological diagnosis. Therefore, any diagnostic procedures (e.g. fine needle aspirate, biopsy/histopathology) should be performed prior to cryosurgery.

There are several cryogens that can be used to freeze tissue, and the two most used in veterinary dermatology are liquid nitrogen and compressed nitrous oxide. To be effective at destroying the tissue, critically cold temperatures must be obtained, which are defined by the type of tumor. For the most part, lethal temperatures range from -35ºC to -60ºC for most types of epithelial tumors (most cite -50ºC as the mean critical temperature).[2] Liquid nitrogen is -196ºC (-320ºF) while nitrous oxide is -89ºC (-127ºF), so theoretically both of these cryogens should be effective at tissue ablation with proper technique.[2,3] When the tissue is exposed to the cryogen, intracellular ice crystals develop within the cells creating irreversible direct damage to critical cellular components and organelles, including the cell membrane. Upon slowly thawing the tissue, intracellular fluids leak out leading to cellular dehydration. Once the tissue thaws, water quickly re-enters the damaged cellular membranes creating swelling and cell lysis. Repeated freeze-thaw cycles induce rapid cellular damage, and apoptosis occurs within the first 12 hours. The rapid cold temperature changes also induce vasoconstriction and direct endothelial damage leading to tissue ischemia. Inflammation, vasodilation and edema develop within 3-5 days after cryosurgery and can be painful.[2-4] Post cryoablation, pro-inflammatory cytokines (IL-1b, IL-6, TNF-a) increase, changing the tumor environment towards tumor destructive TH1 immune response.[5] The coldest freezing will occur in the most superficial layers of the skin where direct contact with the cryogen takes place. This means that the critical freezing temperature required to kill tissue may not be achieved in the deeper portions of larger-sized tumors, and repeated cryosurgery episodes may be required to treat the tumor completely. In these situations, spacing out episodes for several weeks will be useful to determine the effectiveness of each treatment episode.

Healing Time – What to Expect		
Minutes	**Hours**	**Days to Weeks**
Local burning	Hemorrhagic blister	Blister sloughs
Throbbing		Crust forms
Edema		Eschar
Erythema		Heals 2-4 weeks if superficial, 6 weeks if deep

Pros	Cons
Small lesions < 2 cm require 1 treatment	Multiple treatments on large lesions

Continuous spray penetrates ~10 mm into skin	Scarring
No to minimal sedation required	Pain over nerves or boney prominences
Low cost	Avoid areas with poor circulation
Efficacious	No histopathology possible
Good cosmetic results	Bleeding, pain, and blistering post-op
Minimal wound care post-op	Training & safety considerations
Low risk for infection	Equipment sourcing – liquid nitrogen

CRYOSURGERY SAFETY CONSIDERATIONS

Cryogens are fairly easy to use but can be dangerous if not handled properly. The biggest concern is thermal injury to the skin or ocular fluids from accidental exposure during handling or treatments, and liquid nitrogen carries a higher risk potential for operator safety errors since direct contact with the cryogen is more likely during equipment transportation and preparation. Nitrous oxide usually is purchased in pre-loaded cartridges which limits direct handling contact risks.

Liquid nitrogen is considered an asphyxiation risk since it rapidly expands into a gas when it vaporizes, which reduces room oxygen. Additionally, it has no odor or color so operators may not realize room oxygen deprivation is occurring. If room oxygen drops below 19.5% from a rapid gas displacement (perhaps secondary to a large liquid nitrogen spill), this could render the operator unconscious and may result in death in extreme cases. Liquid nitrogen is stored in large containers called Dewars for long-term storage; however, it will vaporize even within these storage containers. Gas pressure may build up inside of canisters and storage devices that are improperly vented or those without properly functioning pressure relief valves, which may result in explosion.

Risk for injury is greatest when cryogens are being transferred/poured from a large storage canister into the treatment cylinders (e.g. Brymill® Cryogun). Important safety practices include using proper personal protective equipment (PPE), maintaining a well-ventilated environment, handling the cryogen slowly to avoid splashes and boiling (pour slowly when transferring into different canisters), using proper storage equipment/Dewars with functional pressure relief valves, avoiding touching non-insulated storage units ungloved as skin will get stuck to canister, filling canisters to 80% capacity to allow for expansion of gases, and avoiding storing uncovered for long periods of time. PPE used when pouring/transferring liquid nitrogen from one canister into another includes safety goggles, face shields, long clothing and closed-toe shoes/thermal safety shoes, and loose-fitting thermal insulated gloves (so that they can be removed quickly if spill into the glove occurs). PPE that should be worn when performing a treatment on an animal includes protective eyewear +/- face shield if using open-spray technique, long-sleeved protective clothing, closed toe shoes, and gloves. Wearing thermal protective gloves during treatments is usually difficult due to decreased dexterity, and the risk of injury is lower during this aspect of handling. Wearing nitrile or latex gloves will not protect from large spills but may help reduce injury from minor splatter during treatment application. All personnel handling liquid nitrogen should be trained in proper safety and handling techniques.

CRYOSURGERY EQUIPMENT AND TECHNIQUE

A common veterinary cryosurgery canister is the Brymill® Cryogun, which is equipped with a variety of removable tips/probes to allow for closed- and open-spray techniques for improved versatility and precision using liquid nitrogen. Canisters are steel and brass, insulated, and have a relief valve to provide constant, controlled pressure within the canister without the concern for pressure overload. Veterinary canisters come in large and small sizes, though the small size is generally large enough for most routine procedures. Cryoplates and Cryocones can be used to protect nearby tissue from unintended contact with the liquid nitrogen. Cryo tweezers are useful for treating skin tags in a controlled, localized fashion. Sourcing liquid nitrogen may be a limitation for smaller practices in more rural communities if a local human hospital, human dermatologist, or referral veterinary hospital is not nearby. Direct cryoprobe contact achieves deeper tissue penetration, approximately 1.3 times the radius of the ice ball (frozen tissue), compared to the spray technique, which reaches only half the radius deep into the tissue.[6]

Cryopens or cryoprobes are used in human and veterinary medicine and provide improved accessibility to cryosurgery with fewer risks associated with equipment handling since the cryogen, nitrous oxide, is stored in cartridges. There are numerous manufacturers and these units use a nitrous oxide canisters to deliver

the cryogen through interchangeable open spray tips. There are several device options each with variable power of performance. Benefits of these units include accessibility to equipment, high margin of error, low to no pain, improved safety to operator and patient, improved dexterity, ease of operation, precision, and good results for small to medium sized lesions. As with liquid nitrogen, damage to the operator or patient may occur with improper technique. Larger lesions may require more than one treatment episode. Cartridges are ordered directly from the company and are replaced routinely. The lifespan of each cartridge depends on time since it was punctured and the number and length of uses. Cartridges are stored at room temperature and reportedly maintain shelf-life after puncturing for several weeks. They are available in a variety of sizes (e.g., 8g, 16g, and 23.5g). The number of treatments available per cartridge is variable based on the device used. For example, The CryoProbe™ XP (H&O Equipments) uses a 16g cartridge and provides about 11-12 treatments for standard skin lesions, whereas the CryoProbe™ X+ uses a 16g cartridge and provides 4-6 treatments. Interchangeable autoclave-safe tips can be used to control spray over the treated area.

Cryosurgery is used in veterinary dermatology for the treatment of numerous skin tumors including both benign and malignant types.[7-11] Additionally, cryotherapy has been used in the treatment of infectious diseases such as leishmaniosis and deep fungal infections, wherein cryonecrosis of affected tissues destroys pathogens and elicits an immune response through the release of antigenic substances.[9,12] Biopsy and histopathology must be performed prior to cryosurgery to achieve an accurate diagnosis. Occasionally, cryosurgery can be combined with traditional scalpel blade surgery or CO_2 surgical laser mass removal.[13] In these techniques, the mass is marginally excised for submission for histopathology, followed by treatment with cryosurgery to kill any remaining tumor cells.

WHAT IS THE DIFFERENCE BETWEEN CRYOTHERAPY AND CRYOSURGERY?

The terms “cryotherapy” and “cryosurgery” are used interchangeably in the veterinary literature; however, the medical terms are slightly different. Cryotherapy is a broader term and is considered any medical technique that uses cryogens to treat a disease, which includes cryosurgery. Cryotherapy sometimes is used to describe treatment with a cryogen that is less intensely cold for the therapeutic treatment of pain, inflammation and swelling, and tissue recovery following injury. The proposed mechanism by which cryotherapy reduces pain and inflammation is that cryogens induce vasoconstriction, decreased blood flow to the affected area, decreased nerve conduction, decreased inflammation and swelling, decreased bleeding, and decreased pain.[14] The reduction in pain is proposed to promote a favorable environment for tissue repair and healing.[14] A practical example of using cryotherapy in everyday practice is placing an ice pack on a surgical incision to reduce inflammation and pain post-operatively. Medical devices may also be utilized including cold compression units, submersion baths, and cryopens. Cryotherapy is most effective during acute inflammatory phases of tissue healing. The effects of cryotherapy are temporary, and the treatment must be repeated to maintain the beneficial effects. Cryosurgery is a more specific surgical form of cryotherapy that uses a critically cold cryogen to destroy tissue, and this modality is primarily used to treat skin lesions that are cancerous. Cryosurgery induces cryoablation and death of living tissue.

CONCLUSION

Cryosurgery is a modality that is readily accessible in general practice, well-tolerated by patients, and easy to learn. It provides the advantages of treatment of skin masses and tumors in sites not amenable to surgical resection, particularly distal extremities, pinnae, eyelids, and the oral cavity. It is relatively affordable and requires local anesthesia and possibly sedation depending on the treatment location and surface area.

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