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TREATMENT OPTIONS FOR MELTING ULCERS IN DOGS AND CATS

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ABSTRACT

Melting ulcers are rapidly progressive corneal ulcers associated with excessive proteolytic enzyme activity leading to degradation of stromal collagen. An imbalance between collagenases and their endogenous inhibitors results in accelerated breakdown of corneal tissue, often exacerbated by secondary infections. In dogs and cats, these ulcers represent a significant clinical challenge, particularly in brachycephalic breeds, which are predisposed due to their prominent sclera and reduced blink reflex. Without early intervention, melting ulcers often progress to corneal perforation, severe visual impairment, and in some cases, the need for enucleation. Given their severity, rapid progression, and poor prognosis, prompt and aggressive treatment is essential. Therapeutic options include intensive topical therapy, various surgical procedures, and novel techniques such as cross-linking, which aim to increase stromal resistance. This review provides a comprehensive overview of these therapeutic strategies, discussing their benefits, limitations, and applicability in veterinary clinics, focusing on optimizing ocular health in dogs and cats.

Keywords: keratomalacia, cornea, canine, feline

INTRODUCTION

The treatment of corneal ulcers in dogs has evolved over time, with many veterinarians contributing to the development of effective treatments. While it is difficult to pinpoint a single individual as the "first" to treat corneal ulcers in dogs, veterinary medicine has gradually advanced with increasing knowledge about ocular conditions in animals. Historically, the treatment of corneal ulcers in animals was based largely on basic wound management and a trial-and-error approach. The American College of Veterinary Ophthalmologists (ACVO), founded in 1968, has played a key role in formalizing the field of veterinary ophthalmology. It has helped establish methods and standardize available treatment options in practice, enabling physicians to make evidence-based medical decisions.

A melting ulcer, also known as stromal liquefactive necrosis or keratomalacia, occurs acutely or with rapid progression (**Estrada *et al.*, 2013**). It is not a primary corneal disease but a complication of an existing corneal ulcer. It develops as a result of an imbalance between proteinases and proteinase inhibitors, both of which are present in the cornea and precorneal tear film as components involved in normal corneal tissue maintenance and wound healing but can also be released by neutrophils, macrophages, keratocytes, and some invading bacterial and fungal species. Dramatic liquefaction of the corneal stroma occurs when the counteracting effects of proteinase inhibitors are overwhelmed by an excess of these proteolytic enzymes (**Tsvetanova *et al.*, 2021**). Corneal ulceration can occur secondary to a variety of etiologies including conformational abnormalities, tear film deficiency, neurological dysfunction, trauma, and/or microbial contamination. Tissue lysis by enzymatic proteases is a normal part of corneal metabolism, healing, and remodeling; however, uncontrolled lysis or melting of corneal tissue as a result of excessive protease activity has the potential to cause significant pathology (**Esson and Calvarese, 2022**). Proteolytic enzymes released by bacteria and/or fungi, corneal and conjunctival epithelial cells, and leukocytes are responsible for corneal destruction. Collagenases and proteinases are normally present in the tear film and cornea in a fine balance with their endogenous tissue inhibitors and are required for normal ocular surface homeostasis. The imbalance of these enzymes with their inhibitors leads to excessive collagen destruction and corneal degradation (**Hartley, 2021**).

Melting ulcers can progress over a matter of hours (**Lim, 2023**). They usually occur in the center and/or near the center of the cornea. They rapidly spread to the remaining surface and layers of the cornea. Melting ulcers (Figure 1A, 4A) are characterized by a grey, soft, mucoid, gelatinous appearance of the cornea (**Ion and Ionascu, 2015**). The ulcer, which extends deeper into the corneal stroma, is usually associated with a secondary microbial infection that initiates stromal destruction (**Mezzadri *et al.*, 2021**), as keratomalacia is often complicated by a severe secondary bacterial infection (**Esson and Calvarese, 2022**).

Brachycephalic breeds of dogs and cats are particularly susceptible to the development of melting ulcers. This is due to shallow orbits and an excessively large palpebral fissure, which exposes the ocular surface to excessive light. Corneal ulcers can lead to scarring or perforation of the cornea and even blindness. Nasal folds also contribute to their development as their hairs irritate the corneal surface. Brachycephalic dogs are twenty times more likely to develop corneal ulcers than other breeds (**Felska-Błaszczyk and Seremak, 2021**). According to the authors of a comprehensive study conducted in England that focused on monitoring the predisposition of brachycephalic dogs to develop corneal ulcers, brachycephalic breeds were 11.18 times more likely to develop corneal ulcers than mongrel dogs, spaniels were 3.13 times more likely, and purebred dogs were 2.23 times more likely. The breeds with the highest prevalence of corneal ulcers were pugs (5.42% of affected breeds), boxers (4.98%), shih tzus (3.45%), cavalier king Charles spaniels (2.49%), and bulldogs (2.41%) (**O'Neill *et al.*, 2017**).

The diagnosis of corneal ulcers is based on their characteristic appearance. The primary treatment goals for corneal ulcers include stopping collagenolysis, controlling infection, managing intraocular inflammation, relieving ocular pain, and providing physical support to the eye. Patients should be referred to a veterinary ophthalmologist immediately. If referral is not possible or is delayed, medical treatment should be started immediately (**Lim, 2023**). Depending on the depth of the stromal defect, treatment of melting corneal ulcers may be medical or surgical (**Williams et al., 2017**). The long-term prognosis for maintaining a comfortable eye in cases of melting corneal ulcers is good if prompt referral and treatment are provided. However, there is a significant risk of globe rupture and potential loss of the eye. In addition, corneal scarring can limit vision even after the ulcer has healed. Medical management alone requires a prolonged period of treatment, often several weeks to months, for complete resolution (**Lim, 2023**).

MEDICAL TREATMENT

Acute ulcerative keratitis with progressive melting requires aggressive topical therapy. Appropriate broad-spectrum antibiotics and atropine are used (**Ledbetter and Gilger, 2013**). Treatment requires vigorous topical therapy to control infection and neutralize the activity of collagenase and other proteases on the cornea (**Whitley and Gilger, 1999**). Collagenase inhibitors counteract the damaging effects of proteolytic enzymes that destroy the corneal stroma (**Jaksz and Busse, 2017**). Anti-collagenase treatments used in veterinary ophthalmology include topical: serum, plasma, fresh frozen plasma (FFP), freeze-thaw cycled plasma (FTCP), platelet-rich plasma (PRP), ethylenediaminetetraacetic acid (EDTA),

acetylcysteine and tetracyclines (topical and/or oral) (**Hartley, 2021**). Clinically, they appear to have their greatest beneficial effect in the first 48 to 72 hours of the ulcerative process (**Whitley and Gilger, 1999**). In general, proteinase inhibitors should be instilled into the eye every 1-2 hours until healing begins, as indicated by a reduction in pain, a static or contracting ulcer, and smoothing of the epithelial margin. Thereafter, application can be reduced to four to six times per day (**Ollivier *et al.*, 2007**). Due to the high risk of eye rupture, all ophthalmic medications should be in the form of solutions rather than ointments, as ointments can aggravate uveitis if they enter the eye. Ophthalmic corticosteroids should never be used on ulcerated corneas as they interfere with healing and increase the risk of infection and corneal melting (**Lim, 2023**).

The disadvantage of medical treatment is its low efficacy and the need for constant handling by the owner. The results of topical therapy are variable and depend not only on the degree of corneal damage but also on the owner's willingness to cooperate in the treatment and ability to administer medication to the patient (**Trbolová *et al.*, 2018**). In addition to the owner's willingness and ability to comply with medication administration, the effectiveness of medical treatment is influenced by the stage of disease at which veterinary patients are presented to the ophthalmologist, antimicrobial resistance of pathogens, and challenges with patient compliance. In a significant number of cases, corneal melting leads to progressive ulceration and even perforation, necessitating globe stabilization, tectonic surgery, or enucleation. Some clinicians and owners may even feel compelled to choose euthanasia over treatment in extreme cases (**Spiess *et al.*, 2014**). Failure of the treatment can lead to loss of vision because of the evolution of keratomalacia and corneal perforation. These failures are usually managed by tectonic surgery (**Famousse, 2014**).

SURGICAL TREATMENTS

When the depth of a corneal defect is ≥ 50% of the corneal thickness, specific surgical procedures are required to prevent disease progression and reduce its duration (**Ledbetter & Gilger, 2013**). Several techniques for corneal reconstruction have been developed for use in dogs and cats (**Sanchez *et al.*, 2024**). The choice of technique depends primarily on the size, location, and stage of the ulcer, as well as the facilities available and the experience of the surgeon. All these techniques require microsurgical skills, specialized instrumentation, and an operating microscope for adequate magnification. They also require general anesthesia for the patient and are more expensive for the owner than medical treatment. The primary goal of these procedures is to restore sufficient corneal stability and, if possible, remove infiltrated and unhealthy tissue to facilitate healing (**Jaksz and Busse, 2017**). In some cases, when corneal tissue loss is significant, structural support may be required (**Hartley, 2021**), using autogenous ocular tissue, homologous or heterologous donor tissue.

Autogenous ocular tissue

The use of the animal's tissue for corneal reconstruction (autogenous ocular tissue) has several obvious advantages, including the availability of tissue without the need for a donor bank or the costs typically associated with the purchase of commercially available biomaterials, and the absence of an immune response to the tissue used. However, depending on the surgical technique chosen, tissue availability may be limited, and the donor site may be subjected to some degree of surgical trauma (**Sanchez *et al.*, 2024**). In veterinary medicine, autologous materials are used to treat melting ulcers in techniques such as third eyelid suturing across the eye, conjunctival autografting, and corneoconjunctival transposition (CCT). Corneal transplantation can also be classified as autografting if the patient's cornea is used for transplantation.

Suturing the third eyelid across the eye (preferably to the bulbar conjunctiva rather than through the upper eyelid) remains a treatment option used by some veterinarians. The major disadvantage of this technique is that the cornea cannot be observed, so the deepening of the ulcer will not be apparent until perforation occurs. If this technique is used, care should be taken to ensure that the sutures do not abrade the cornea (**Peiffer and Petersen-Jones, 2008**).

Conjunctival autografting is the most commonly used technique to treat deep corneal ulcers in dogs and cats. Its advantages include providing protection and structural support to the weakened cornea (**Peiffer and Petersen-Jones, 2008**), being free of the risk of host rejection (**Gelatt *et al.*, 2022**) and promoting healing by providing blood flow that delivers growth factors, protease inhibitors and fibroblasts, as well as facilitating access of systemic antibiotics to the defect (**Jaksz and Busse, 2017**). Conjunctival grafts are dissected pieces of conjunctiva that are transplanted into the corneal defect. They consist of either bulbar or palpebral conjunctival mucosa transplanted and sutured directly to the edges of the corneal ulcer or defect to provide additional support and tissue to a cornea weakened by deep ulceration, descemetocele and perforation with or without iris prolapse (Gelatt et al., 2022). Conjunctival grafts have been described in a variety of patterns, with the rotational bulbar pedicle graft being optimal for small animal corneas (**Wilkie and Whittaker 1997; Wanichanon *et al.*, 1996**) and the graft most commonly used by veterinary ophthalmologists. The advantages are that vision is maintained while the graft is in place, the technique can be performed to cover any part of the cornea, the graft moves about the globe no tension is created by eyelid movement and topical medications can be applied (**Damasceno and Joffily. 2023**). Conjunctival pedicle graft (Figure 1B, 2) is a surgical treatment with a successful rate exceeding 90% (**Wilkie and Whittaker 1997**). Despite these advantages, graft dehiscence can occur for the following reasons: incomplete corneal debridement, aqueous leakage, excessive tension, pedicle angulation greater than 45º to the vertical axis, presence of melting and large lesions (**Ramos et al., 2019**). Failure of a conjunctival pedicle graft has numerous causes such as poor surgical technique, including inadequate debridement of the recipient site, improper suture placement, excessive graft tension or thickness, excessive size of the graft, which overlaps the ulcer edge failing to achieve epithelial-to-epithelial apposition. Above all, failure of conjunctival pedicle graft may be caused by the use of conjunctival graft in a situation in which a corneal graft would have been more appropriate and failure to control infection (**Wilkie and Whittaker 1997; Tuntivanich et al. 2001; Soontornvipart et al., 2003**). To be effective, the graft must extend beyond the keratomalacic area. In very extensive keratomalacia, a full conjunctival graft may be preferable. The main disadvantage of conjunctival grafts is residual corneal opacity, which may affect vision, especially if the lesion is in the axial cornea or is very large (**Vanore *et al.*, 2007**).

Corneoconjunctival transposition (CCT) has been adapted from the original corneoscleral transposition described by Parshall in 1973. It consists of removing the affected corneal tissue and replacing it with a peripherally harvested corneoconjunctival graft (**Dulaurent *et al.*, 2023**). This surgical technique involves sliding transposition of the adjacent healthy cornea and attached bulbar conjunctiva, which allows a clearer visual axis compared to other surgical techniques (**Wilkie and Whittaker 1997**). CCT is a good option for treating corneal ulcers, although it can leave a scar in the peripheral cornea. Graft rejection is one of the major complications of corneal transplantation and the most common cause of postoperative graft failure. In addition, graft rejection can lead to suture dehiscence and corneal opacity (**Kim *et al.*, 2019**). This technique provides a continuous blood supply to the affected area and does not require donor material. It provides an immediate source of corneal stromal tissue to fill the defect, and this technique can be used for full-thickness lesions. An advantage of CCTs over conjunctival grafts is the superior axial transparency and therefore better preservation of vision (**Yang *et al.*, 2019**).

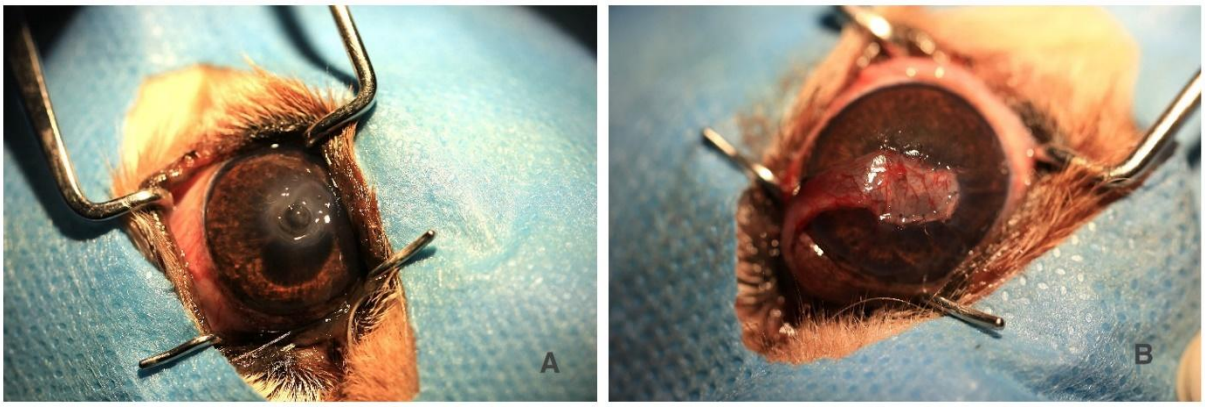

Figure 1 Melting ulcer with descemetocele in a 10-year-old Chihuahua. (A) Note the surrounding malacic corneal tissue and lack of vascular response, before surgery. (B) Surgical treatment of corneal ulceration and keratomalacia using conjunctival pedicle, immediately after surgery.

Another method of treating deeper ulcers is corneal lamellar transplantation. Fresh autologous lamellar grafts do not experience graft rejection. However, as the graft is taken from the same cornea, the area of the cornea that can be treated with this technique is necessarily limited by the amount of normal corneal tissue available (**Hansen and Guandalini, 2002**). The use of corneal transplantation (keratoplasty) to treat corneal defects in dogs and cats is not as common as in human medicine. This is partly due to cost, but also to the efficacy and versatility achieved with conjunctival autografts. Unlike humans, most animals have adequate clinical vision with less than clear corneas (**Gelatt *et al.*, 2022**).
Autologous buccal mucosa grafts appear to successfully treat severe corneal ulcers in dogs and cats, providing a useful and economical alternative to other corneal transplants (**Mezzadri *et al.*, 2021**).

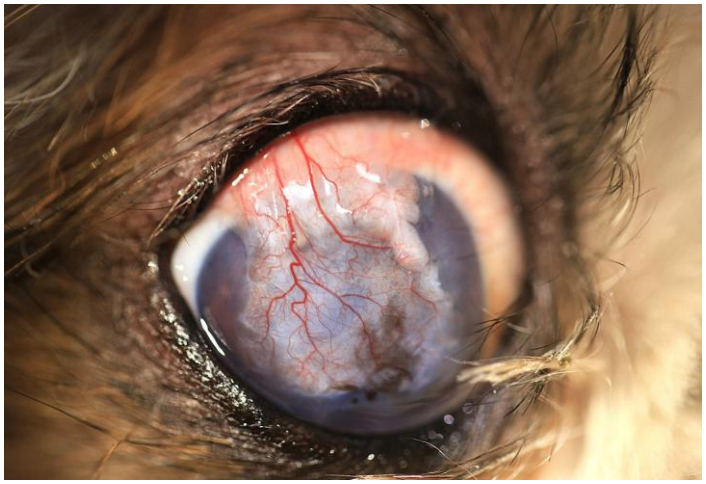

Figure 2 Right eye of a Shih Tzu dog 3 months after placing axial conjunctival pedicle flap. Cornea and conjunctival tissues are well integrated, the surrounding cornea is clear, the flap is vascularized.

Donor tissue

Homologous and heterologous donor corneas can also be used to treat corneal ulcers in dogs and cats. Based on their origin, keratoplasties can be classified as homologous corneal grafts (HoCG), homografts, or allografts when the donor tissue is obtained from an animal of the same species as the recipient, and heterologous corneal grafts (HeCG), heterografts or xenografts when the donor tissue is obtained from an animal of a different species (**Sanchez *et al.*, 2024**).
Based on the preservation method used and the length of time the corneal tissue can be viably stored, donor tissue can be classified as fresh, including 'short-term' (i.e. up to 48 h), 'medium-term' (i.e. 2-4 days) and 'long-term' (i.e. average of 25 days), and frozen, including 'very long-term' (i.e. years) (**Costa *et al.*, 2017**). Most veterinary clinics do not have the necessary equipment to maintain biological cultures, leading to a preference for very long-term preservation methods. Although not ideal, these methods account for up to 90% of canine keratoplasty procedures. Cryopreservation at sub-zero temperatures (-20°C to -30°C and -40°C) using a broad-spectrum antibiotic solution is widely used for homografts and heterografts. However, its main limitation is the loss of endothelial and epithelial cells, which limits the preserved tissue to the corneal stroma for tectonic support. Despite this, cryopreservation can potentially extend the usability of donor tissue for up to eight years without structural or microbiological problems (**Sanches *et al.*, 2024**). Fresh lamellar keratoplasty can provide good visual results, although scarring of the graft-host interface always occurs. This grafting technique provides sufficient corneas for multiple recipient eyes. By dividing the corneas into sections, there is always enough material for transplantation. The advantages of a frozen lamellar corneal graft are the tectonic support and the immediate restoration of corneal integrity. Compared to pedicled conjunctival and transconjunctival grafts, it allows vision through the graft itself **(Hansen and Guandalini, 2002**). The main obstacle to the wider use of keratoplasty in small animals is the reliable availability and storage of donor corneas **(Gelatt *et al.*, 2022**).
Many bioengineered materials have been used in veterinary ophthalmology as grafts for corneal reconstruction. These materials serve as scaffolds for cellular migration, provide tectonic tissue support, and are variably transparent, biocompatible, and biodegradable (**Ledbetter *et al.*, 2024**). The amniotic membrane (AM) is the inner layer of the fetal membranes and consists of three distinct layers: a monolayer of epithelium, the basement membrane, and the stroma. The amniotic membrane contains cytokines, proteoglycans, collagen, laminin, and fibronectin and serves as a substrate for epithelial cell growth, migration, and adhesion. It is inherently transparent, lacks immunogenicity, and possesses numerous properties that can be exploited in ocular surface reconstruction, including anti-inflammatory, antifibrotic, anti-proteolytic, antiangiogenic, and antimicrobial properties (**Baum, 2002**). This biomaterial contributes to both the cornea's structural strengthening and the healing process's acceleration. This is due to its ability to preserve the biochemical properties of the corneal material while providing essential extracellular matrix components to the damaged cornea (**Hao *et al.*, 2024**). They also promote the reduction of infection, pain, scarring, and anti-proteinase activity (**Rozin *et al.*, 2020**). Amniotic membrane transplantation materials are prepared from many species, including human, equine, canine, bovine, rabbit, and porcine sources (**Ledbetter *et al.*, 2024**). They can be used "fresh" or preserved. Several methods have been developed to preserve AM for prolonged storage, including lyophilization and cryopreservation with glycerol or dimethyl sulfoxide (DMSO) (**Yassin, *et al.*, 2021**). Cryopreservation often requires the use of specialized equipment, such as ultra-low temperature freezers, and maintaining these conditions can be a logistical challenge for transport and storage (**Ledbetter *et al.*, 2024**). Despite these limitations associated with the transport and storage of amniotic membranes, its use has great potential in the treatment of deep keratolytic ulcers.
Porcine urinary bladder acellular matrix (UBM) is a lyophilized and dehydrated extracellular matrix product derived from the lamina propria and basement membrane of the porcine urinary bladder. It is composed of collagen and growth factors. It acts as a scaffold to promote cell proliferation, integration, and tissue regeneration and is eventually degraded and replaced by host tissue (**Mancuso *et al.*, 2014**).
The porcine small intestinal submucosal (SIS) graft may be an effective alternative surgical treatment to the traditional conjunctival grafts commonly used to repair ulcers in dogs and cats. The advantages of using an SIS graft include good corneal transparency, preservation of corneal integrity, and preservation of vision (**Vanore *et al.*, 2007**). There is increasing interest in the use of SIS grafts in the surgical management of severe corneal disease. SIS is a porcine jejunum-derived biomaterial composed of three layers: the tunica muscularis mucosa, the tunica submucosa, and the stratum compactum of the tunica mucosa. A combination of mechanical and chemical methods is used to remove the serosa, muscular, and superficial mucosal layers, leaving an acellular extracellular matrix that acts as a three-dimensional scaffold for tissue repair and remodeling (**Badylak, 1993**). The SIS also contains growth factors (TGFβs, bFGF), collagen (types I, III, and V), fibronectin, hyaluronic acid, chondroitin sulfate A and heparin sulfate (**Pasquale *et al.*, 1993**). A study by **Vanore *et al*. (2007**) reported the successful use of SIS to repair melting ulcers after extensive debridement of necrotic and collagenolytic corneal tissue.
Another biomaterial that has been successfully used to treat deep or perforated corneal ulcers in dogs is acellular porcine corneal stroma (APCS). This is processed and lyophilized porcine stroma that is produced in 10mm and 12mm diameter discs, available in a range of graft thicknesses (150-600 μm) and has a relatively long shelf life. The APCS graft material is thicker and stiffer than many other biomaterials used for corneal reconstruction and has improved handling characteristics for some surgical applications (**Ledbetter *et al.*, 2024; Xu *et al.*, 2017; Hao *et al.*, 2023**). APCS may be a viable alternative to other corneal transplant procedures and is an attractive treatment option due to the readily available donor source, excellent tectonic support, and tissue biocompatibility (**Lavaud, *et al.*, 2021**).

Figure 3 Treatment of a melting ulcer in 12-year-old Persian cat using the corneal cross-linking method.

COLLAGEN CROSS-LINKING

A more recent treatment modality used in human and veterinary medicine is corneal collagen cross-linking (CXL), which uses riboflavin and UV-A irradiation to increase corneal stability (**Williams et al., 2017**). Natural covalent cross-links between corneal collagen fibers improve the biomechanical stability of the cornea. Corneal collagen cross-linking (CXL) uses riboflavin (vitamin B2), which acts as

a photosensitizer when exposed to UV-A light with a wavelength at the riboflavin absorption peak of 370 nm (Figure 3). This results in a photopolymerization process driven by free oxygen radicals that introduce additional cross-links within and between collagen fibers in the corneal stroma to a depth of 300 µm (**Spoerl et al., 2007**). The result is an increase in the biomechanical and biochemical stability of the cornea and reactive oxygen species (ROS)-induced damage to cells and microorganisms in the irradiated area. In a riboflavin-saturated cornea of ≥400 µm thickness, the UV-A irradiance generated at the level of the endothelium with the standard CXL procedure is less than half the endothelial damage threshold. All structures behind a 400-µm thick corneal stroma, including the corneal endothelium, iris, lens epithelium, and retina, are exposed to a residual UV exposure that is considered safe for these structures (**Pot *et al.*, 2014**).

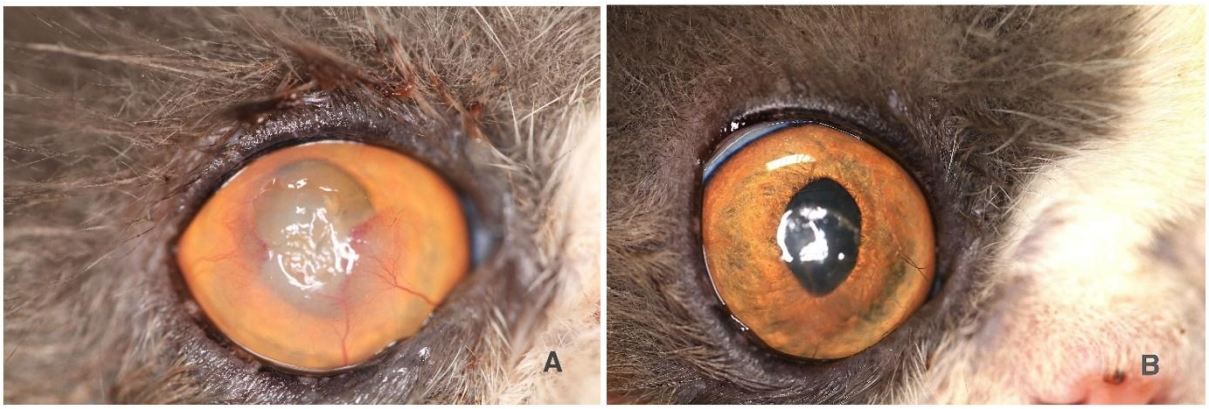

Figure 4 (A) Clinical presentation associated with stromal ulcerative keratitis with significant vascular response in the right eye of a 12-year-old cat. The cornea appears to be affected by tissue lysis and edema. The patient did not respond to conservative medical treatment. Appearance before starting corneal cross-linking treatment. (B) Appearance 28 days after corneal cross-linking treatment. Substantial enhancement in clinical condition.

As **Famose (2015)** emphasizes, the CXL procedure requires precise focusing of the UV beam, thereby necessitating general anesthesia. While the accelerated CXL protocol reduces anesthesia duration compared to the traditional approach, offering a potential practical advantage while maintaining equivalent biological effects, it is important to note that the cost of commercially available riboflavin (Vibex™) is significantly higher than that of compounded alternatives. Therefore, when selecting appropriate treatment, these factors, anesthesia requirements and financial considerations—must be carefully evaluated.

Corneal collagen cross-linking (CXL) is a viable alternative to complex surgical treatments. Unlike conservative medical therapy, which is often ineffective, CXL offers a safe and effective treatment option for keratomalacia in various species (Figure 4B), especially in light of the increasing problem of antimicrobial resistance (**Zubrický, 2021**).

This review aimed to present and evaluate various methods available in veterinary practice for the treatment of melting corneal ulcers in dogs and cats. Although there are several approaches documented in the literature for treating corneal defects, not all are applicable to corneal ulcers accompanied by keratomalacia. To the authors' knowledge, this is the first comprehensive review article that analyzes and describes the most current and effective therapeutic methods for managing melting ulcers in small animal practice, offering valuable insights to enhance clinical decision-making in the management of these complex ocular conditions.

Anatomically there are no differences between dogs and cats, in both the cornea consists of 4 layers (epithelium, stroma, Descemet membrane, and endothelium). Both cats and dogs do not have a Bowman's membrane **(Gelatt *et al.*, 2022**). The difference in the thickness of the cornea varies between species, in contrast, central thickness of the canine cornea is 138.8 +/- 9.6, while in feline patients it has 97.1 +/- 5.5 micrometers. Analysis of corneal histological and immunohistochemical in various species demonstrated differences in the distribution of cytokeratins and aquaporins suggesting species differences in the maintenance of structural integrity and fluid balance. Epithelial staining patterns varied markedly between species, and the widest distribution of aquaporins (which contribute to corneal transparency) was demonstrated in feline epithelial cell layers (**Nautscher et al., 2016**).

Corneal diseases differ between cats and dogs, especially when it comes to metabolic problems (corneal dystrophies) or autoimmune proliferative keratitis. For instance, eosinophilic keratitis in cats has never been observed in dogs. In the case of corneal defects, the methodology of treatment is very similar due to the similar pathogenesis. This means that the available methods described can be used in dogs, cats and horses, which often suffer from keratomalacia. Additionally, given the high prevalence of feline herpesvirus-1 (FHV-1) in cats, clinicians should consider the role of FHV-1 in the development of their patient's corneal ulceration and hence consider starting anti-viral therapy **(Gelatt *et al.*, 2022**). .

CONCLUSIONS

Melting ulcers are a serious problem in veterinary ophthalmology and require urgent therapeutic intervention. Their rapid progression and poor response to medical therapy make them a high-risk diagnosis, threatening both the vision and the overall health of the patient. Successful management of melting ulcers requires a thorough understanding of the available treatment options, including the advantages and limitations of each method. Several factors must be considered when selecting a therapeutic approach, including the extent of corneal involvement, the rate of disease progression, the material and technical capabilities of the veterinary facility, and the expertise of the ophthalmologist. Medical treatment is the first-line approach, but its effectiveness is often limited and highly dependent on the cooperation of the pet owner. Surgical procedures offer the potential to stabilize the cornea and preserve vision, but their success depends on the availability of specialized equipment in the veterinary hospital and the skill of the surgeon. Emerging therapies such as corneal collagen cross-linking (CXL) offer a promising alternative by improving corneal stability and reducing the risk of infection through photopolymerization. Despite current challenges related to cost and accessibility, CXL represents a significant advance in the treatment of melting ulcers and has the potential to become a valuable tool in veterinary ophthalmology.

With the development of medicine, both surgical techniques and biomaterials used in veterinary ophthalmology are evolving. Available methods, although effective in saving the eye after severe trauma, are often associated with the occurrence of secondary corneal scarring, Further research is needed to investigate and develop biomaterials that can support corneal healing without scar formation, with the potential for use in reconstructive corneal surgery. These materials would not only promote eye healing but also ensure complete restoration of vision with the minimum or lack of scar formation.

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REFERENCES

Badylak, S.F. (1993). Small intestine submucosa (SIS): a biomaterial conducive to smart tissue remodelling. Tissue Engineering: Current Perspective. (ed. E Bell) Burkhauser, Cambridge, 179–189. https://doi.org/10.1007/978-1-4615-8186-4_17

Baum, J. (2002). Thygeson lecture. Amniotic membrane transplantation: why is it effective? Cornea. 21(4), 339-341.

Costa, D., Leiva, M., Naranjo, C., Ríos, J., Peña, M.T. (2017). Cryopreservation (−20°C) of canine corneoscleral tissue: histological, microbiological, and ultrastructural study. *Vet Ophthalmol*, *11*(Suppl 1), 29-104. https://doi.org/10.1111/vop.12544

Damasceno, A.G., Joffily, D. (2023). Conjunctival Pedicle Graft for the Treatment of Deep and Perfuraded Corneal. Ulcers in Dogs. *Int J Zoo Animal Biol*, 6(4), 000499. https://doi: 10.23880/izab-16000499

Dixon, C. (2024). Corneal ulcers update in canine and feline pets. *VetTimes*. 54(9), 8-12.

Dulaurent, T., Rozoy, M., Steun, L., Isard, P.F. (2023). Multidirectional corneoconjunctival transposition in the treatment of large keratomalacia in 7 dogs and 5 cats. *Vet Ophthalmol*, *00*, 1-11. https://doi.org/10.1111/vop.12085

Esson, D., Calvarese, S. (2022). Keratomalacia ("Melting Ulcer"). In Clinical Atlas of Canine and Feline Ophthalmic Disease (eds. D. Esson and S. Calvarese).196. https://doi.org/10.1002/9781119665854.ch92

Estrada, D., Penagos, S., Viera, E., Angulo, P.A., Arias, M.P. (2013). Melting ulcer in a colt: clinical management and evolution. *Revista Colombiana de Ciencias Pecuarias*, *26*(1),31-36.

Famose, F. (2015). Evaluation of accelerated collagen cross-linking for the treatment of melting keratitis in ten cats. *Vet Ophthalmol*, *18*,95-104. https://doi.org/10.1111/vop.12112

Famose, F. (2014). Evaluation of accelerated collagen cross-linking for the treatment of melting keratitis in eight dogs. *Vet Ophthalmol*, *17*(5),358–67. https://doi.org/10.1111/vop.12085
Felska-Błaszczyk, L., Seremak, B. Negative Health Changes in Brachycephalic Dogs Resulting From Breeding Pressure– A Review. *Rocz. Nauk. Zoot*, *48*(1),15–28.
Gelatt, K.N., Shlomo, G.B., Gilger, B.C., Hendrix, D.V.H., Kern, T.J., et al. (2021). Veterinary ophthalmology. 6th (Edn.), John Wiley & Sons. ISBN 10: 1119441838.
Gelatt, K.N., Gelatt, J.P., Plummer, C.E. (2022). Veterinary Ophthalmic Surgery. Saunders Ltd. 206- 216. https://doi.org/10.1016/C2019-0-01710-4
Hansen, P.A., Guandalini, A. (1999). A retrospective study of 30 cases of frozen lamellar corneal graft in dogs and cats. *Veterinary Ophthalmology*, 2:233-241. https://doi.org/10.1046/j.1463-5224.1999.00084.x
Hao, Y., Zhou, J., Tan, J., et al. (2023). Preclinical evaluation of the safety and effectiveness of a new bioartificial cornea. *Bioact Mater*, 29:265-278. https://doi.org/10.1016/j.bioactmat.2023.07.005
Hao, L., Wei-Hsiang, H., Yi-Chen, S., Chung-Tien, L. (2024), Investigation of topical amniotic membrane suspension and ReGeneraTing Agent on early corneal stromal healing in rats. *Veterinary and Animal Science*. 24. https://doi.org/10.1016/j.vas.2024.100344
Hartley, C. (2021). Outcomes of treatments for keratomalacia in dogs and cats: a systematic review of the published literature including non-randomised controlled and non-controlled studies. *Journal of Small Animal Practice, 62*(10), 840-849. https://doi.org/10.1111/jsap.13326
Ion, L., Ionascu, I., Birtoiu, A. (2015). Melting keratitis in dogs and cats. *Agriculture and Agricultural Science Procedia*, *6*,342-349. https://doi.org/10.1016/j.aaspro.2015.08.090
Jaksz, M., Busse, C. (2017). VetTimes. Treating corneal ulceration in dogs part 2: deep ulcers. https://www.vettimes.co.uk/app/uploads/wp-post-to-pdf-enhanced-cache/1/treating-corneal-ulceration-in-dogs-part-2-deep-ulcers.pdf
Kim, S.Y., Kim, J.Y., Jeong, S.W. (2019). Long-term evaluation of autologous lamellar corneal grafts for the treatment of deep corneal ulcer in four dogs: a case report. *Vet Med-Czech*, *64*(2),84-91. https://doi.org/10.17221/139/2017-VETMED
Lavaud, A., Kowalska, M.E., Voelter, K., Pot, S.A., Rampazzo, A. (2021). Penetrating Keratoplasty in Dogs using Acellular Porcine Corneal Stroma (BioCorneaVet™): A prospective pilot study of five cases. *Vet Ophthalmol*, *24*,543-553. https://doi.org/10.1111/vop.12884
Ledbetter, E.C., Sanchez, R.F., Repiso. M.L. (2024). Reconstruction of deep and perforating corneal defects in dogs—A review (Part II/III): Biomaterials and keratoprosthesis. *Vet Ophthalmol*, *00*,1-11. https://doi.org/10.1111/vop.13287
Ledbetter, E.C, Gilger, B.C. (2013): 18. Diseases and surgery of the canine cornea and sclera. In: Gelatt KN, Gilger BC, Kern TJ (eds): Veterinary Ophthalmology. 5th edn. Wiley- Blackwell. 976–1049. ISBN 10: 1119441838.
Lim, C.C. (2022). Chapter 14. Cornea. In Small Animal Ophthalmic Atlas and Guide. Second Edition. 175-177. https://doi.org/10.1002/9781119804284.fmatter
Mancuso, L.A., Lassaline, M., Scherrer, N. (2014). Porcine urinary bladder extracellular matrix grafts (ACell vet® corneal discs) for keratomalacia in 17 equids (2012–2013). *Vet Ophthalmol*, *19*(1),3-10. https://doi.org/10.1111/vop.12240
Mezzadri, V., Crotti, A., Nardi, S., Barsotti, G. (2021). Surgical treatment of canine and feline descemetoceles, deep and perforated corneal ulcers with autologous buccal mucous membrane grafts. *Vet Ophthalmol*, *24*(6),599-609. https://doi: 10.1111/vop.12907
Nautscher, N., Bauer, A., Steffl, M., & Amselgruber, W. M. (2016). Comparative morphological evaluation of domestic animal cornea. *Veterinary ophthalmology*, *19*(4), 297–304. https://doi.org/10.1111/vop.12298
Ollivier, F.J., Gilger, B.C., Barrie, K.P., et al. (2007). Proteinases of the cornea and preocular tear film. *Veterinary Ophthalmology*, 10,199–206. https://doi.org/10.1111/j.1463-5224.2007.00546.x
O'Neill, D.G., Lee, M.M., Brodbelt, D.C., Church, D.B., Sanchez, R.F. (2017). Corneal ulcerative disease in dogs under primary veterinary care in England: epidemiology and clinical management. *Canine Genet Epidemiol*, *4*(1),171. doi:10.1186/s40575-017-0045-5
Pasquale, L.R., Dorman-Pease, M.E., Lutty, G.A. (1993). Immunolocalization of TGF-β1, TGF-β2 and TGF-β3 in the anterior segment of the human eye. *Investigative Ophthalmology and Visual Science*, *34*,23–30.
Peiffer, R., Petersen-Jones, S.M. W.B. Saunders, 2009. Small Animal Ophthalmology. A Problem-Oriented Approach Fourth Edition. https://doi.org/10.1016/B978-0-7020-2861-8.X0001-3
Pot, S.A., Gallhöfer, N.S., Matheis, F.L., Voelter-Ratson, K., Hafezi, F., Spiess, B.M. (2014). Corneal collagen cross-linking as treatment for infectious and noninfectious corneal melting in cats and dogs: results of a prospective, nonrandomized, controlled trial. *Vet Ophthalmol*, *17*, 250-260. https://doi.org/10.1111/vop.12090
Ramos, R.M.T., Rodrigues, L.M.N., Passos, Y.D.B., Palácio, L da P. (2019). Pedicled conjunctival graft in the surgical treatment of ocular perforation in a canine patient. *Science animation* (Print), *29*(S3), 41-44.
Rozin, A., Cardoso, K.M., Guimarães, T.G. (2020). Clinical Aspects of Amniotic Membrane Implants in Corneal Repair in Dogs with Complicated Ulcers. *Acta Scientiae Veterinariae*, *48*(Supl1),534.https://doi.org/10.22456/1679-9216.101085
Sanchez, R.F., Ledbetter, E.C., Leiva, M. (2024). Reconstruction of deep and perforating corneal defects in dogs—A review (Part I/III): Autogenous ocular tissues, donor tissues, and corneal clarity scoring. *Vet Ophthalmol*. *00*,1-13. https://doi.org/10.1111/vop.13286
Soontornvipart, K., Tuntivanich, N., Kecová, H., Rau, P. (2003). Conjunctival Pedicle Graft in Dogs and Cats: A Retrospective Study of 88 Cases. *Acta Veterinaria Brno*. 72. https://doi.org/10.2754/avb200372010063
Spiess, B.M., Pot, S.A., Florin, M. and Hafezi, F. (2014). Corneal collagen cross-linking (CXL) for the treatment of melting keratitis in cats and dogs: a pilot study. *Vet Ophthalmol*, *17*,1-11. https://doi.org/10.1111/vop.12027
Spoerl, E., Mrochen, M., Sliney, D., Trokel, S., Seiler, T. (2007). Safety of UVA-riboflavin cross-linking of the cornea. *Cornea*, *26*(4),385-9. http://dx.doi.org/10.1097/ICO.0b013e3180334f78
Trbolová, A., Balická, A., Lapšanská, M. (2018). Použitie rohovkového kolagénového cross linking (CXL) pri terapii infekčných a neinfekčných vredov u psov, mačky a koňa, pilotná štúdia. Vetžurnál, 02,6-12.
Tsvetanova, A., Powell, R.M., Tsvetanov, K.A., Smith, K.M. and Gould, D.J. (2021). Melting corneal ulcers (keratomalacia) in dogs: A 5-year clinical and microbiological study (2014–2018). *Vet. Ophthalmol*, *24*,265-278. https://doi.org/10.1111/vop.12885
Vanore, M., Chahory, S., Payen, G., Clerc, B. (2007) Surgical repair of deep melting ulcers with porcine small intestinal submucosa (SIS) graft in dogs and cats. *Veterinary ophthalmology*, *10*(2), 93–99. https://doi.org/10.1111/j.1463-5224.2007.00515.x
Wanichanon, C., Boonvittaya, J., Tuntivanich, N., Tuntivanich, P., Brahmasa, A., Soontornvipart, K. (1996). Conjunctival Pedicle graft in Dogs. *Thai J Vet Med*, *26*:33-49. https://doi.org/10.56808/2985-1130.1679
Whitley, RH., Gilger, BC. (1999). Diseases of the Canine Cornea and Sclera. In: Gelatt, K.N. Veterinary Ophthalmology, 3rd Ed. Lippincott Willians & Wilkins, Cap.19,635-673. https://doi.org/10.1016/S0195-5616(00)05012-9
Wilkie, D.A., Whittaker, C. (1997). Surgery of the cornea. *Vet Clin North Am Small Anim Pract*, *27*(5),1067-1107. https://doi.org/10.1016/S0195-5616(97)50104-5
Williams, D. L., Wirostko, B. M., Gum, G., & Mann, B.K. (2017). Topical cross-linked HA-based hydrogel accelerates closure of corneal epithelial defects andrepair of stromal ulceration in companion animals. *Investigative Ophthalmology and Visual Science*, *58*(11), 4616–4622. https://doi.org/10.1167/iovs.16-20848
Xu, B., Song, Z., Fan, T. (2017). Construction of anterior hemi-corneal equivalents using nontransfected human corneal cells and transplantation in dog models. *Artif Organs*, *41*(11), 1004-1016. DOI: https://doi.org/10.1111/aor.12878
Yang, V.Y., Labelle, A.L, Breaux, C.B. (2019). A bidirectional corneoconjunctival transposition for the treatment of feline corneal sequestrum. *Vet Ophthalmol*, *22*:192-195. https://doi.org/10.1111/vop.12586
Yassin, B., AbdElKader, N., AbuBakr, H., Khattab, M., Emam, I., Farghali, H. (2021). Fresh versus cryopreserved canine amniotic membrane: Physical and histological comparisons. *Veterinary Medical Journal (Giza)*, *67*(1), 174-182. https://doi.org/10.21608/vmjg.2021.212208
Zubrický, P. (2021). Liečba keratolytického vredu mačky metódou rohovkového kolagénového cross-linkingu (CXL). Treatment of keratolytic ulcers in cats with the corneal collagen cross-linking method (CXL). *Infovet*, *28*(3),123-126.