Management of Deep Corneal Ulcers

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ABSTRACT: Deep corneal ulcers are one of the most common vision-threatening ocular disorders in domestic animals. Rapidly progressing corneal ulcers—those that have progressed despite medical therapy and those that involve one-half to two-thirds of the depth of the corneal stroma—should be repaired surgically because of the danger of perforation. Both medical and surgical approaches to the management of deep corneal ulcers are reviewed. The choice of surgical procedure is determined by the location and depth of the corneal lesion, as well as by the desired optical result.

Corneal ulceration is a relatively common, potentially vision-threatening disease of the cornea of companion animals. Although many corneal ulcers are superficial and heal quickly, a progressive or deep ulcer requires more aggressive therapy.

NORMAL CORNEAL WOUND HEALING

Within 1 hour of the formation of a corneal wound, the epithelial cells lose their surface microvilli and begin to flatten in preparation for migrating to fill the epithelial defect. As the individual cells begin to migrate, fibronectin, which lines the corneal ulcer bed, helps mediate temporary transmembrane adhesions between the epithelial cells and the extracellular matrix. Contact inhibition assists in halting the migration of the cells after the defect has been corrected.

Factors that may further speed epithelialization of the wound include human epidermal growth factor, transforming growth factor-β, and hyaluronan. The presence of excessive polymorphonuclear cells associated with inflammation within the wound may slow the epithelialization process. Even though an ulcer may quickly epithelialize, the attachment of the epithelium to the underlying basement membrane may be fragile for the first 6 to 8 weeks.

If a wound extends to the corneal stroma, healing is more complicated and protracted. Because the hydrophobic barrier of the corneal epithelium is lost, fluid is imbibed by the collagen fibrils of the stroma, which results in corneal edema. Exposure of the corneal stroma results in chemotaxis of leukocytes. Within 24 hours, leukocytes from the tear film and limbus coat the bottom of...
Because the normal lamellar architecture of the corneal stroma is not preserved, transparency is lost and a scar results.

**CLINICAL SIGNS**

Animals with a corneal ulcer exhibit the classic signs of ocular pain: blepharospasm, excessive lacrimation, and photophobia. Conjunctival hyperemia and a miotic pupil may be seen as a result of reflex uveitis caused by irritation of the ophthalmic branch of the trigeminal nerve. Various degrees of corneal opacity result from edema, leukocytic infiltration, and neovascularization (Figure 1).

**ETIOLOGY**

It is always important to identify and, if possible, eliminate the cause of a corneal ulcer. The causes are numerous and include trauma, foreign bodies, diseases of the eyelashes, and anatomic deformities of the eyelids such as entropion. Exposure of the cornea because of a prominent eyelid fissure or facial nerve paralysis can also result in corneal ulceration. Decreased tear production in keratoconjunctivitis sicca can be an important contributing factor to the genesis of corneal ulcers. In cats and horses, infection of the cornea with herpesvirus may lead to ulceration. Ulcers may also occur after exposure of the cornea to caustic chemicals, such as strong acids or bases, and dysfunction of the corneal endothelium that results in diffuse severe edema may predispose an animal to develop recurrent ulcers.

**DIAGNOSIS**

A corneal ulcer is diagnosed by use of fluorescein staining. When the corneal epithelium is denuded, the hydrophilic corneal stroma interacts with the sodium fluorescein stain, which results in typical green staining in the area of the ulcer. A full ophthalmic examination, including a Schirmer tear test and assessment of the palpebral and corneal reflexes, should be performed to identify any predisposing ophthalmic conditions or concurrent ocular diseases. Ancillary tests to facilitate identification of infectious organisms that may complicate healing include culture and antibiotic sensitivity assays and cytology of the edges of the ulcer with subsequent Gram’s stain. Routine hematoxylin and eosin staining may reveal intranuclear inclusion bodies that occur with herpesvirus infection.

**THERAPY**

**Medical Management**

Medical therapy is a mainstay of the management of corneal ulcers. For superficial uncomplicated ulcers, prophylactic use of a broad-spectrum topical antibiotic assists in preventing a corneal infection from becoming established. For infected corneal ulcers, culture and sensitivity testing, as well as cytology of the ulcer edges, help guide the choice of topical antimicrobial. Frequent, up to hourly, application of a topical antimicrobial may be necessary in patients with severe corneal infection. Topical atropine to dilate the pupil is also important to prevent synechiae formation, to stabilize the blood aqueous barrier, and to relieve pain by relaxing spasm of the iridal muscles. The frequency of topical atropine application varies according to the degree of intraocular inflammation. In uninfected superficial ulcers, one to three applications may be sufficient; in more complicated ulcers, application even four to six times a day may not achieve maximal papillary dilation. Elizabethan collars, by preventing self-trauma and thereby exacerbation of the ulcer, are a useful adjunct to medical management. Systemic NSAIDs such as carprofen can help address the intraocular inflammation that accompanies severe corneal disease. Medical management alone, however, is not always successful in achieving resolution of corneal ulcers.

**Surgical Repair**

As a rule, ulcers that involve one-half to two-thirds of the depth of the stroma should be surgically repaired because of the danger of perforation. Rapidly progressing ulcers, or those that have progressed despite medical therapy, may also require surgical intervention. Various surgical techniques have been proposed for repair of deep corneal ulcers.

**Controversial Techniques**

Direct suturing of descemetoceles or deep ulcers up to 5 mm in diameter has been described, but it is not currently recommended. Use of this technique may result in distortion of the globe. Also, the cornea at the edges of the descemetocele may not be healthy enough to retain the sutures.

Third eyelid flap placement has been used in the treatment of deep ulcers in dogs. The flap helps minimize exposure of the damaged cornea by providing a physical barrier that covers the ulcer. This therapy is not ideal, however, in that it obstructs visualization of the cornea and thereby precludes frequent monitoring of
Figure 1—(A) Rapidly progressing, melting corneal ulcer illustrating conjunctival hyperemia and corneal opacity caused by edema and infiltration of leukocytes. (B) The same eye 1 week after placement of a conjunctival pedicle graft.

healing. Third eyelid flaps may even impede the efficacy of topically applied medications and trap necrotic debris on the corneal surface. In addition, third eyelid flaps do not provide a corneal lesion with a direct blood supply. Used as a sole therapeutic entity, they are of limited value and are considered by some practitioners to be potentially detrimental.

Application of ophthalmic tissue adhesive (e.g., N-butyl cyanoacrylate) has been advocated as a means of primary repair for corneal ulcers as well as corneal perforations and lacerations. Not only does the tissue glue serve to “bandage” the cornea, it also has antibacterial properties. The ulcer bed will epithelialize underneath the glue, which causes sloughing of the glue as healing progresses. It is critical that the ulcer bed be thoroughly dried before glue application. A 1-ml syringe with a 30-gauge hypodermic needle allows for precise application of a thin layer of glue to the ulcer bed. The animal must not be allowed to blink until the glue has completely dried. Although some authors advocate the use of cyanoacrylate adhesives with small descemetoceles, this use is controversial. In clinical experience, the heat caused by polymerization of the glue can be deleterious to Descemet’s membrane, and perforation can result after application of the glue to the descemetocele. Although general anesthesia may provide optimal conditions for glue application, this technique is commonly performed with compliant patients under sedation or without sedation. This method may, therefore, be an especially attractive choice for patients that are poor candidates for general anesthesia.

Conjunctival Flaps

Conjunctival flaps have been used successfully to repair deep corneal ulcers. This type of flap consists of a thin sheet of conjunctival tissue that has been cut away from the underlying episcleral fascia and pulled over the corneal defect. Conjunctival flaps can assume a variety of configurations, the size and shape of which are determined by the nature of the defect (Figure 2). All flaps provide mechanical strength to the ulcer bed by filling the defect with fibrovascular tissue.
Conjunctival flaps also provide the lesion with an immediate blood supply and a source of epithelial cells and fibroblasts, thereby facilitating healing. Conjunctival flaps provide some antimicrobial and anticollagenase or antiprotease properties as well.7

In conjunctival pedicle flaps, a strip of conjunctiva that is slightly wider than the corneal defect is cut from the conjunctiva adjacent to the limbus5,7,12 (Figures 2A and 1B). The base of the pedicle remains attached, the free end of the conjunctival pedicle is rotated to cover the corneal defect, and the pedicle is sutured to the edge of the ulcer. It is essential that the ulcer bed is free of corneal epithelium because the conjunctival flap will not adhere to any epithelialized tissue. In preparing the ulcer bed for a conjunctival flap or a corneal graft, it is important to remove any necrotic or malacic tissue from the edges of the ulcer. Absorbable suture material is most commonly used to secure the pedicle, thereby obviating the need for suture removal. For dogs and cats, 7-0 to 9-0 polyglactin 910 (Vicryl, Ethicon) on a micropoint spatula needle is often chosen, whereas 6-0 to 7-0 polyglactin 910 may be selected for horses.2 The suture pattern may be a simple interrupted, a simple continuous one, or a combination of the two patterns. Sutures should be placed at least two-thirds into the depth of the corneal stroma without penetrating the full thickness of the cornea. All varieties of conjunctival flaps typically result in significant scarring of the cornea.3,5,12 This scarring is confined to the nonepithelialized area that has been covered by conjunctiva.

Conjunctival “hood” flaps are created by making a single incision in the conjunctiva adjacent to the limbus, undermining the tissue, pulling the conjunctiva down to cover the defect, and suturing it to the opposite edge of the defect7 (Figure 2B). Hood flaps are particularly suited to peripheral or perilimbal corneal defects.3 Another variation of the conjunctival flap is the bridge flap (Figure 2C). In bridge flaps, two incisions parallel to the limbus are made for approximately 180° so that both ends of the flap are left attached to the globe.7 The strip of tissue is freed from the underlying fascial attachments and pulled centrally to cover the defect. This type of flap is especially useful for providing additional support to linear corneal lesions such as lacerations.3

Severing the blood vessels supplying both conjunctival pedicle flaps and bridge flaps is recommended at approximately 3 to 8 weeks to allow atrophy of the grafted tissue and decreased scar formation.3,5 The hood flap, in contrast, may be left in place permanently if it does not pose a significant obstruction to vision.

Another variant flap is the 360° or total conjunctival flap, which can be used for extensive lesions of the cornea. In this flap, the conjunctiva is incised circumferentially at the limbus, undermined, pulled together in purse-string fashion over the cornea, and sutured to itself (Figure 2D). The conjunctival tissue will adhere to the cornea where the epithelium is absent. This technique is easy to perform because direct suturing to the cornea is not required. Graft failure may be increased with this technique because direct conjunctiva to cornea apposition is not achieved by suturing.7 Additional disadvantages of this flap include the fact that vision is severely, if not totally, compromised in the operated eye during the healing period. Furthermore, monitoring of the eye during the healing phase is not possible because of obstruction by the flap.3 Some authors assert that the delivery of topical medications is impeded by 360° flaps.7 General anesthesia is usually required a second time to cut the flap free from the cornea. Usually, a large corneal scar remains after the cornea has healed. This scarring may be a reflection of the fact that the initial corneal lesion is extensive when a 360° flap is chosen.

Island Graft

The conjunctival island graft is a variant of a conjunctival flap.15 In the island graft, the attachment of a piece of bulbar conjunctiva to the globe is severed, creating a free “island” of conjunctival tissue (Figure 2E). The diameter of the island of conjunctival tissue should be slightly larger than the diameter of the corneal defect. The island of tissue is then sutured to the defect, thereby serving a tectonic purpose. Another option is a tarsoconjunctival graft, harvested from the center of the upper eyelid of the affected eye. An inherent blood supply is not provided with either type of island graft; instead, the graft
eventually becomes vascularized by means of corneal neovascularization. Island grafts may result in less dramatic scarring of the cornea than that seen with conjunctival flaps. However, because island grafts do not provide a ready blood supply, they are not as efficacious as flaps for infected ulcers.7

**Keratoplastic Procedures**

The use of various keratoplastic procedures for repair of deep corneal ulcers has also been described. Grafts used in these procedures are classified according to the source of the grafted tissue, as autografts, allografts, or xenografts. An autograft is composed of tissue from the same animal, whereas an allograft consists of tissue from an animal of the same species. A xenograft is composed of tissue from an animal of a different species; the term *xenograft* is also used to indicate graft material that is not of corneal origin (e.g., porcine small intestinal...
submucosa). Grafts are also defined according to the extent of the cornea that is replaced (e.g., lamellar versus penetrating). Lamellar grafts are partial-thickness grafts, whereas penetrating corneal grafts replace a full-thickness piece of cornea. Another consideration affecting keratoplastic procedures is the manner in which the graft has been stored. Is it frozen? Has it been stored in specialized tissue medium? Is it fresh? All these factors—source of tissue, extent of cornea replaced, type of graft storage—play a role in determining the optical clarity of the resultant graft.

Corneal tissue is obviously the most physiologic choice for grafting into a diseased cornea. Compared with conjunctival flaps or xenografts consisting of non-corneal tissue, grafts of corneal origin are expected to minimize scarring. Corneal transplantation has become common in human ophthalmic practice, but it is not used routinely in veterinary ophthalmology. There are several explanations for this difference. First, accessibility to fresh donor material is limited in veterinary practice. The practice of eye banking requires a well-developed system of communication and network of persons involved in the collection of cadaver eyes. Corneal storage materials are expensive. Because of difficulties in harvesting and maintaining a supply of fresh donor corneas, frozen corneal tissue has been used.2,16,17 These corneas are stored in antibiotic solution in the freezer section of a standard refrigerator. The corneas can be stored for months (possibly years) and still serve as a tectonic graft for a corneal defect. Unfortunately, corneal endothelial and epithelial cells do not survive frozen storage. Because these cells are vital for maintaining corneal clarity, grafts lacking the cells are often opaque.

Corneal grafting of any variety, partial thickness or full thickness, necessitates the use of microsurgical instruments and adequate magnification, preferably provided by an operating microscope. The surgeon must also be skilled at microsurgery, with a thorough understanding of microsurgical techniques and procedures.

Partial-thickness (i.e., lamellar) keratoplasty has been described for repair of deep ulcers, descemetoceles, and perforated corneas.3,18,19 In these and other keratoplastic procedures, as for conjunctival flaps and grafts, the ulcer bed must first be debrided of any necrotic or unhealthy tissue. A partial-thickness piece of cornea is sutured directly over the corneal lesion, thereby providing mechanical support to the diseased area. The potential sources of donor tissue include self (autogenous lamellar keratoplasty), another animal of the same species (allogenic lamellar keratoplasty), or possibly an animal of another species (lamellar keratoplasty with xenograft).

Corneoscleral or corneoonconjunctival transpositions are similar to autogenous lamellar grafts, except that the grafts remain attached to their original base.3,20 In corneoscleral transpositions, a partial-thickness strip of cornea and adjacent sclera is advanced into the defect and sutured in place. Corneoscleral transpositions are particularly suited for repair of a central corneal defect. Clear, healthy cornea from a peripheral area is used to repair the central diseased region, thereby attempting to preserve the clarity of the visual axis. Because tissue from the same animal is used, concern about rejection of the graft is reduced. Also, fresh corneal tissue is advanced into the defect, thereby theoretically reducing the amount of scarring.

Penetrating keratoplasty employs a full-thickness graft of corneal tissue, either fresh or frozen, to correct a full-thickness corneal defect.3,16,17,21–24 Penetrating keratoplasty may be used to repair deep corneal ulcers or descemetoceles, to excise corneal stromal abscesses in horses (Figure 3) or corneal sequestra in cats, and to provide a clear visual axis in severely scarred or edematous corneas. A corneal trephine is used to prepare both the donor and the recipient bed. Typically, the diameter of the trephine used to harvest the donor corneal tissue is slightly larger (0.2 to 0.5 mm) than that used to prepare the recipient bed to allow slight shrinkage of the donor graft.3 Viscoelastic materials can be used intraoperatively to fill the anterior chamber and prevent its collapse until the donor cornea is sutured in place.3

**Xenografts**

Because of the difficulty and expense of obtaining and storing fresh donor corneas of the same species to be used in keratoplastic procedures, alternative tissues have been proposed as graft materials. Experimental penetrating keratoplasty has been performed with fresh porcine corneal tissue but resulted in vascularization and opacification in almost all cases.30 Equine amnion and equine renal capsule have been used to repair corneal defects in dogs.26–28 The cartilage of the third eyelid has also been described as a possible xenograft for corneoscleral defects.30 Other tissues that have been applied in human surgical procedures include split-thickness dermal grafts30 and peristomal-fascia temporalis pedicle flaps.31

Perhaps the most commonly used xenograft today is a biomaterial manufactured from porcine small intestinal submucosa (Vet Bio SIS T, Cook Veterinary Products). It is theorized that the submucosa provides a dense acellular collagen matrix that serves as a scaffold ingrowth of cells, in this case, keratocytes. Vet Bio SIS T has been used with a conjunctival graft in the repair of a corneoscleral defect in a dog.12 Other authors have used this material in cats as a lamellar graft for deep corneal ulcers with minimal scarring.30 We have used this product to replace corneal tissue after excision of corneal stromal abscesses in horses. We have also used it in conjunction
with a conjunctival pedicle flap to repair very deep or perforated ulcers in dogs, cats, and horses. In eyes with perforating ulcers, a conjunctival pedicle graft does not always prevent the leakage of aqueous humor because sutures are not placed around the entire circumference of the lesion. When the Vet Bio SIS T graft is placed in the ulcer bed, it can be circumferentially sutured to achieve a watertight seal. The addition of the conjunctival pedicle over the submucosa graft then facilitates growth of blood vessels, which speeds healing and resolution of a corneal infection, if present. Compared with other xenografts, Vet Bio SIS T used alone may result in less significant scarring. Further controlled studies are warranted to document the usefulness and tissue reactions to these xenografts.

Postoperative Care

Postoperative care of these eyes, regardless of the surgical procedure performed, is similar to postoperative care of deep corneal ulcers that have been treated by nonsurgical means. For tissues to heal well after surgery, infection must be aggressively controlled by topical use of antimicrobials. Both medical and surgical therapy can have a role in the management of deep corneal ulcers. Often, a combination of both approaches is necessary to effectively treat ulcers that are deeper than one-half to two-thirds of the depth of the stroma, are rapidly progressing, or do not respond to medical therapy alone. The various surgical procedures can be tailored to suit the location and depth of a particular lesion, as well as to achieve the desired optical result.

ACKNOWLEDGMENT

The authors would like to thank Drs. Will Eward, Stephen Swaim, and James Winkler for their review of this manuscript.

REFERENCES

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The article you have read qualifies for 1.5 contact hours of Continuing Education Credit from the Auburn University College of Veterinary Medicine. Choose the best answer to each of the following questions; then mark your answers on the postage-paid envelope inserted in Compendium.

1. Possible indications for surgical management of corneal ulcers include all of the following except
   a. a rapidly progressing corneal ulcer.
   b. an ulcer that has not responded to medical therapy.
   c. an ulcer that has eroded one-half of the depth of the corneal stroma.
   d. an ulcer that has abundant corneal neovascularization.

2. Which of the following is not an advantage of conjunctival flaps?
   a. They provide increased mechanical strength to the ulcer bed.
   b. They cause decreased scarring of the cornea compared with that achieved by medical management.
   c. They are a source of anticollagenases and antiproteases from serum.
   d. They provide a source of fibrovascular tissue to line the ulcer bed and fight infection.

3. The main disadvantage of conjunctival flaps is
   a. opacification of the graft site that can interfere with vision.
   b. the high rate of dehiscence.
   c. the high rate of corneal perforation during surgery.
   d. the prolonged period until the flap heals in the corneal ulcer bed.

4. Which of the following is not considered an advantage of frozen corneal tissue used in grafts?
   a. graft clarity once healing is complete
   b. stronger wound closure compared with conjunctival grafts
   c. decreased scarring compared with conjunctival grafts
   d. inexpensive storage in the freezer section of a standard refrigerator

5. What is the main disadvantage of frozen corneal grafts?
   a. the need for microsurgical instruments and clinician experience in microsurgical technique
   b. the need for expensive corneal storage media that must be replaced frequently
   c. a high rate of wound dehiscence
   d. the need for extensive tissue typing

6. Cyanoacrylate ophthalmic tissue adhesive can be employed in which of the following situations?
   a. extensive perforating corneal lacerations
   b. corneoscleral lacerations
   c. temporary tarsorrhaphy
   d. deep stromal ulcer

7. Which of the following is not considered a problem of direct suturing of descemetoceles?
   a. Distortion of the globe is possible.
   b. Unhealthy edges of the descemetocele may not be strong enough to retain sutures.
   c. With large descemetoceles, the sutures may be under substantial tension.
   d. Substantial corneal scarring may result.

8. Which of the following is not considered an advantage of corneoscleral transpositions?
   a. The central visual axis is preserved.
   b. Peripheral corneal scarring is substituted for central corneal scarring.
   c. Autogenous corneal tissue is used, thereby reducing the potential for scarring.
   d. The potential for scarring is reduced because full-thickness tissue is used.

9. Which of the following does not characterize medical therapy for deep corneal ulcers?
   a. Culture and sensitivity testing help in determining the proper choice of antimicrobial.
   b. Aggressive medical therapy is often required in addition to surgical therapy.
   c. Cytology and Gram’s staining are useful for determining the initial choice of antimicrobial, until results of definitive testing become available.
   d. Surgical therapy often obviates the need for intensive medical therapy.

10. Possible causes of corneal ulcers include all of the following except
    a. prolonged exposure to ultraviolet light.
    b. keratoconjunctivitis sicca.
    c. viral infections.
    d. trauma.