

Back to Basics: Diagnostic and Treatment Recommendations for Superficial Ulcerative Keratitis

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Introduction

Ulcerative keratitis is one of the most common causes of ocular discomfort in both canine and feline patients. Although treatment plans can vary depending on species and type of ulceration, principles of superficial corneal ulcer management have been well established among veterinarians. However, superficial does not mean simple. Not all superficial corneal ulcers will heal in a timely manner or without complication. In addition, treatment recommendations are changing as antibiotic resistance has surfaced in the ophthalmology community. Therefore, this article will review tips and tricks to keep in mind during the initial and recheck exams and current treatment recommendations for non-healing and potentially infected superficial corneal ulceration.

Initial examination and diagnostic testing

Most pets with ulcerative keratitis are in significant pain. Although topical anesthetic medication (i.e. proparacaine or tetracaine) can help decrease this discomfort, consider administering an injectable opioid, such as buprenorphine or methadone, to improve comfort and compliance. Other opioids such as butorphanol and hydromorphone should be avoided, if possible. Specifically, butorphanol decreases pupil size, thereby interfering with the retinal exam and also affects tear production and intraocular pressure.(1-3) Hydromorphone should not be used as this opioid commonly induces vomiting, which could result in rupture of a deep corneal ulcer. By utilizing appropriate pain management protocols, a thorough and most importantly fear-free examination can be performed, in addition to important diagnostic testing.

After pain medications are administered, the next step should be a neuro-ophthalmic examination. Minimally, the neuro-ophthalmic exam should include menace response, direct and consenting pupillary light reflexes (do not forget about the consenting!), dazzle reflex and palpebral reflex. As a reminder, if the patient is non-visual in the affected eye and has negative direct and consenting pupillary light reflexes and negative dazzle reflex, prognosis for vision is poor, and depending on severity of the ulcer, enucleation may be considered.

It is also strongly recommended to assess tear production and intraocular pressure prior to applying fluorescein stain. These components of the minimum ophthalmic database are just as important as, if not more than, the fluorescein stain test in patients with corneal ulceration. Keratoconjunctivitis sicca often results in the delayed healing of corneal ulcers. The buphthalmos, corneal edema and/or decreased corneal sensitivity of glaucomatous globes can

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promote corneal ulcer formation, especially in the axial cornea. The diagnosis of other ocular comorbidities will not only guide treatment recommendations but will impact client education.

Now for the remainder of the ocular exam and assessment of the corneal ulcer. At this point, the following should be determined:

- 1. Depth of the corneal ulcer
- 2. Presence of a secondary infection and/or a much needed vascular response
- 3. Concurrent eyelid abnormalities such as an eyelid mass or entropion that may account for the corneal ulcer formation
- 4. Presence of reflex uveitis (miosis, hypopyon, hyphema and/or flare)

Collectively, the neuro-ophthalmic and ocular exam findings and results of the minimum ophthalmic database will determine treatment plans and referral recommendations.

Medical management for superficial corneal ulceration

Most superficial corneal ulcers that are not infected typically heal within 72 hours with (and sometimes without) medical management. In these cases, the treatment plan should include:

- 1. Topical antibiotic solution or ointment, with the choice of solution or ointment made by the client (i.e., which formulation will be easier to administer). Anecdotally and in the literature, resistance has been observed (see below) to certain ophthalmic antibiotics, and judicious antibiotic use is recommended.
- 2. Topical atropine or tropicamide if reflex uveitis is present. However, if intraocular pressure is at the high end of normal range use topical cycloplegics judiciously, and do not use either medication in glaucoma patients. If IOP is at the high end of normal range, a dose of topical atropine can be administered in hospital (rather than dispensed for daily use at home).
- 3. Topical lubricant. Although seemingly unnecessary in the face of reflex tearing, topical lubricants have been shown to stabilize the pre-corneal tear film and accelerate corneal wound healing.(4-6) They may also help improve comfort.
- 4. **Systemic** non-steroidal anti-inflammatory and analgesic medications to help decrease inflammation and discomfort. Topical non-steroidal and steroidal medications should never be used in patients with ulcerative keratitis.
- 5. Systemic or topical anti-viral medication in any feline patient with a corneal ulcer. In a recent review article from UC Davis, the recommended famciclovir dose is 90 mg/kg, q12hr.(7) However, most clients find it difficult, if not impossible, to treat with famciclovir due to its large size and need for frequent administration. Therefore, although more expensive, topical anti-viral medications may be preferable. Topical cidofovir (0.5%, q12hr) or idoxuridine (0.1%, q4-6hr) can be formulated by

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- compounding pharmacies such as Stokes or Wedgewood and sent directly to the client.
- 6. A plastic, firm Elizabethan collar is a must for all canine patients. An inflatable or foam cone is unacceptable as dogs will still be able to rub their faces/eyes against pillows, blankets or rugs. Anecdotally, I find that most feline patients do not rub at their corneal ulcers. Therefore, I do not use E-collars as often in cats with ulcers, unless clients report self-trauma, or a deep ulcer is present.

In dogs, most superficial corneal ulcers will re-epithelialize within 3-4 days, so typically I recommend a recheck in 5-7 days. Because feline herpes virus (FHV) can play a role in ulcerative keratitis in cats and clinical signs associated with FHV can take 2-4 weeks (or longer) to improve, I recommend starting with a 2 week recheck for feline patients.

Management of refractory superficial corneal ulceration in dogs

It is always frustrating to find that a corneal ulcer is persisting at the first recheck. If no additional ophthalmic abnormalities are noted, the ulcer remains superficial and non-infected and has a redundant epithelial margin, then the ulcer is likely a spontaneous chronic corneal epithelial defect or SCCED. Although exact pathophysiology is unknown, it is hypothesized that SCCEDs are the result of an acellular hyalinized stromal membrane and atypical/dysplastic epithelial cells.(8) Therefore, a variety of techniques have been developed to remove both the membrane and abnormal cells, including cotton tip applicator (CTA) debridement, burr keratectomy, grid keratotomy, combination of burr keratectomy and grid keratotomy, anterior stromal punctate keratotomy, thermokeratoplasty, corneal glue placement and superficial keratectomy.(9-13) Reported success rates of 75-90% are quite similar among most of these techniques (9-12, 14) with CTA debridement having the lowest success rate of 20-50% and superficial keratectomy having the highest success rate approaching 100%.(15) The preferred treatment method is dependent on training and resources. Following these procedures, a contact lens is also typically placed to improve patient comfort and medical management is continued for 2-3 weeks as described above. These ulcers need time to heal, so repeat debridement is recommended only if appropriate duration of time has passed. If debrided every few days, then the SCCED may never heal.

Success rate is also dependent on appropriate case selection as not all refractory ulcers are SCCEDs. Therefore, before you pick up your cotton tip applicator, 27 gauge needle or algerbrush, reassess your patient and repeat the ocular exam. Is there a cellular infiltrate or yellow discoloration in or around the ulcer? If so, a secondary infection may now be present as show in Figure 1a. Is the ulcer no longer superficial (Figure 1b)? Is there a mass (Figure 1c) or eyelid abnormality that may be mechanically debriding the ulcer and therefore, preventing healing? You may consider rechecking tear production. Even though only a week has passed, it is possible the patient has developed a quantitative or qualitative tear film deficiency and is in

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need of a tear stimulant such as tacrolimus or cyclosporine, which can be used safely in non-infected corneal ulcers.

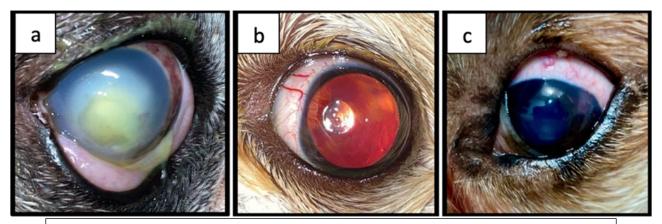


Figure 1a. Infected corneal ulcer; note the yellow-green discoloration of the ulcer bed typical of a bacterial keratitis. Figure 1b. Corneal ulcer with approximately 80% stromal loss; there is no evidence of infection. Figure 1c. Non-healing ulcer in the lateral cornea secondary to upper eyelid tumor

Therefore, be certain that the ulcer is a SCCED (Figure 2a) prior to performing one of the above techniques. Otherwise, the patient may return with a descemetocele, keratomalacia or even a corneal rupture. However, even when performed appropriately, there is a small risk of infection with any of the above treatments, especially in brachycephalic patients (Figure 2b).

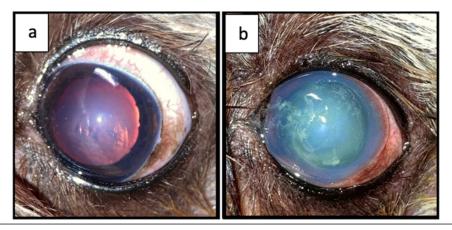


Figure 2a. Superficial non-healing ulcer with redundant epithelial margin characteristic of a SCCED in a Shih tzu. Figure 2b. Same eye as shown in Figure 2a, one week post burr keratectomy; patient has now developed diffuse keratomalacia, reflex uveitis and secondary glaucoma. Tobramycin was utilized prior to referral and post keratectomy



Management of refractory superficial corneal ulceration in cats

CTA debridement and burr keratectomy are typically not recommended in feline patients. The corneal ulcer may be persisting due to underlying infectious keratoconjunctivitis. Inappropriate debridement may also delay corneal wound healing and lead to sequestrum formation (Figure 3). That being said, select cases may benefit from corneal debridement or superficial keratectomy and contact lens placement and should be referred to a veterinary ophthalmologist for evaluation.



Figure 3. Corneal sequestrum developed following chronic corneal ulceration in one year old brachycephalic cat.

Antibiotic selection for corneal ulceration

The goal of antibiotic therapy in a superficial corneal ulceration is to prevent infection. However, even with appropriate medical management, secondary infection can occur. The most common bacteria isolated from infected corneal ulcers include *Streptococcus* spp., *Staphylococcus* spp. and *Pseudomonas* spp., and unfortunately, antibiotic resistance among these isolates is becoming a critical problem in veterinary ophthalmology.

Most reports describing antimicrobial susceptibility in bacterial keratitis focus on canine patients. For instance, methicillin resistance was noted in approximately 24% of staphylococcal isolates from dogs with ulcerative keratitis. Not surprisingly, dogs belonging to veterinary and other medical/health care professionals were four times more likely to have methicillin resistant staphylococcal keratitis.(16) *Staphylococcus* spp. and *Pseudomonas* spp. isolated from canine corneal ulcers have shown significant increases in MIC values over time for commonly used antibiotics such as erythromycin (*Staphylococcus* spp.) and moxifloxacin (*Pseudomonas*

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spp).(17) Additionally, chronic topical fluoroquinolone use in dogs can affect the ocular flora, promote resistance to ofloxacin and increase MIC values not only for other fluoroquinolones but also for other antibiotics.(17, 18) Finally, bacteria have been isolated from SCCEDs in dogs that were receiving topical antibiotic medications prior to burr keratectomy, with tobramycin being the most common antibiotic used in indolent ulcers with bacterial isolates.(19)

At this time, antibiotic resistance may be less prevalent in feline bacterial keratitis. Although *Staphyloccocus* spp. is still one of the most common isolates, these bacteria in cats are still highly susceptible to ofloxacin, ciprofloxacin, gentamicin and moxifloxacin.(20)

In addition to the antibiotic resistance arising in *Staphylococcus* spp. and *Pseudomonas* spp., treatment plans also need to address atypical infections as a variety of other bacteria have been reportedly isolated. Therefore, corneal cytology and culture should be performed to identify the causative pathogen and help guide antimicrobial therapy. However, culture and sensitivity results can be delayed by several days and so empirical broad spectrum antibiotic therapy must be started while results are pending. With emergent antibiotic resistance in mind, empirical antibiotic recommendations are as follows:

- a. Dogs:
 - i. Neomycin polymyxin B bacitracin
 - ii. Neomycin polymyxin B gramicidin
 - iii. Gentamicin
 - iv. +/- Tobramycin (may be beneficial in cases of suspected *Pseudomonas* keratitis)
- b. Cats:
 - i. Erythromcyin
 - ii. Ofloxacin
 - iii. Ciprofloxacin (although anecdotally may causes ocular irritation)

**Please note that any antibiotic containing polymyxin B (NPB, NPG or terramycin) should be used cautiously or not at all in cats due to potential for anaphylaxis.(21)

Conclusion

Although prognosis for most superficial corneal ulceration is fair to good, these cases can be frustrating to you, the patient and the owner. But, with a thorough exam, thoughtful antibiotic selection and appropriate recommendations for ancillary procedures and/or referral, you can limit a patient's duration of discomfort and subsequently the duration of time in the dreaded E-collar. Most importantly, you can limit antibiotic resistance of ocular pathogens. However, if the ulcer is persisting or developing a secondary infection, do not hesitate to reach out to your local, board-certified veterinary ophthalmologist for advice or to discuss referral.

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