Abstract

Indolent corneal ulcers—also known as refractory ulcers, "boxer" ulcers, spontaneous chronic corneal epithelial defects, and recurrent erosions—are a special type of superficial ulcer. They are always nonhealing, superficial corneal ulcers with loose edges and can have varying amounts of ocular discomfort, a characteristic "halo" stain pattern, and corneal vascularization. Indolent ulcers are never infected. It is critical to rule out other underlying causes before diagnosing an indolent ulcer. Always look for reasons that an ulcer may not be healing. As with many ophthalmic conditions, indolent ulcers can often be managed in a primary care setting. However, accurate diagnosis, appropriate therapies, and proper postoperative care are critical for successful outcomes. A variety of medical and surgical options are available for the treatment of indolent ulcers in a general practice setting, including cotton-tipped applicator debridement, grid keratotomy, and diamond burr debridement.

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OPHTHALMOLOGY

When Is It Indolent? Diagnosis and Treatment of Indolent Corneal Ulcers

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The cornea is the transparent, anterior portion of the fibrous tunic of the globe. Damage to the cornea, resulting in epithelial cell loss with exposed corneal stroma, creates an ulcer on the corneal surface. Squinting (blepharospasm) or holding an eye shut and tearing (epiphora) are often the signs owners will first notice in pets with corneal ulcers. Fluorescein stain uptake in the ulcerated region confirms the diagnosis of an ulcer. Categorization of the ulcer is based on a combination of clinical signs and visual inspection of the eye.

Indolent corneal ulcers, also known as refractory ulcers, "boxer" ulcers, spontaneous chronic corneal epithelial defects (SCCEDs), and recurrent erosions, are a special type of superficial ulcer that fails to resolve through the normal wound-healing process.[1] Hallmark clinical and histologic features of SCCEDs include a superficial corneal ulcer that (1) does not extend into the stroma; (2) is associated with redundant, nonadherent corneal epithelial borders that may be associated with an acellular hyaline zone in the anterior stroma; (3) persists

Take-Home Points

- Indolent ulcers can often be managed in a primary care setting.
- Accurate diagnosis, appropriate therapies, and proper postoperative care are critical for successful outcomes when treating indolent ulcers.
- A variety of medical and surgical options are available for the treatment of indolent ulcers in a general practice setting.
- It is critical to always numb the eye thoroughly with an appropriate topical anesthetic (e.g., proparacaine ophthalmic solution) prior to performing any of the described surgical procedures (i.e., cotton-tipped applicator debridement, grid keratotomy, diamond burr debridement).
- Only allow sterile instruments to touch the surface of the eye due to the open wound/active ulcer.
- Indolent ulcers are never infected. Ulcers that are infected must be treated differently.
- A grid keratotomy should never be performed in cats due to the risk of corneal sequestrum formation.
- Placement of an Elizabethan collar is always recommended until the ulcer is healed.

for weeks or months if not adequately addressed; and (4) may or may not include neovascularization and edema.[2-8]

The underlying pathophysiology of SCCEDs is not completely understood, and there is some thought that these ulcers may be the shared end result of a variety of pathways.[1] Ultimately, indolent corneal ulcers result from dysmaturation of corneal epithelia that do not properly attach to the underlying stroma of the eye, creating a lesion composed of loose, poorly adhered epithelia overlaying corneal stroma (lipping).[1,9]

Nonhealing ulcers are often incorrectly labeled as "indolent" without exclusion of other causes of improper healing first, which can lead to inappropriate treatments and catastrophic consequences for the affected eye. Possible underlying issues that could be the cause of a nonhealing ulcer aside from the category of "indolent" include infection, tear film deficiencies (qualitative or quantitative), exposure due to conformation or buphthalmia, a foreign body, an eyelid mass, aberrant hairs (ectopic cilia, distichia, trichiasis), and entropion.[2] *It is critical to rule out underlying causes* ***before*** *a diagnosis of an indolent ulcer. Always look for reasons that an ulcer may not be healing, especially in younger animals.*

As with many ophthalmic conditions, indolent ulcers can often be managed in a primary care setting. However, accurate diagnosis, appropriate therapies, and proper postoperative care are critical for successful outcomes. This article discusses diagnosis of indolent ulcers, treatment options, and conditions for referral.

DIAGNOSIS

Indolent corneal ulcers are always nonhealing, superficial ulcers with loose edges and can have varying amounts of ocular discomfort, a characteristic "halo"

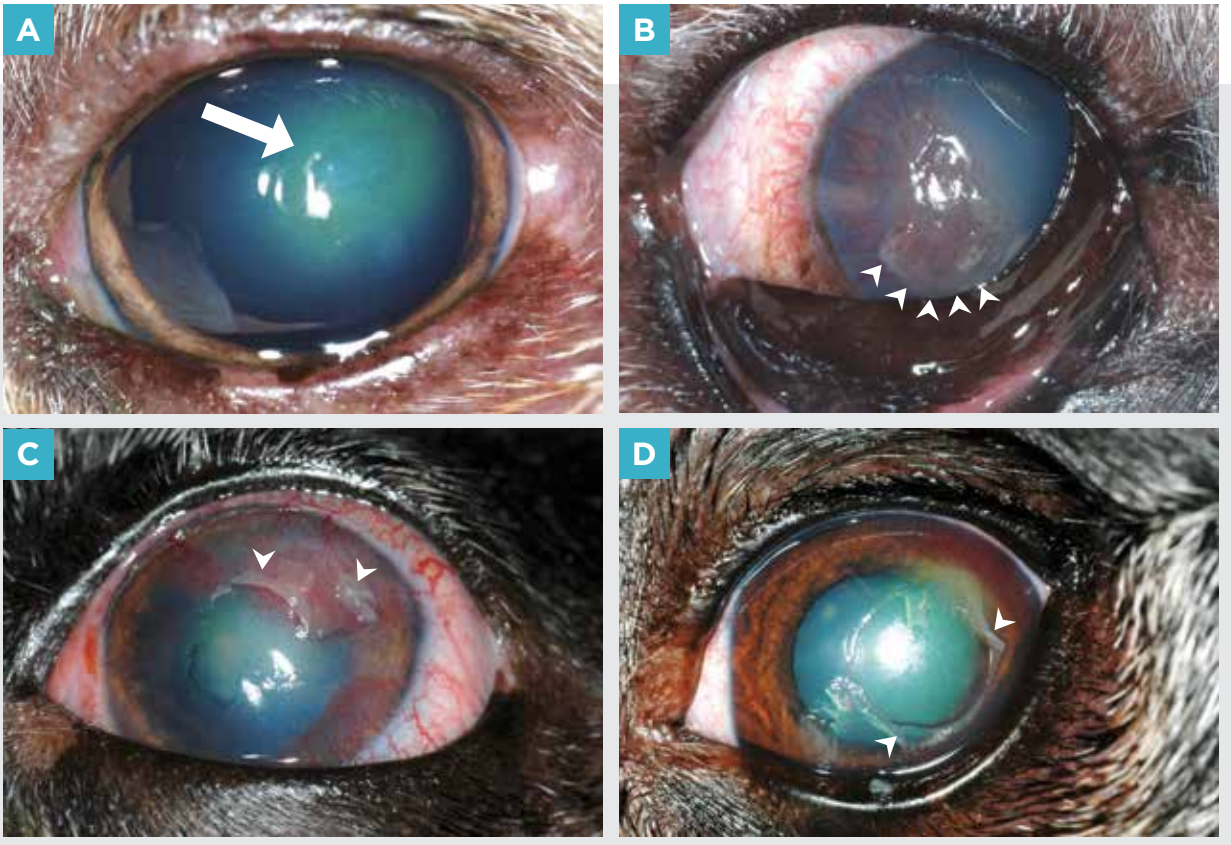

FIGURE 1. Examples of indolent ulcers on presentation, prior to treatment, with variable amounts of edema, vascularization, and scrolled epithelium. **(A)** Note the "halo" effect **(arrow)** where stain has leaked under the loose ulcer margins, but no corneal vessels or scrolled epithelium. **(B)** Moderate focal vascularization and corneal edema with thickened, loose scrolled epithelium **(arrowheads)**. **(C)** Moderate focal vascularization and loose scrolled epithelial edges **(arrowheads)**. **(D)** Short focal vessels but moderate loose scrolled epithelial edges **(arrowheads)**.

TABLE 1 Summary of the Relative Success Rates of Different Interventions

METHOD	SUCCESS RATE[a]
Cotton-tipped applicator debridement	50%–65%
Grid keratotomy	65%–87%
Diamond burr debridement	85%–90%
Superficial keratectomy[b]	Approaching 100%

[a]Success rates are reported for healing between 10 and 21 days postprocedure. These are averages compiled across several studies. In some cases, it may take 2 or more treatments before clinical resolution is seen.[7,12,14,15]
[b]This is a referral-only surgery performed under general anesthesia and results in stromal loss. It is not a benign surgery and should not be considered a first-line treatment.

stain pattern, and corneal vascularization (**FIGURE 1**). They are most commonly found in middle-aged to older dogs (average age of 8 to 9 years), although they can be found at any age.[7,9-11] Indolent ulcers have been documented in almost every canine breed, but some studies suggest that boxers may be overrepresented.[8,11] Nonhealing superficial corneal ulcers with indolent characteristics can occur in cats; however, the pathophysiology is likely different, involves feline herpesvirus, and has yet to be extensively studied.[12,13]

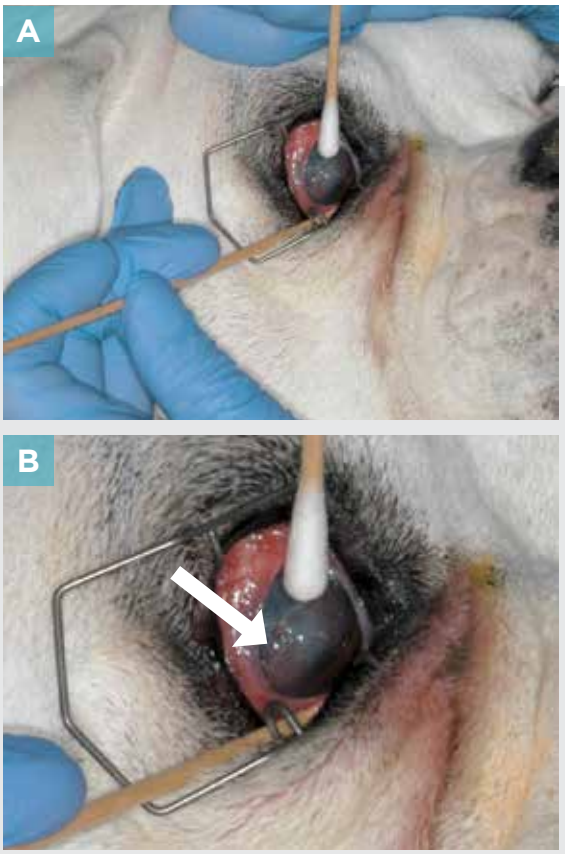

FIGURE 2. The first step of any surgical treatment is to debride any loose epithelia with a sterile cotton-tipped applicator (CTA). **(A)** A sterile eyelid speculum is being used to retract the eyelids, and a second sterile CTA is being used in the clinician's nondominant hand to retract the third eyelid. **(B)** Note the thin demarcation of loose epithelia between the lesion and normal cornea **(white arrow)**.

TREATMENT

A number of medical and surgical interventions are available for the treatment and management of canine indolent corneal ulcers (**TABLE 1**). Several of the more common and accessible interventional modalities are discussed below, with an emphasis on those that can be performed in a general practice setting. These include cotton-tipped applicator (CTA) debridement, grid keratotomy, and diamond burr debridement.

Usually, these procedures can be performed with just a topical anesthetic. Anxious or excessively moving patients often benefit from light sedation; heavy sedation and anesthesia are typically avoided unless the patient is aggressive, as they cause ventral globe deviation and make the procedure more difficult to accomplish.

Corneal cytology may be performed before executing any of the following procedures to ensure there is no infection. A corneal debridement is *not* an appropriate treatment if the ulcer is infected. **Note:** It is critical to always numb the eye thoroughly with an appropriate topical anesthetic (e.g., proparacaine ophthalmic solution) prior to any of the outlined procedures and to only allow sterile instruments to touch the surface of the eye due to the open wound/active ulcer.

Cotton-Tipped Applicator Debridement

Epithelial debridement has long been considered the frontline treatment for indolent corneal ulcers.[2] Sterile, dry CTAs can be used to gently remove the loose epithelium starting from the center of the lesion and working out toward the margins of the erosion (**FIGURE 2**).[1,2] CTAs should be replaced frequently so

that they remain dry. Normal, healthy epithelium cannot be removed with CTAs; therefore, debridement should continue until no additional epithelium is being removed and only firmly adhered epithelium remains.[1,2] This may be a larger area of epithelial loss than is initially obvious, as the fluorescein stain may not have reached the margins of the ulcer, and sometimes the epithelium from the entire cornea is removed. To show the full extent of the ulcer prior to performing a keratotomy or diamond burr, the eye can be restained after this step.

Grid Keratotomy

Another common treatment technique involves making linear scratches in the affected cornea. There are many approaches to these techniques, but it is important to note that all of them require initial CTA debridement *before* performing any variation of a keratotomy to declare the extent of the abnormal cornea and remove the unhealthy epithelium.

One technique describes grasping a small-gauge (i.e., 25-gauge) needle by a *sterile* hemostat so that only the very tip of the needle is exposed; however, the needle can be held at the hub with or without a syringe as well (**FIGURE 3**), and commercially available needles are also designed specifically for these procedures.[1] Holding the needle with a hemostat allows the depth of the puncture to be controlled while still providing a handle. To perform a grid keratotomy, small lines are made with the tip of the needle 0.5 to 1 mm apart in a crosshatched pattern extending across the entire defect just into the normal cornea.[1,2] These gridlines should remain within the superficial corneal stroma; thus, the needle should be lightly scratched across the tissue.

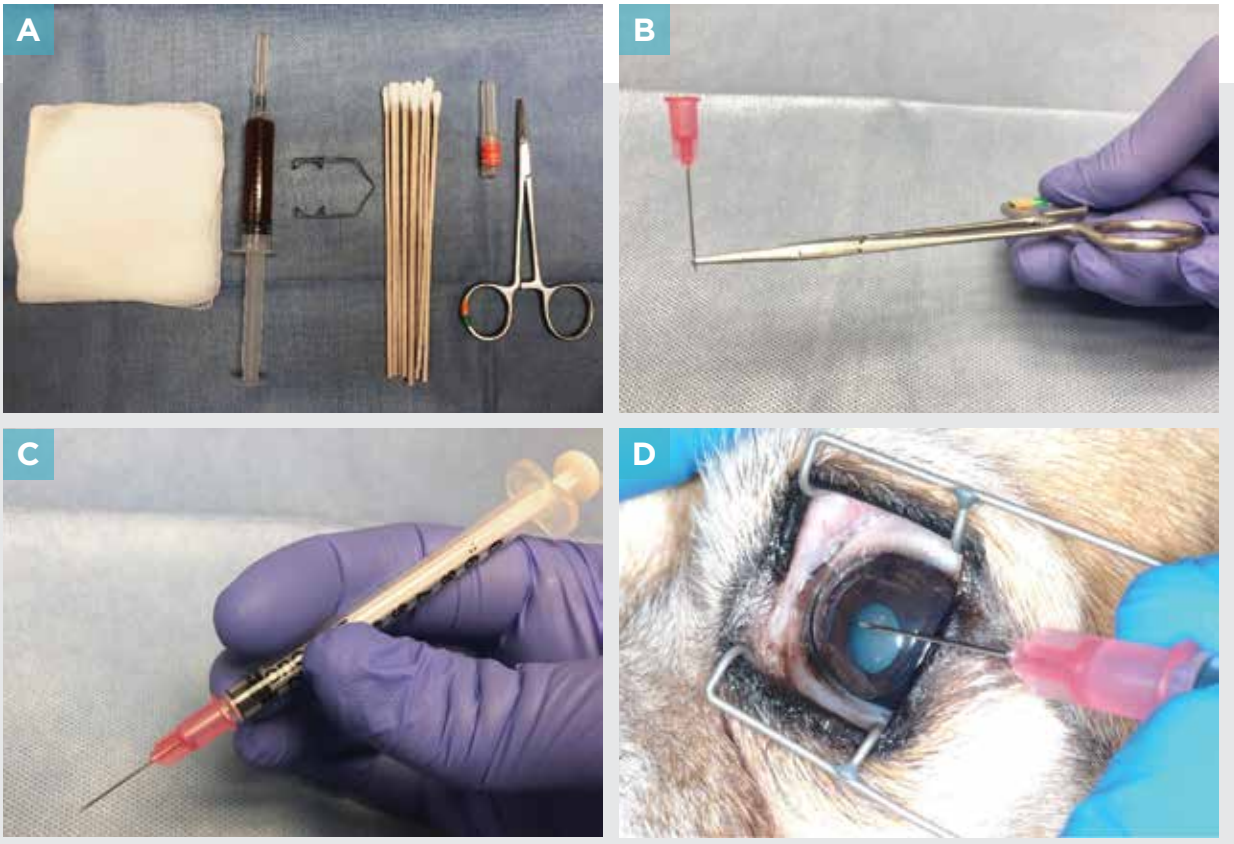

FIGURE 3. Grid keratotomy. **(A)** An example of the tools needed for a grid keratotomy from left to right: 4×4 gauze, dilute betadine solution, sterile eyelid speculum, sterile cotton-tipped applicators (CTAs), 25-gauge needle, and a sterile hemostat. **(B)** If using a standard 25-gauge needle for a grid keratotomy, it can be grasped near the tip by the sterile hemostat with approximately 1 mm of the needle exposed. **(C)** Alternatively, a sterile syringe attached to a 25-gauge needle can be used to perform a keratotomy. Some individuals may find this simpler or more comfortable; it's a personal preference. **(D)** Preparing to start a grid keratotomy on a patient. An eyelid speculum may be used to keep the lids open, and/or a sterile CTA can be used to keep the third eyelid out of the way, as seen in **FIGURE 2**. Note the acute (almost parallel) angle of the needle in relation to the surface of the eye. The needle should never be perpendicular to the eye's surface. Note: This photo is staged as an example and this cornea is normal.

A grid keratotomy should never be performed in cats due to the risk of corneal sequestrum formation.[1]

Diamond Burr Debridement

A diamond burr is a small, handheld, battery-powered instrument that can be used for superficial corneal debridement in cases of indolent ulcers (**FIGURE 4**). The diamond burr is gently passed over the ulcerated area in a circular motion to etch microscopic defects into the acellular hyalinized zone of the corneal stroma. Efficacy and outcome are comparable to those seen with grid keratotomy. Studies have shown that the instrument does not damage the surrounding normal epithelium and does not remove corneal stroma when used properly in gentle, slow, circular motions.[16]

Pro Tips

- Improve burr efficiency by performing a CTA debridement prior to using the diamond burr, so that the excess epithelium does not clog the grooves between the diamond particles.
- A slight indentation of the cornea ensures adequate contact between the instrument and the ulcer.

Diamond burr debridement is often considered the gold standard for treating indolent corneal ulcers in a general practice setting. Benefits include safety and efficiency, as no needle is involved; therefore, sedation or anesthesia is typically not needed. Another benefit is that the cornea subjectively scars less from an uncomplicated burr than from a grid keratotomy (**FIGURE 5**).

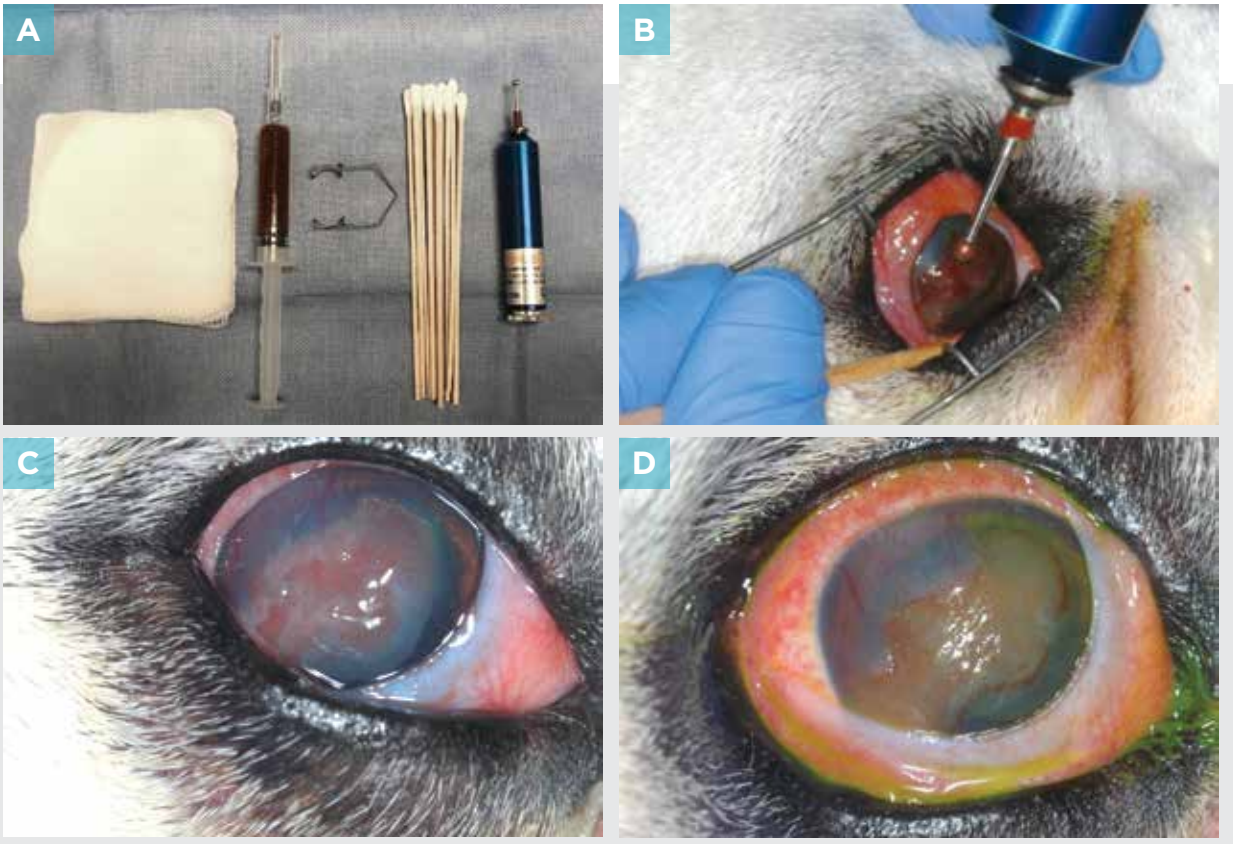

FIGURE 4. Diamond burr debridement. **(A)** An example of the tools needed for a diamond burr debridement from left to right: 4×4 gauze, dilute betadine solution, sterile eyelid speculum, cotton-tipped applicators (CTAs), and a diamond burr handpiece with tip inserted. **(B)** A diamond burr procedure being performed in a dog. An eyelid speculum may be used to keep the lids open and/or a sterile CTA can be used to keep the third eyelid out of the way, as seen in **FIGURE 2**. **(C)** An example of an indolent ulcer that was present for months prior to presentation. Although proper medical management to prevent infection was instituted, no procedures had been performed to stimulate healing. Note the vascularization indicating chronicity and thickened loose epithelial lip at the edge of the ulcer before debridement. **(D)** The same eye after diamond burr debridement. This ulcer healed within 14 days of the debridement.

Diamond burr debridement in cats has been shown to be a safe, noninvasive treatment for nonhealing corneal ulcers, with a reported success rate of 81%.[17] Some clinicians recommended treating feline patients with an antiviral at the time of the corneal burr as a link between feline herpesvirus and feline indolent ulcers is suspected.[14]

The costs associated with purchasing this instrument and the burrs are quite reasonable and will quickly be recouped, even after just a handful of procedures.[18] As with all treatment options for indolent ulcers, the trick is not the procedure itself, but instead determining which patient needs the procedure.

The burrs themselves are reusable with proper cleaning between patients but will need to be replaced periodically (after approximately 50 uses). There are a number of protocols describing cleaning and sterilizing the burr tips between procedures; however, ultrasonic cleaning is recommended to achieve adequate particulate removal prior to sterilization.[18] This protocol will cause burrs to break down over time; therefore, they should be replaced regularly.[18]

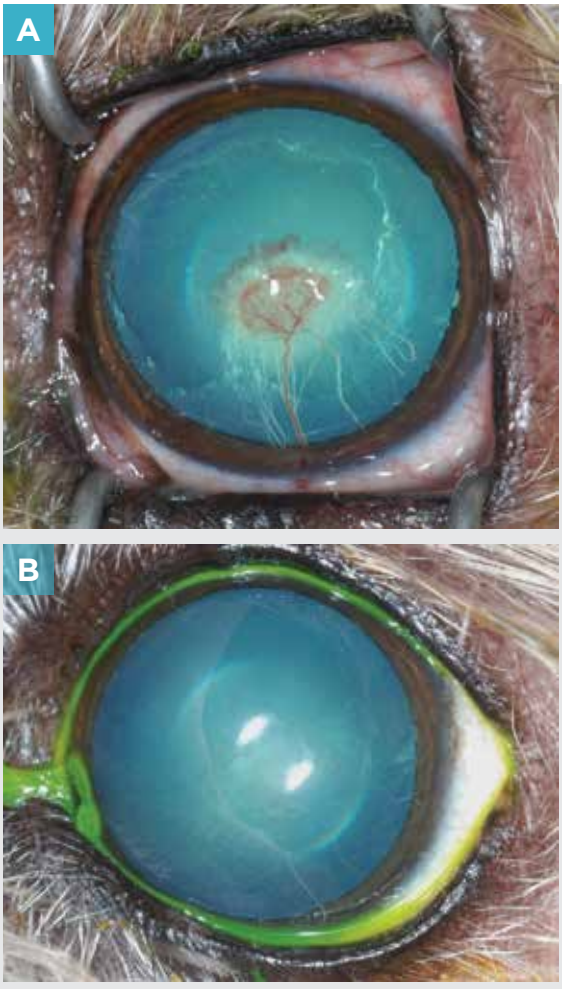

FIGURE 5. An example of an indolent ulcer through the healing process. **(A)** Immediately after diamond burr debridement and **(B)** 14 days after the debridement, by which time the ulcer was healed with minimal scarring.

ADJUNCTIVE THERAPIES/ AFTERCARE

Elizabethan Collar

Placement of an Elizabethan collar is recommended until the ulcer is healed. Due to the fragile connection of the epithelial cell to the stroma, this is especially important in an indolent ulcer. The use of an Elizabethan collar also prevents the patient from introducing infectious organisms onto the open wound through rubbing.

Bandage Contact Lens

Multiple studies have demonstrated accelerated healing times for an indolent ulcer following placement of a bandage contact lens (BCL). A variety of BCLs are available; however, nonprescription, human contact lenses may have better retention rates and are often less expensive than veterinary-specific lenses.[5,14] The trick in placing a BCL is ensuring that the contact is correctly placed under the third eyelid; however, even with proper placement, the contact can be lost quickly in some patients. It is not necessary to replace these contacts; if they fall out, owners should be discouraged from attempting to replace them.

Antibiotics

Many ophthalmologists recommend prophylactic, topical, broad-spectrum antibiotics 3 to 4 times daily.

- ***Remember:*** *An indolent ulcer is never infected.* If there is evidence of infection, the ulcers should be treated differently. However, secondary infections can potentially occur and there is an ~3% risk of corneal melting post–diamond burr debridement; thus, it is important to monitor for signs of corneal infection (yellow discharge, yellow appearance in the cornea, acute worsening in comfort) after the procedure.[14]
- Terramycin (Zoetis, zoetisus.com) may speed up the resolution of indolent ulcers.[19]

A cycloplegic agent, such as atropine, is often recommended to improve patient comfort. Atropine

can be given every 12 to 24 hours to effect (the goal is maintaining a dilated pupil and a more comfortable eye). It is also commonly administered once at the hospital before or after the debridement procedure due to its moderate cost to dispense. Oral analgesics are also recommended to improve comfort in patients that are exhibiting blepharospasm, as the cornea is highly innervated and corneal ulcers are painful.

Regenerative Agents

Multiple studies have looked at a variety of topical regenerative agents, but no therapeutic advantages have been demonstrated to date.[15,20]

Topical application of serum, a commonly used agent that reduces proteinase activity in infected or "melting" ulcers, was well-tolerated by dogs with SCCEDs but did not reduce time to corneal reepithelialization.[21]

FOLLOW-UP

Patients should be rechecked in 10 to 14 days. If the indolent ulcer does not heal, repeated procedures can be performed every 14 days, as this allows adequate time for the ulcer to attempt to heal between treatments.

SUMMARY

Nonhealing ulcers are often incorrectly labeled as "indolent" without first excluding other causes of improper healing. This can lead to inappropriate treatments and poor outcomes for the affected eye, pain or discomfort for the patient, and unwarranted financial strain on the owners. Accurate diagnosis, appropriate therapies, and proper postoperative care are critical for successful outcomes.

As is the case with many ophthalmic conditions, general practitioners can diagnose, treat, and manage indolent ulcers. A variety of medical and surgical options are available for the treatment of indolent ulcers in a general practice setting. Armed with the appropriate knowledge and equipment, managing cases of indolent ulcers can be rewarding, provide excellent outcomes for patients and clients, and serve as an additional source of revenue. **TVP**

VIDEO DEMONSTRATIONS
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The trick in placing a BCL is ensuring that the contact is correctly placed under the third eyelid; however, even with proper placement, the contact can be lost quickly in some patients.

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