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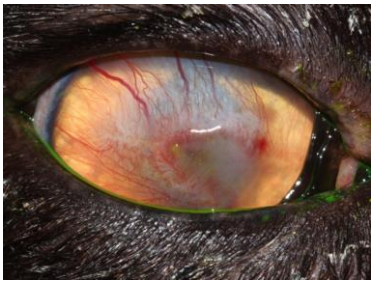
Ophthalmic Surgery Mini Series

Session 2: The surgical options for the non-healing ulcer

Claudia Hartley
BVSc CertVOphthal DipECVO MRCVS
European & RCVS Specialist in Veterinary Ophthalmology



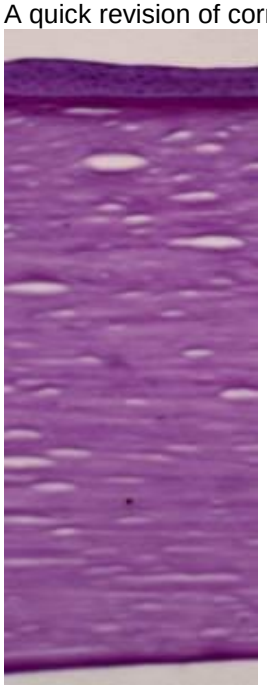
Ophthalmic Surgery Mini Series

The surgical options for the non-healing ulcer

1. Spontaneous Chronic Corneal Epithelial Defects (SCCED) vs. the complicated ulcer

Introduction

A quick revision of corneal anatomy:



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1. Epithelium (6-8 cell layers thick)
2. Basement membrane (secreted by basal epithelial cells)
3. Stroma
4. Descemet's membrane (secreted by endothelial cells)
5. Endothelium (1 cell thick)

The cornea is a transparent window, and together with the tear film, it refracts light onto the retina. Opacities within the cornea, and disruption of the tear film, will scatter and obstruct light passage, degrading the image achievable on the retina. The cornea is also an important barrier between the intraocular structures and the environment.

The transparency of the cornea is maintained by a lack of blood vessels and pigment, regular arrangement of small collagen fibrils, a non-keratinised surface epithelium and a state of relative dehydration.

The epithelium is composed of lipophilic stratified squamous epithelial cells 6-8 layers deep. Basal epithelial cells are cuboidal and lie against a basement membrane. Anterior to the basal cells are layers of wing cells and further anterior to these are stratified squamous cells. Being lipophilic it will not retain the hydrophilic stain fluorescein. The basement membrane below the basal epithelial cells is secreted throughout life and hence is thicker in the older animal.

The corneal stroma is composed largely of collagen that is regularly arranged (and therefore transparent; after healing post injury it loses its transparency due to the newer irregularly arranged collagen). It makes up the bulk of the corneal depth and being hydrophilic it will retain fluorescein stain.

Descemet's membrane is secreted by the endothelium cell layer below it (i.e. it is a true basement membrane). It is an elastic lipophilic membrane that will not stain with fluorescein and therefore a descemetocoele will appear as a green halo (of stromal fluorescein uptake) surrounding a central clear area. The endothelium layer is one cell thick and has very limited regenerative ability. Loss of endothelial cells results in surrounding cells elongating and spreading out to cover a larger surface area (at a critical threshold of cell loss complete coverage is not possible and endothelial cell decompensation occurs with corneal oedema).

The thickness of Descemet's membrane and the endothelium is less than the thickness of a red blood cell (7um).

The total depth of the canine cornea is 0.45mm (centrally) – 0.65mm (peripherally).
The stroma is kept in a relatively dehydrated state by the epithelium and endothelium (as barriers and active NA/K transport pumps in endothelial cells), which maintains its transparency. A breach of the epithelium, or damage to the endothelium, results in stromal hydration and corneal oedema.

The cornea receives its nutrition from the tears, the aqueous and direct diffusion of oxygen from the atmosphere. Innervation of the cornea is from branches of the ophthalmic nerve (trigeminal nerve), which enter the mid-stromal level of the cornea circumferentially at the limbus. The trunks run radially to the central cornea and form sub-epithelial plexi in the anterior stroma. Free nerve endings extend to the epithelial wing cell layers.

Corneal Healing

An epithelial ulcer will heal in three main phases. The initial rapid cell-sliding phase occurs as neighbouring epithelial cells spread themselves thinly to cover the defect. This is followed by a mitotic phase during which the normal number of epithelial cell layers is restored by mitosis. And finally the adhesion phase where basal epithelial cells adhere to the underlying stroma. The adhesion phase may not be complete until some weeks after fluorescein is not longer retained by the cornea.

Restoration of a stromal defect may take weeks as keratocytes and fibroblasts produce new collagen. Initially the collagen fibrils are irregularly arranged leading to the classic fibrotic scar appearance, but with time they line up more regularly and transparency is improved.

Recurrent Epithelial Erosions /Indolent ulcers /Spontaneous Chronic Corneal Epithelial Defects (SCCED))

Spontaneous chronic corneal epithelial defects (SCCEDs) in dogs are chronic superficial (epithelial) ulcers that fail to resolve through normal epithelial wound healing. Various names have been used for this condition including: boxer ulcers, indolent erosions or ulcers, canine recurrent erosions, recurrent epithelial erosions, refractory corneal ulcers, non-healing erosions, and idiopathic persistent corneal erosions. Although these ulcers are common in Boxers (where the mean age of onset is 6.6 years) they can be seen in any breed with age, and are more common in the over 8year old age group.

Clinically, SCCEDs resemble recurrent erosions in people and often associated with superficial trauma although spontaneous occurrence is thought to be possible. It is important to look for an inciting or exacerbating cause (foreign body in the conjunctival sac or behind the third eyelid, lid abnormalities, distichia, ectopic cilia, KCS etc.).

They have a characteristic appearance of a non-infected superficial loss of epithelium surrounded by a redundant non-adherent margin of epithelium. This non-adherent rim of epithelium will often stain characteristically with fluorescein as fluorescein leaks underneath the loose epithelium providing a 'halo' effect.

SCCEDs do not involve the stromal layers of the cornea. **This is an important distinction as stromal ulcers should never be treated with the techniques we use specifically for SCCEDs (e.g. cotton bud debridement, grid/punctate keratotomy, diamond burr debridement or superficial keratectomy – see later), as they may cause rapid deterioration in these cases.**

The complicated ulcer

A simple ulcer is a non-infected superficial ulcer that heals uneventfully within 7 days. A complicated ulcer is strictly all other ulcer types, including the SCCED ulcer, however, most ophthalmologists would put SCCEDs into a separate group. So a complicated ulcer is one or more of the following:

- stromal
- infected
- malacic
- secondary to an underlying pathology: e.g. neurotrophic, KCS, entropion, FB

2. Aetiopathogenesis and its impact on choice of surgical procedure

A SCCED has been shown to involve an abnormality of epithelial binding to the anterior stroma. Affected cases treated by superficial keratectomy have been studied by histopathology and electron microscopy and the samples demonstrated some characteristic findings:

- non-adherent and frequently dysplastic adjacent epithelium
- absent or discontinuous fragments of basement membrane
- a hyaline-like membrane overlying the ulcerated stroma

These findings were not demonstrated in an experimental study looking at repeated epithelial debridement of the canine cornea, suggesting that these changes are not simply a manifestation of chronic ulceration.

Treatments of SCCED have therefore focused on removal of non-adherent epithelium, and removal of the hyaline like membrane that is proposed to be acting as a barrier to stromal adherence of basal epithelial cells. An excellent reference for the aetiology and treatment of SCCED in dogs is

Bentley E. Spontaneous Chronic Corneal Epithelial Defects in Dogs: A Review. *Journal Of American Animal Hospital Association* 2005:41(3);158-165.

Ulcers secondary to an underlying entropion, distichiasis, ectopic cilia, or foreign body will require surgical attention aimed at these causes or ulcer healing will be stubbornly elusive. Corneal ulcers secondary to KCS, trigeminal nerve paralysis (neurotrophic), or with malacia, are frequently rapidly progressive and will usually require surgical support (grafting) to aid healing.

Infected or malacic corneal ulcers need to be addressed with appropriate anti-microbial agents and anti-collagenases respectively. Frequently, stabilisation of the cornea is attempted prior to corneal surgery if sufficient tissue remains to allow this delay. This has the advantage of potential reversing some tissue pathology and leaving more cornea available to graft/give a better visual outcome. These cases do require very intensive medication and are generally best hospitalised.

3. Debridement, grid & punctate keratotomies, & corneal burr procedures

Treatments for SCCED include:

1. Cotton-tip debridement of redundant epithelium – under topical local anaesthesia
2. Corneal burr procedure or grid or punctate keratotomy – under topical local anaesthesia or sedation/GA - **NEVER use on a stromal ulcer. NEVER use in cats > sequestrum**
3. (Phenol cautery) – use with extreme care (and **NEVER in cats > sequestrum**) and always flush liberally with saline afterwards. **NEVER use on a stromal ulcer.** Phenol no longer available (carcinogenic)
4. Superficial keratectomy – requires magnification (operating microscope) and anaesthesia.

4. Complicated deep ulcers and their surgical options

Stromal ulcers need careful assessment for depth and likelihood of progression. For instance, if they are less than half stromal depth with a healthy edge, medical treatment (with careful frequent monitoring) may be appropriate. Be extra cautious in brachycephalic breeds as they can progress extremely fast e.g. Pug, Pekingese and Shih Tzus. Also in cases with subnormal tear production. Look carefully for an inciting cause – lid abnormalities, distichia, ectopic cilia, foreign bodies, inadequate/absent palpebral reflex etc. as getting a successful outcome for the ulcer when these underlying issues have not been addressed is frequently disappointing.

The most commonly isolated bacteria are *Staphylococcus spp*. and *Streptococcus spp..* Fusidic acid (Isathal™) should cover these gram positive commensal bacteria, although resistance is unfortunately on the rise. Chloramphenicol drops penetrate the cornea well and are also an excellent choice for corneal ulceration. Brachycephalic breeds (Pugs, Pekingese, Shih Tzus +/- Lhasa Apsos) are (in my experience) often carrying *Pseudomonas spp.* and a fluoroquinolone, such as ofloxacin (Exocin™) drops could be considered. Gentamicin (Tiacil™or Clinagel™) can be epitheliotoxic so it is wise to reserve this for the cases where culture and sensitivity results indicate. Keratoconjunctivitis sicca (KCS) cases have an altered normal conjunctival flora, with increased presence of gram negative bacteria and therefore antibacterial choice may need to be modified where this is present.

Cytology is easy to perform and can help in choosing an appropriate antibiotic. Differentiating cocci bacteria and rod bacteria as well as characterising the inflammatory cell population is invaluable and can be done at the patient side without the delay and costs encountered with bacterial culture and sensitivity testing. More recently, cases of fungal keratitis have been reported in dogs and require aggressive anti-fungal treatment +/- surgery. A cytology brush (available from Veterinary Speciality Products) is excellent for gathering samples and rolling on to a microscope slide, as the cell capture and non-rupture is much improved. It is worthwhile making several slides and stain 1-2 with Diff Quik in the practice, and unstained slides can be submitted to a cytopathologist for more advanced examination (and selective stains) if required.

Stromal ulcers that are greater then half stromal depth, or are progressing, are candidates for conjunctival pedicle or corneoconjunctival transposition (CCT) grafts. Also consider grafting early in KCS associated ulceration as the cornea is already compromised. Cases where fungi have been identified can often benefit from early surgical intervention for keratectomy to reduce the fungal load, and bringing in a graft with vascular supply.

Descemetocoeles
These are surgical emergencies that require immediate support in the form of a conjunctival pedicle graft, CCT or other grafting technique. The descemetocoele will not retain fluorescein stain. Paradoxically, as most of the corneal nerve endings are found in the anterior stroma and epithelium, when ulcers deepen often the owner will report decreasing ocular pain. Do not be fooled, as the dog is only a whisker away from a ruptured globe.

Perforations
Again these are surgical emergencies. Frequently the perforation will plug with iridal tissue. Alternatively an aqueous clot may form to temporarily plug the perforation. Leave any fibrin-aqueous clot in situ until ready to graft (intraoperatively) as this will reduce the chance of globe deflation, increased inflammation, and reduced chance of success.

Melting Ulcers (Keratomalacia)
Keratomalacia is a result of liquefaction of corneal stroma by collagenases (matrix metalloproteinases (MMPs) and serine proteases e.g. neutrophil elastase), which are liberated by bacteria and white blood cells (largely neutrophils). Anti-proteases found within autologous serum can be used topically (intensively) to try and halt collagenolysis. Chelating agents such as EDTA chelate zinc and calcium required by proteases, so can also have anti-collagenase action. Other anti-collagenases include acetylcysteine and tetracyclines.

Autologous serum should be prepared aseptically and stored in the fridge. Serum is an excellent medium for bacterial growth. In humans, autologous serum is usually dispensed in daily vials that the patient keeps in his/her freezer retrieving a fresh vial each day. In our patients, topical autologous serum is generally best reserved for in-hospital use only due to the risk of bacterial contamination.

Keratomalacic cases should be hospitalised for intensive (hourly to 2-hourly) treatments and monitoring for progression. Frequently progression is fast and conjunctival pedicle or corneoconjunctival transposition (CCT) grafting is usually warranted. Grafting brings a blood supply, with its anti-collagenases, directly to the area most in need.

Foreign Bodies

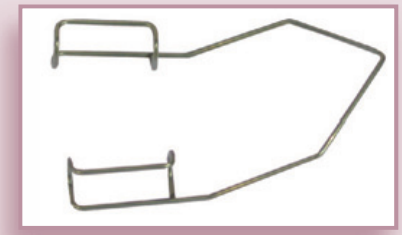
Foreign bodies should be removed by impaling the FB perpendicular to the plane it entered the cornea. Be prepared for intraocular surgery, as many will enter the anterior chamber if they haven't already. It is important to assess if the lens is involved as if the lens capsule is ruptured lens protein leakage incites an aggressive uveitis (phacoclastic uveitis).

Corneal surgery

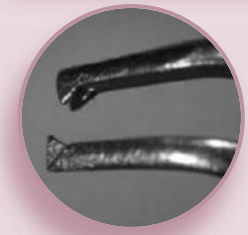
Corneal surgery should be performed using an operating microscope. This provides sufficient illumination and magnification that accurate suture placement and graft dissection can be safely achieved. It really does make a difference to the outcome success. In a lot of cases this does mean referral, but there will be instances where this is not possible for financial or logistical reasons. With adequate owner preparation and informed consent you may be left with performing corneal grafting procedures in less than ideal situations and here are some basics to help you.

Surgical instruments

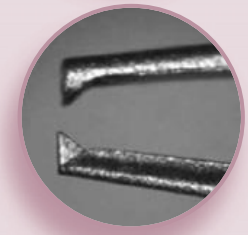
The figure below is an excerpt from: Hartley C. Treatment of corneal ulcers: when is surgery indicated? *Journal of Feline Medicine and Surgery: Clinical Practice* 2010; **12**: 398-405. This article covers some of the basics of corneal surgery including equipment & instruments, positioning, and preparation for corneal surgery, as well as some of the techniques we will discuss in this webinar.



Barraquer eyelid speculum. *Courtesy of AcriVet*



Colibri forceps. *Courtesy of AcriVet*

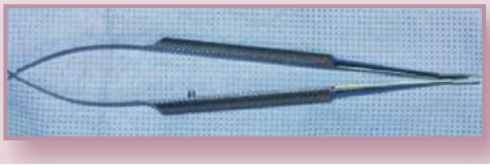


Fine rat-tooth forceps. *Courtesy of AcriVet*

Westcott tenotomy scissors. *Courtesy of AcriVet*

Sharpoint restricted depth knife (300 µm) – the button on the blade prevents the knife incising deeper than desired

Sharpoint angled bevel-up crescent knife (performing a superficial keratectomy in a horse)



Microneedle holders suitable for use with 8/0 vicryl or finer suture material

Another very useful resource is Eisner's Eye Surgery: An Introduction to Operative Technique (Springer-Verlag 2nd edition; 1990) which is a medical textbook but covers suture patterns and techniques that are useful to be familiar with when undertaking corneal surgery.

Conjunctival pedicle grafts (CPG)

These are a good option where some tectonic and vascular support is required (although conjunctiva alone has limited tectonic ability this is less of a concern unless you have a full thickness deficit or descemetocoele where additional support in conjunction with a pedicle graft might be required.

Classically the donor graft is raised from the dorsal to dorsolateral conjunctiva as this is the most accessible. Of course, the ulcer location may dictate the more appropriate site of conjunctiva donor tissue (if the ulcer is ventromedial you may be faced with raising a graft from the bulbar conjunctiva behind the third eyelid, which is technically more difficult).

The conjunctiva is incised perpendicular to the limbus at the distal limit of the intended graft. The conjunctiva is then undermined via this small incision to lift the desired area of graft. It is wise to make the graft 1-2mm larger than the deficit as contraction of the tissue once dissected is expected. The conjunctiova is then incised along the limbus and a second incision parallel to this one at an appropriate width to cover the corneal defect (i.e. 1-2mm wider than defect). The pedicle is trimmed to remove excess Tenon's capsule that can cuase contracture of the graft and retraction from the corneal sutures post-operatively. Extreme care is required not to button hole the graft at this stage and where an operating microscope really demonstrates its benefit.

The ulcer bed should be adequately prepared so that the epithelium of the ulcer margin will meet the conjunctival epithelium of the prepared graft. If a conjunctival pedicle graft is sutured over corneal epithelium the graft is unlikely to incorporate into the cornea and slough prematurely, or a corneoconjunctival cyst may form requiring future surgical intervention.

The conjunctival graft is then sutured into the defect, starting with cardinal sutures at each corner and then bisecting sutures. It is important that the conjunctival epithelium should appose the corneal epithelium accurately and there isn't excessive tension on the graft (that will cause devitalisation of this delicate tissue). Limbal tacking sutures are preferred by some surgeons to improve the stability of the graft on the cornea and resist contraction of the pedicle.

The pedicle can be sectioned after 6-8 weeks if a vascular supply is no longer needed (healing is complete and no ongoing requirement for a blood supply) to reduce scarring/visual compromise, although many grafts will thin significantly with time to be relatively innocuous even without pedicle sectioning.

Corneoconjunctival transpositions (CCT)

It is not appropriate to attempt this surgery without the aid of an operating microscope as it involves the creation of a split thickness corneal graft (using either a Beaver™ blade or restricted depth and crescent knives) and adjacent conjunctiva that is then moved into the defect and sutured in place. It has the advantage of additional tectonic support and often an excellent cosmetic outcome.

Diverging cornea incisions are made from the defect to the limbus at approximately half stromal depth (300µm). The adjacent conjunctiva is then undermined using Westcott's corneal scissors (similar to pedicle graft) and lastly the limbus is incised to connect the corneal plane with the conjunctival. The conjunctiva is further undermined so that the transposition can cover the defect without tension. Again cardinal sutures are usually placed at the corners and then followed by bisecting simple interrupted sutures or a continuous suture.

The conjunctiva will become incorporated into the peripheral cornea so there will be no pedicle to section (in 6-8 weeks time) with this procedure.

Collagen / Other Material Grafts

A-Cell™ is a commercially available graft material that is compromised of collagen and can be used to add additional tectonic support (for example underneath a conjunctival pedicle graft). The graft material can be fashioned to the appropriate size and shape for the ulcer/deficit and then sutured in place and overlain by a conjunctival pedicle graft.

Another material that can be used, and can have advantages for some situations (e.g. fungal keratitis, keratomalacia) includes amnion. This is now commercially available as Omnigen™, which is a freeze-dried preparation of human amnion. Some ophthalmologists may have the facilities to harvest, prepare, and store equine amnion that can be used in canine and feline patients as well as equine cases.

Lastly corneal tissue is sometimes available to some ophthalmologists, although rarely as a fresh tissue (where corneal clarity might be maintained e.g. penetrating keratoplasty for endothelial degeneration with long term immunosuppression of host vs. graft disease), and more commonly as frozen tissue. This effectively acts as a collagen scaffold and provides excellent tectonic support for very deep deficits, but would not be expected to be transparent long-term.