Deep corneal ulcers are defined by a defect of the epithelium and stromal loss that may extend as far as the Descemet’s membrane.

Figure 1a. Deep corneal ulcer in two pugs, frontal view. Note the visible indentation and change of contour of the ocular surface.

They may be the result of a traumatic injury (for example, a cat scratch or corneal foreign body) or may arise from the deterioration of superficial defects due to an infection, corneal melt or the ongoing presence of complicating factors. The deeper the stromal ulcer is, the more fragile the eye becomes.

Any ulcer that extends to more than two-thirds the stromal depth should be considered as an emergency, as even minimal trauma can cause a perforation of the globe. This article will address the diagnosis and treatment of deep corneal defects.

Diagnosis

The diagnosis of a deep corneal ulcer is based on a complete and thorough ophthalmic examination (see part one, VT47.08). Generally, any visible indentation of the corneal surface
suggests stromal loss (Figure 1) and should be taken very seriously. In cases of very deep corneal defects, the Schirmer tear test and tonometry should be avoided to prevent a corneal rupture. Nevertheless, it is especially important to perform the Schirmer tear test on the opposite eye, if it is safe to do so, as it may hold the key to the diagnosis of a contributing dry eye condition.

Figure 1b. Deep corneal ulcer in two pugs, lateral view. Note the visible indentation and change of contour of the ocular surface.

Corneal sampling for cytology and, ideally, culture and sensitivity is recommended for the evaluation of a possible infection and the adjustment of therapy if needed. Unfortunately, the results of culture and sensitivity are not instantly available, therefore on-site cytology allows immediate checking for the presence and type of bacteria involved. The most common organisms found in infected corneal ulcers are Gram-positive cocci (Staphylococcus or Streptococcus) or Gram-negative rods (Pseudomonas), or both. Large amounts of neutrophils may be seen in the case of an infectious or a sterile melting process.

Infected deep ulcers often have soft edges and associated corneal oedema with stromal thickening. They may be accompanied by a varying degree of white and yellow corneal opacity due to a combination of oedema and leukocytic infiltration. The presence of corneal vessels suggests a longer-standing pathology as vascularisation develops after a 48-hour lag period and progresses about 1mm per day.

Keratomalacia, or corneal melting, is a process of excessive destruction and softening of the
corneal stroma. It is caused by elevated levels of proteolytic enzymes released by bacteria and host cells (leukocytes, epithelial cells or fibroblasts) in response to a corneal insult. A melting ulcer has a creamy, gelatinous, liquefied appearance with ill-defined margins (Figure 2). Without very quick intervention these rapidly progressive defects may lead to a corneal perforation.

When the stroma is completely destroyed, exposing Descemet’s membrane, the defect is called a descemetocele (Figure 3). It often appears as a crater-like defect with a transparent base, which does not stain with fluorescein. Due to its fragile nature and potential for imminent globe perforation, any descemetocele is a surgical emergency.

Corneal perforations are usually the result of a traumatic injury or the consequence of a progressive deep corneal ulceration (Figure 4). Iris prolapse and/or a positive Seidel test are diagnostic for a corneal perforation. For a Seidel test, sterile fluorescein is gently applied to the suspected perforation. In the case of an aqueous humour leak, this is seen as a green stream of fluid coming from the eye as the dye is diluted. A stream of aqueous humour across the corneal surface may be also noted. A negative Seidel test does not rule out a perforation as the defect may be sealed by fibrin or a prolapsed iris (Figure 5).

Other changes that may be observed on examination include a shallow anterior chamber, alterations of the pupil shape (dyscoria) and position. A corneal perforation requires a prompt diagnosis and treatment, as failure to do so can lead to further ocular damage (such as an endophthalmitis or cataract formation) and carries a poorer prognosis for preservation of the eye and functional vision.

Most corneal ulcers are associated with a varying degree of reflex uveitis. The release of inflammatory mediators causes miosis and pain and, in more severe cases, accumulation of pus (hypopyon), blood (hyphaema) and/or fibrin in the anterior chamber.
Figure 2. Deep melting ulcer. Note the creamy appearance and ill-defined edges. Leukocytic infiltrate (hypopyon) and blood (hyphaema) is present in the anterior chamber, indicating secondary uveitis.
Figure 3. Descemetocele. Note the crater-like appearance and fluorescein-negative centre of the defect where all stroma has been destroyed.
Figure 4. Perforated central corneal defect. The anterior chamber is collapsed, there is an aqueous leakage from the eye and the iris is prolapsing through the defect.

Medical treatment

The decision as to whether a deep corneal ulcer should be treated conservatively is based mainly on the depth of the defect, but other factors, such as the dog’s temperament and owner compliance, should also be taken into account to achieve the best possible outcome for the patient.

Medical treatment involves targeted topical therapy with antimicrobial agents, collagenase inhibitors and management of the pain and inflammation. The initial antibiotic selection should be guided by results of cytological evaluation. The presence of rods and cocci allows an indication as to which antibiotic is likely to be effective. Antibiotics commonly used as a first-line antimicrobial therapy in stromal ulcers with rod-shaped bacteria are fluoroquinolones (ofloxacin or ciprofloxacin),
aminoglycosides (gentamycin or tobramycin) and, in the case of cocci, chloramphenicol.

The antibiotic regimen should be altered in case of a poor response and ideally based on the results of culture and sensitivity to more specifically target the infectious agent. The frequency of applying eye medication depends on the severity of the lesion. Rapid progression and melting require aggressive application of drops every 1 to 2 hours for at least 24 to 48 hours. In cases of deep corneal defects, the use of systemic antibiotics with good ocular penetration should be considered.

Keratomalacia must be addressed with collagenase inhibitors to counteract detrimental effects of proteolytic enzymes, which cause destruction of the corneal stroma. The most commonly used agent is autologous serum because, apart from its excellent anti-collagenase properties, it also contains numerous growth factors and immunoglobulins. Ethylenediaminetetraacetic acid and acetylcysteine also inhibit proteolytic enzymes, but to a lesser degree. The frequency of application should initially be every 30 to 60 minutes and can be reduced or stopped once the cornea starts to heal.

The control of pain and inflammation is achieved by administering NSAIDs and, if required, systemic opioids. A topical mydriatic (atropine to effect) will relieve any accompanying painful ciliary muscle spasm and dilate the pupil to prevent adhesions in case of more prominent uveitis with hypopyon. Repeat applications may be required to achieve this effect in severely inflamed eyes. The use of topical corticoids or NSAIDs are usually contraindicated as they can dramatically worsen corneal ulceration by inhibiting corneal healing and potentiating the effect of destructive enzymes.

**Surgical management**

Every patient with a deep corneal ulcer should ideally be hospitalised or re-evaluated at least every 12 to 24 hours after the onset of therapy. Corneal surgery should be considered if the ulcer does not improve or deteriorates. Surgery is usually also recommended in all ulcers that are deeper than two-thirds of the corneal thickness. The aims of surgical treatment are to restore sufficient corneal stability and remove infiltrated and unhealthy tissue where possible to facilitate healing.

The choice of the procedure depends mainly on the size, location and stage of the ulceration, as well as the available facilities and experience of the surgeon. These techniques require microsurgical skills, instrumentation and an operating microscope for adequate magnification. Ideally, neuromuscular blocking agents are used for optimal positioning of the eye and to prevent any movement during surgery. If at all possible, patients needing corneal surgery should be referred to a specialist in ophthalmology.

**Conjunctival grafts**
Conjunctival grafts are dissected parts of the conjunctiva transposed into the corneal defect. Aside from providing some mechanical support, they encourage healing by providing blood supply (supplying growth factors, protease inhibitors or fibroblasts) and a route for systemic antibiotics to reach the defect. Conjunctival grafts have been described in a variety of patterns. A pedicle graft is most commonly placed (Figure 6). A strip of conjunctiva is moved on to the defect and sutured to the surrounding cornea with a simple interrupted or continuous suture pattern. It is important to debride the diseased corneal tissue to allow healing between normal tissues at the ulcer margins. Other variations of conjunctival grafts include total 360°, the hood, bridge and island (free) grafts:

- The 360° graft is used mainly to save eyes affected by extensive corneal lesions. The bulbar conjunctiva is cut circumferentially and closed in the middle in a purse string or horizontal fashion. This type of flap is easy to perform, but covers the whole cornea and, therefore, completely impedes vision and precludes adequate monitoring of the lesion and inflammation within the eye.
- A hood flap may be helpful in peripheral defects. The conjunctiva adjacent to the lesion is undermined and advanced to cover the defect.
- A bridge graft is similar to a pedicle graft, except it is attached at both ends rather than at one end. It is advantageous in long, linear ulcers or when a more reliable blood supply is needed.
- An island (free) graft may serve as a mechanical support for the lesion; however, it lacks the benefits of providing vascular supply.

In very deep corneal ulcers or perforations, conjunctival tissue may not be strong enough to provide good structural support to maintain corneal integrity and watertightness. Recurrent problems are possible (Figure 7). It also results in significant scarring as the conjunctival tissue is integrated into the ulcerated cornea, even if the pedicle is dissected when not needed anymore. Therefore, cornea, or other tissues with better structural integrity, can help to overcome these problems.
Figure 5. Peripheral corneal laceration with iris prolapse. Note the change in pupil shape (dyscoria), which appears more horizontally elongated towards the defect.
Figure 6. Conjunctival pedicle graft in a dog with a peripheral melting ulcer unresponsive to medical treatment. Note the hypopyon in the anterior chamber.
Corneoconjunctival transposition

Corneoconjunctival transposition is a type of sliding lamellar keratoplasty where a pedicle of cornea attached to the limbus and conjunctiva is used to repair a corneal defect (Figure 8). The advantage of this procedure is the use of own tissue, which results in decreased corneal scarring and, therefore, a more transparent cornea postoperatively. Moreover, vessels supplied from the attached conjunctiva enhance the graft’s viability and, after a lag period, provide vascularisation of
the defect.

This technique is reserved for patients where there is enough healthy adjacent cornea to cover the defect and often results in good transparency of the transposed cornea (Figure 9). A disadvantage of this procedure is a significant part of the originally healthy cornea will be covered by conjunctiva that integrates into the corneal tissue and will lead to a loss of transparency in this area.

**Corneal grafting**

Corneal grafting involves the use of tissue harvested from the adjacent normal cornea (autologous graft; Figure 10), from a donor animal of the same species (homologous grafts), or from a species that differs from the recipient (heterologous grafts).

Corneal grafts are divided into partial thickness (lamellar) and full thickness (penetrating) keratoplasties. Corneal tissue collected from donors can be fresh or frozen. The main advantage of fresh tissue is the presence of viable endothelial and epithelial cells, which minimises any postoperative corneal opacity. Because fresh cornea is not often available, the use of frozen grafts is possible. Given the lack of viable cells in these corneas, they are mainly used for their excellent tectonic properties. However, they often cause significant corneal vascularisation and scarring, although this can be influenced by the choice of suture material and postoperative anti-inflammatory medication.

A variety of other natural and synthetic materials have been used as patches to cover ulcers, such as oral or vaginal mucosa, porcine small intestinal mucosa, peritoneum, pericardium or amniotic membrane.
Figure 8. Corneoconjunctival transposition in a French bulldog with a central descemetocele. The transposition was taken from the ventromedial part of the cornea to cover the defect.
Figure 9. The same dog as in Figure 8, six weeks after surgery. The graft has integrated well with the surrounding cornea. This patient was started on topical ciclosporin to help reduce corneal vascularisation and possible corneal pigmentation.
Figure 10. Autologous corneal graft harvested from the lateral cornea of the same eye to cover a deep central ulcer.

Summary

A range of surgical techniques are available to repair deep corneal defects. In all patients, the potential long-term visual outcome should carefully be considered when choosing a technique, as corneal transparency has to be at the heart of any treatment plan.

Advances in veterinary ophthalmology often allow not only the preservation of the eye, but of functional vision, which is what makes the true difference to patients.
Treating corneal ulceration in dogs part 1: superficial ulcers

Further Reading