Diagnosis and Management of Corneal Ulcers

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Corneal ulceration is a common problem. The presenting signs are usually epiphora, photophobia, blepharospasm and a change in the appearance of the eye.

The diagnosis, prognosis and aetiology of corneal ulcers are discussed and appropriate medical and surgical methods of treatment reviewed.

Introduction

Corneal ulcers are a common reason for consulting a veterinary ophthalmologist and certainly a frequent cause of blindness among pets.

In addition to the risk of corneal perforation leading to loss of the eyeball (due to either phthisis or secondary glaucoma), areas of opacity may form that seriously or permanently impair vision. Where such a condition exists, as much attention must be given to preserving the integrity of the anterior chamber as to the measures to be taken to enable the cornea to heal without losing its transparency.

Patients are brought to the surgery either because they present with epiphora, photophobia or blepharospasm or because the appearance of the eye has changed.

It is sometimes necessary to apply local anaesthesia to correct any blepharospasm, but the use of local anaesthetics should be confined to diagnostic purposes. Repeated use may cause lesions of the corneal epithelium, and all therapeutic use of these products is contraindicated.

When the appearance of the eye is changed, the lesions that can be seen are either corneal only (oedema, loss of substantia, keratitis) or lesions of the other ocular structures (conjunctiva, anterior chamber, uvea).

Diagnosis

Ideally, the eye should be examined with a slit lamp combined with a system of enlargement, i.e. a biomicroscope, which has a lighting system that can be focused into a thin line of light, the slit. With this, virtual sections of the cornea can be illuminated, thus making it possible to evaluate the increase (oedema, keratitis) or decrease (loss of substantia) in thickness. In the absence of this instrument, a good-quality source of lighting, combined with a magnifying glass, will suffice. An otoscope with its aural speculum removed can perfectly well be used as an examination lamp.

A full ophthalmological examination should be made to ascertain the causes or consequences of the corneal changes. The eyelids and their margins, which may be abnormal in shape or function, should first be studied.

The most common abnormality of shape is entropion, which leads to corneal trauma due to friction by the hair of the upper or lower eyelids. Ectopic hair may also emerge from the openings in the meibomian glands (distichiasis). Finally, and although they are not strictly speaking part of the palpebra, the size of the nasal plicae, which are a common cause of corneal traumatism in brachycephalic animals, should be noted.

Lagophthalmos (the inability to close the lids over a proptosed globe) and no, or insufficient, blinking (e.g. due to paralysis of the facial nerve) can result in ulceration. In these cases, a central ulcer results in the area where the lacrimal film is not properly spread.

The conjunctiva should next be examined, beginning with the palpebral conjunctiva, where an ectopic cilium or a tumour may be growing, the fornix of the conjunctiva, which may contain a foreign body, and finally the nictitating membrane, the posterior part of which is in direct contact with the cornea and may also conceal a foreign body or tumour.

The use of Schirmer's test to measure lacrimal secretion is useful, especially where there are other clinical
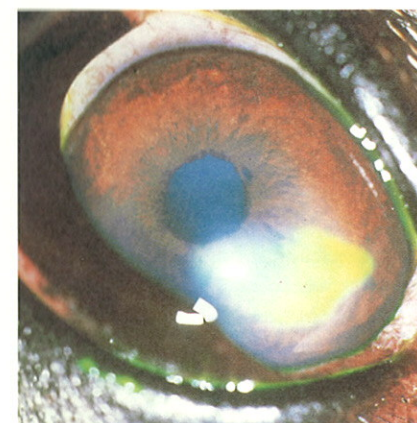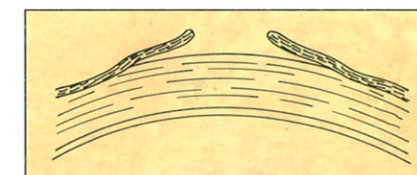
Figure 1 *Superficial ulcer.*
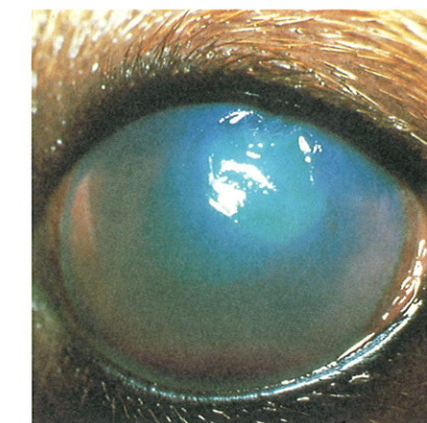

Figure 2 *Ulcer with detached edges.*

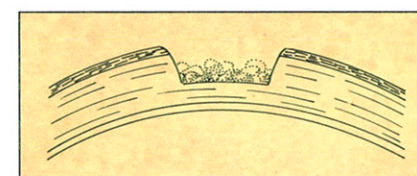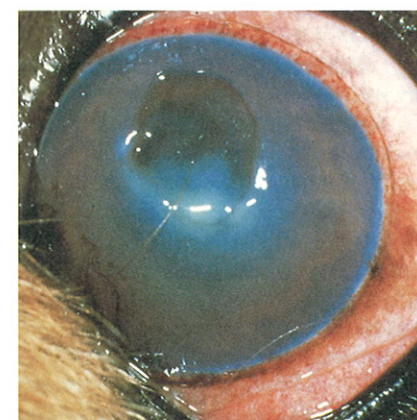
Figure 3 *Medium ulcer.*
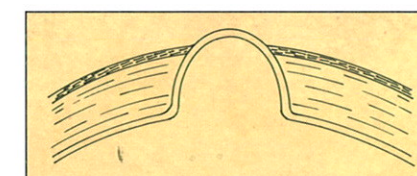

Figure 4 *Deep ulcer.*
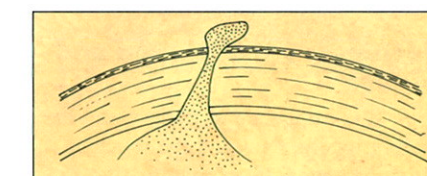

Figure 5 *Descemetocele.*

Figure 6 *Iridial staphyloma.*

signs of keratoconjunctivitis sicca (KCS), conjunctival and palpebral redness, conjunctivitis, oedema, corneal neovascularisation and pigmentation, and particularly where there is a recurrent ulcer after cessation of therapy.

A further examination of the cornea must then be made to evaluate the extent of any lesions:
- Depth of the ulcer (**Figures 1–6**).
- Corneal oedema.
- Neovascularisation.

Where the ulcer is superficial, the use of fluorescein may make diagnosis easier. This hydrophilic stain fixes on the corneal stroma when the epithelial layer has been lost. The stain infiltrates into the space between the epithelium and the stroma, and a much larger area of staining than was suggested by direct examination can then be seen.

Fluorescein is of no value in the diagnosis of deep ulcers because it provides no special information as the lesion can already be seen macroscopically. There may even be false-negative reactions because of a descemetocele, because fluorescein does not fix on Descemet's membrane, or because there is a fibrin plug at the bottom of the ulcer.

Conversely, there may sometimes be false-positive reactions where there are epithelial lesions, such as in certain types of keratitis (KCS or chronic superficial keratitis), or where there is granulation tissue covering the corneal stroma.

This staining technique may, however, be used to monitor epithelial healing.

When a result below 10 mm has been obtained in a Schirmer's test, it is useful to assess the degree of deterioration of the epithelial cells using rose bengal. This stain fixes selectively on the keratinised cells of the degenerating and exfoliating corneal and conjunctival epithelium.

The anterior chamber should then be examined for any signs of infection, intraocular inflammation or sequelae of corneal perforation. This may reveal a deposit at the bottom of the anterior chamber, i.e. a hypopyon, consisting of an accumulation of leukocytes (**Figure 3**). This is generally sterile and is only a sign of considerable inflammatory reaction.

While the uveal reaction cannot

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always be revealed in this way, the miosis that often accompanies ulcers is easy to identify.

Corneal pain causes parasympathetic stimulation: the point of departure of the oculopupillary reflex is in the sensitive fibres of the cornea that connect with the trigeminal nerve (V), and it returns via the parasympathetic fibres of the common oculomotor nerve (III).

In some cases there may be uveitis resulting from intraocular penetration of corneal degradation products and bacterial toxins: in addition to the signs described above, there is then vascular infiltration of the limbus in the form of fine, parallel vessels that creep into the corneal stroma.

As well as a clinical examination, it is useful to take a swab for laboratory diagnosis. The latter can be performed quickly in the consulting room by microscopic examination of a smear of the swab taken from the ulcer margins using a Kimura spatula stained with Gram's stain.

Culture, followed by an antibiogram, will specify the nature of the bacteria present and make it possible to target any antibiotic therapy.

Mechanism of Evolution and Healing

It is important to understand the healing mechanism and the ways in which a corneal ulcer may evolve.

In the case of superficial ulceration, the basal cells of the epithelium on the periphery of the lesion become flattened, to cover the area where there is loss of substantia. In principle, the epithelium covers the bared stroma a few hours after the accident. Cell multiplication then restores the epithelium to its normal thickness.

This mechanism may also operate where the ulceration is deeper, in which case a transparent scar will be seen, hinting at the cornea's thinness at the site of the damage.

More often than not, a deep ulcer is first filled with a fibrin plug. The cell debris is digested by granulocytes, initially brought by tears, then by migration into the stroma; finally, the keratocytes migrate and secrete the collagenous fibrils that reconstitute the cornea.

Bacterial complications prevent the development of these processes. The submerged leukocytes are unable to play their part, and the corneal degradation products modifying the collagen molecules make them sensitive to the effect of other enzymes contained in the granulocytes. This may result in a rapid deterioration of the state of the cornea, which may even continue after institution of treatment and destruction of the pathogenic bacterial flora. The entire thickness of the stroma may be affected, revealing a fine, transparent membrane (descemetocele) at the bottom of the ulcer, ready to rupture at the least impact.

Prognosis

The prognosis may be difficult to evaluate since it depends simultaneously on the clinical findings, the rate of development of the lesion, its duration and the veterinary surgeon's technical abilities.

According to the depth and type of ulcer, there may be rapid perforation of the eyeball (which is what often happens with collagenase ulcers found in brachycephalic animals) or formation of hypertrophic granulation tissue (ulcer with detached edges in the Boxer).

Since each type of ulcer requires specific therapy, the sequelae will also depend on the veterinary surgeon's skill and technical facilities. In all cases where an unfavourable outcome is anticipated, and in the absence of specialised equipment, the best advice that can be given is to perform a Third Eyelid Flap and quickly institute cycloplegic, antibiotic and anticollagenase treatment.

Medical Treatment

Medical treatment has several aims:
- To suppress pain.
- To limit and treat the infection.
- To control lysis.
- To promote healing.
- To avoid neovascularisation.

Suppressing Pain

Pain control is achieved by the use of a cycloplegic parasympatholytic drug and particularly atropine in the form of a 1% collyrium.

This is applied several times a day until mydriasis is achieved, which is a sign of relaxation of spasm. Once mydriasis has been achieved, two applications per day are sufficient. Where there is corneal perforation it prevents the iris from entering the breach, and where there is uveitis it reduces the chances of the formation of synechiae.

Table 1

Antibiotics to use

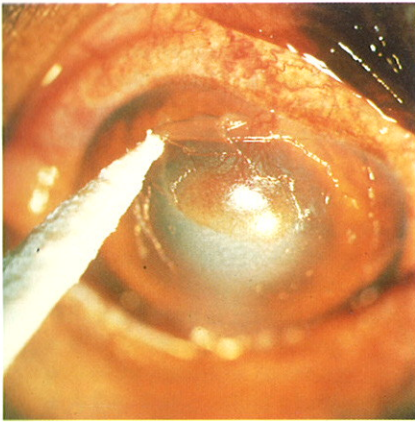|	Micro-organisms	Topical antibiotic	Antibiotic by the systemic or subconjunctival route
Gram + cocci	Staphylococcus Streptococcus Enterococcus	Bacitracin Gentamicin Chloramphenicol Fusidic acid	Penicillin Ampicillin and its derivatives
Gram − cocci	Neisseria	Gentamicin Chloramphenicol Tetracycline	Gentamicin Tetracycline Erythromycin
Gram + bacilli	E. coli Proteus Enterobacter Pseudomonas	Gentamicin Norfloxacin	Gentamicin
Anaerobes	Clostridium Fusobacterium	Chloramphenicol	Penicillin Tetracycline Pristinamycin

Figure 7 *Manual de-epithelialisation.*

Figure 8
Microscopic appearance of an ulcer with detached edges.
Photo by Gilles Chaudieu.

Limiting and Treating Infection

The use of antibiotics is essential in all cases of corneal ulceration because the absence of epithelium leaves the door wide open to all possible intraocular infections. The choice of antibiotic must be made according to the severity of the case and the result of any antibiogram.

Topical therapy with a wide-spectrum antibiotic (gentamicin or chloramphenicol) is recommended.

Table 1 gives information on the antibiotic to be used according to the result of the Gram staining.

Infection can be treated by means of subconjunctival injections. While these are not always easy to perform, they do give more lasting effects and higher antibiotic concentrations in the eye.

Systemic antibiotic administration is necessary where there is a risk of intraocular infection, which is evidenced by the symptoms mentioned above, or even by endophthalmia or panophthalmia.

Controlling Lysis

Bacteria, and the cornea itself when its epithelium is damaged, secrete proteolytic enzymes and collagenase. Their effect is to cleave the collagen molecule, which then becomes sensitive to the activity of other proteolytic enzymes, trypsin or chymotrypsin, aggravating the ulceration process. Disorganisation of the cornea may go so far as softening of the stroma, which is termed keratomalacia.

Collagenase inhibitors may prevent this. Acetylcysteine and ETA (Ethylenediamine Tetra-Acetic acid) in the form of sodium edetate are used, and it is the author's preference to use a collagenase inhibitor routinely.

Promoting Healing

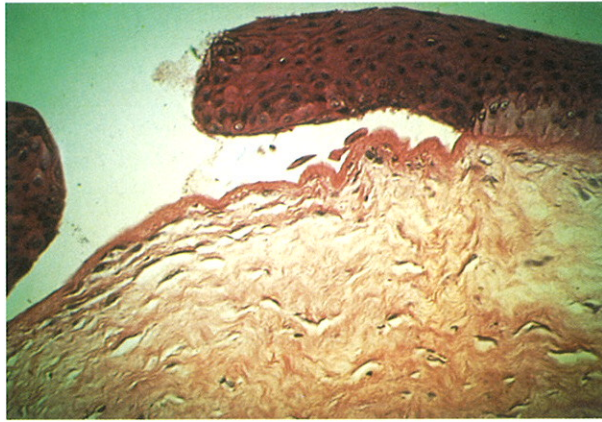The utility of trophic substances in corneal ulcer treatment is disputed.
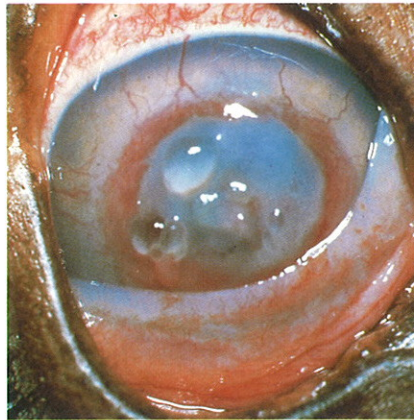

Figure 9 *Corneal oedema, keratitis bullosa and ulcer.*

Indeed, while they increase the possibility of corneal epithelium growth, they also promote neovascularisation, which is the cause of scar formation. Their use must therefore be limited in time and their effects must be controlled, possibly by corticosteroid therapy.

The principal therapeutic agents available are based on anabolic drugs, nucleotides, amino acids and vitamins.

Avoiding Neovascularisation

Corticosteroids inhibit collagen formation, reduce fibroblast activity and delay epithelial recovery. They are thus contraindicated for corneal ulcers, but their use is sometimes valuable to prevent or reduce the neovascularisation reaction that often accompanies the healing of corneal ulceration.

They must, however, only be used under very strict control and, in any case, after a negative fluorescein test.

They are particularly useful in the treatment of the punctate keratitis of the Longhaired Dachshund.

Medicosurgical Treatment

There are three options:
- Manual de-epithelialisation.
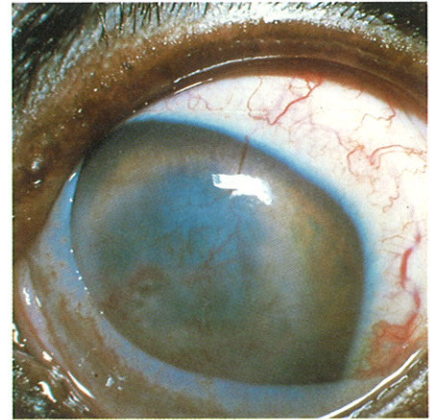- Contact lenses.
- Cyanoacrylate adhesive.

Figure 10 *Result following the fitting of a protective lens.*

Manual De-epithelialisation

The purpose of manual de-epithelialisation is to rid the cornea of epithelium that is not adhering to the stroma. It allows the growth of new epithelium having physiological basal cells that will be able to anchor on the subjacent stroma (**Figures 7, 8**).

Performed under local anaesthesia, it is carried out using a swab that may or may not be impregnated with a caustic product. Tincture of iodine and trichloroacetic acid are used for this purpose, but the author's preference is for a 1% dilute solution of povidone-iodine.

This de-epithelialisation may be performed 2–3 times at intervals of a few days.

Contact Lenses

These are used routinely in human medicine where there is a corneal ulcer, but rarely in cats and dogs. Their price, and the fact that they are so easily lost by the animals, dissuade many owners from considering the advantages that this method of treatment can offer (**Figures 9, 10**):
- Speedy pain relief.
- Maintenance of a high level of therapeutic active principle in the hydrophilic lens.

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- Growth and adherence of epithelium made easier when there is an ulcer with detached edges.

The problem most often encountered is the result of the disparity between the size and curvature of the lens on the market and the size and curvature of veterinary patients' corneas.

Cyanoacrylate Adhesive

Cyanoacrylate adhesive can be used to halt the spread of an ulcer or to repair a cornea (or at least temporarily to repair a perforation). It has outstanding tissue adhesion, proven antiseptic properties and an inhibiting effect on proteolytic enzymes.

It is first necessary to clear the cornea of epithelial and necrosed debris, then to thoroughly dry the area to which the adhesive is to be applied.

When used on a superficial ulcer or an ulcer with detached edges, the adhesive disappears as soon as the cornea has healed sufficiently.

Where there is complete perforation, a temporary repair should be made with a plug of adhesive. A transfixing graft, during which the ring of cornea surrounding the perforated area is removed, will then have to be performed.

Surgical Treatment

For some ulcers, surgical treatment may be required initially, or become necessary when healing is delayed or when there is a risk that overabundant granulation tissue will prejudice corneal transparency. Surgical treatment can be considered under two headings:

1. Methods that do not require special instruments, i.e. blepharorrhaphy, Third Eyelid Flap and conjunctival covering.

2. Methods that require microsurgical instruments as well as thorough training in this field, i.e. conjunctival, corneoscleral, lamellar and transfixing grafts.

Blepharorrhaphy

This technique involves closing the eye by suturing the upper and lower lids. It is easy to perform but nonetheless requires care to ensure that the needle is inserted into and withdrawn from the edges of the eyelid accurately so as to prevent
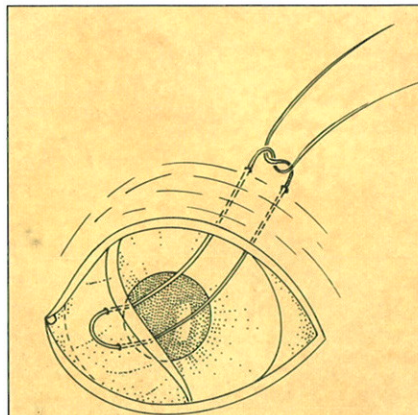

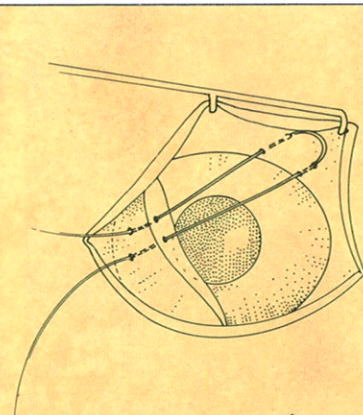**Figure 11** *Third Eyelid Flap: Technique No 1.*
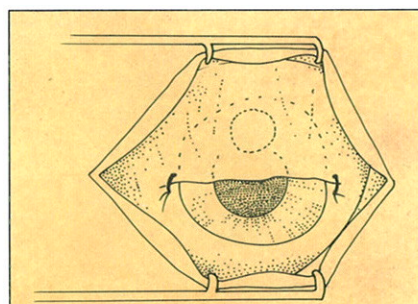

Figure 12 *Third Eyelid Flap: Technique No 2.*
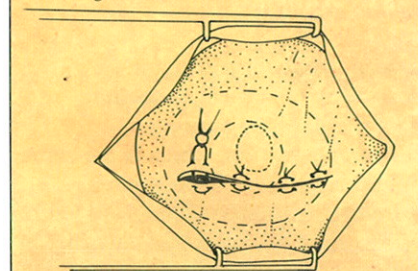

Figure 13 *180° conjunctival lowering or covering.*

Figure 14 *360° conjunctival covering.*
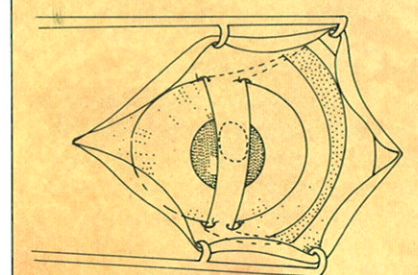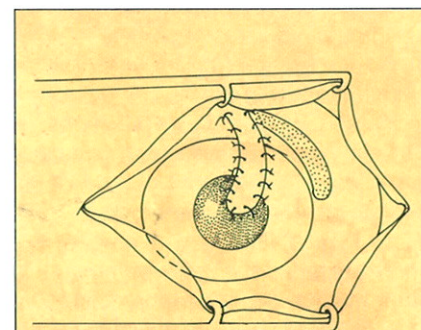

Figure 15 *Bridge covering.*

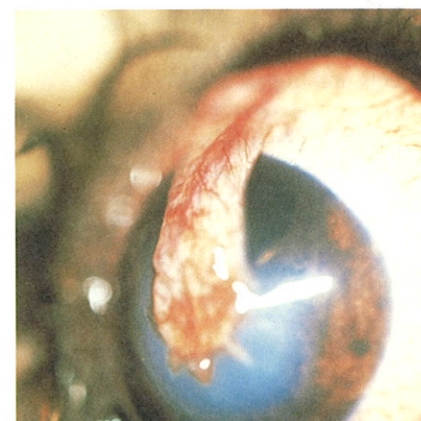**Figure 16** *Pediculate conjunctival graft.*

Figure 17 *Pediculate graft of ocular conjunctiva.*

the suture rubbing on the cornea. This technique should only be used where there is paralysis of the eyelids or where there is luxation of the globe.

Third Eyelid Flap

Involves suturing the nictitating membrane so that it is in permanent contact with the cornea. This technique's usefulness lies in the mechanical and medical properties of

this third eyelid and the ease with which it can be performed on most species and breeds.

There are two alternative methods, either fixing the nictitating membrane to the upper lid by transfixing the latter (**Figure 11**), or suturing it to the palpebral conjunctiva in the upper external quadrant (**Figure 12**).

The nictitating membrane's high permeability allows topical products to be applied, but therapy by systemic administration is preferable. A Third Eyelid Flap is usually left in position for 2–3 weeks.

Conjunctival Covering

Conjunctival covering is slightly more difficult to perform than the various techniques set out above and requires prior dissection of the palpebral conjunctiva. This is relatively slack in the dog, but far less mobile and far less easily accessible in the cat. According to the location, size and depth of the ulcer, the following may be carried out (**Figures 13–15**):

- 180° lowering or covering.
- 360° or complete covering.
- A flap – also called a bridge.

Grafts

Grafts can be performed using conjunctival flaps (pediculate or otherwise), corneoscleral sliding flaps or corneal transplants, which may involve the whole (transfixing graft), or only part (lamellar graft), of the thickness of the cornea.

Conjunctival Graft

The conjunctiva is initially prepared as for conjunctival covering, but the dissected flap is fixed directly to the cornea on the margins of the ulcer by means of a single 9/0 nylon thread (**Figures 16 and 17**). For substantia losses of less than 3 mm, it is not necessary to use a pediculate graft.

After three weeks, the conjunctiva being completely attached to the cornea, the sutures can be removed (and the pedicle, if any, cut).

This operation has the effect of leaving an opaque scar on the cornea, which is inconvenient if the ulcer is on the visual axis.

Corneoscleral Transplantation

This is more difficult and involves sliding healthy cornea adjacent to the lesion extended by a flap of sclera. It requires preliminary preparation of the fringes of the ulcer to prepare the bed for the flap and lamellar dissection of the cornea, then of the sclera. The flap, so made, is sutured with a single 9/0 nylon thread.

This technique can only be used successfully if all associated causes of infection have definitely been removed.

Lamellar Keratoplasty

Rarely carried out on animals, this procedure is used to replace the part of the cornea that has had to be removed by surface keratectomy because of massive destruction of the corneal stroma by enzymes (**Figures 18–21**), or a corneal leucoma. Only corneal stroma is used, which does not necessarily involve recourse to fresh
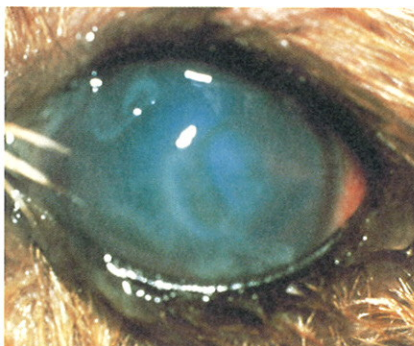

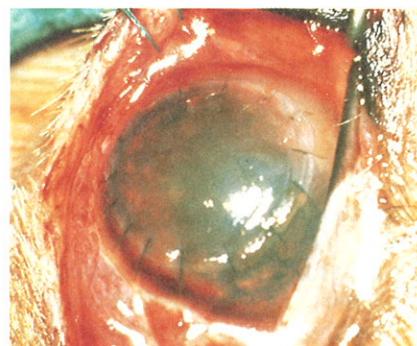**Figure 18** *Keratomalacia in a two-year-old Yorkshire Terrier.*
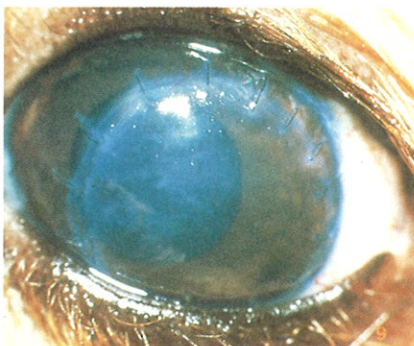

Figure 19 *Lamellar corneal graft.*

Figure 20 *Immediate post-operative appearance: after 15 days.*
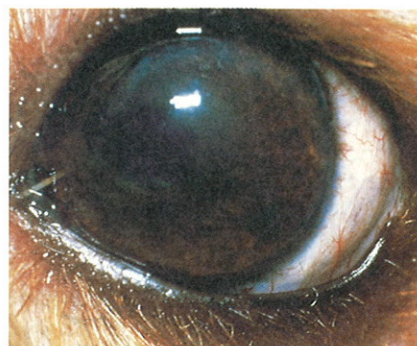

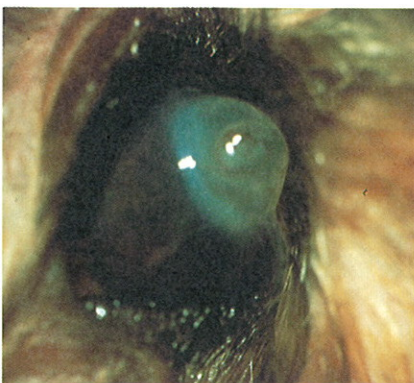**Figure 21** *After 2.5 months.*

Figure 22 *Large descemetocele in a young monophthalmous dog.*

Figure 23 *Thick conjunctival graft, then transfixing keratoplasty.*
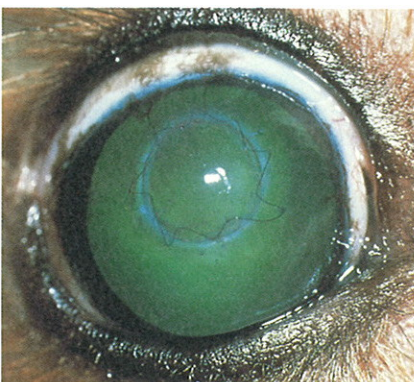

Figure 24 *Appearance of the eye after 15 days.*
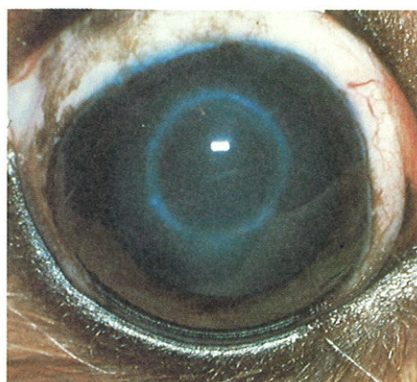
Figure 25 *After 2.5 months.*

grafts and thus obviates organ storage problems.

Transfixing Keratoplasty

Sometimes performed straight away where there is a perforated ulcer, but more often to replace a cornea that has become opaque following healing by granulation or a conjunctival graft (**Figures 22–25**), transfixing keratoplasty is certainly the technique that poses most problems in veterinary medicine – sourcing donors, widely differing eyeball sizes, removal and

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storage of the graft: moreover, the outcome of the operation is not always good.

Be that as it may, the limited indications and technical difficulties confine these last two techniques to a veterinary surgery specialising in ophthalmology.

Therapeutic Review

Treatment of a corneal ulcer should be in several stages:

1. Evaluation of the extent of the ulcer.
2. Investigation of the cause and its removal, if discovered.
3. Therapy aimed at halting its spread.
4. Treatment to promote healing with the minimum of sequelae.

Each ulcer is a special case, and the following is based solely on the depth of the lesion.

Superficial Ulcer

Generally very painful because the sensitive trigeminal nerve endings are located in the superficial layers of the cornea, these ulcers heal rapidly after institution of the standard medical treatment: atropine, antibiotic, anticollagenase. This type of ulcer should normally heal within a week.

Special mention should be made of ulcers with detached edges. Although the ulcer is superficial and has no tendency to become worse, no improvement is seen, or only a very transitory improvement. The abnormality found in the basal cells of the epithelium (**Figure 8**) explains the refractory or recurring nature of this affection, which has to be treated by surgery: after de-epithelialisation (**Figure 7**), carried out under general anaesthetic, the stroma is roughened (using a bistoury or needle), before performing a Third Eyelid Flap.

Medium Ulcer

Two types are recognised:

● If the ulcer does not tend to worsen, the same medical treatment as is used for superficial ulcers is instituted, possibly combined with therapy (anabolic), promoting healing.

● If the ulcer is evolving or seems to be progressing to marginal oedema caused by collagenases and uveal reaction, medical treatment alone may be instituted, monitoring the lesion daily. Topical treatment must be instilled very regularly every hour or every two hours.

The least sign of any deterioration must be noted and prompt surgical treatment considered (Third Eyelid Flap, conjunctival covering).

Deep Ulcer

Surgical treatment must be considered straight away and, according to the veterinary surgeon's facilities or technical skills, it may consist of Third Eyelid Flap, conjunctival covering or a conjunctival graft. It is always best to use the technique that makes it possible to monitor the state of the adjoining cornea and the intraocular structures easily. If there is considerable uveitis, corticosteroid treatment must be instituted promptly. The use of corticosteroid therapy by systemic administration does not seem to have the same effect on healing as topical treatments, and it is essential in order to prevent the sequelae that could be caused by uveitis (synechia, phthisis bulbi, glaucoma).

Descemetocele

Where the lesion is small, the margins of the loss of corneal substantia can be sutured edge to edge, the astigmatism induced not being particularly inconvenient to animals.

Where the lesion is larger, it is necessary to resort to conjunctival covering or, better still, the different grafting procedures: transfixing or, in the absence of a fresh graft, corneoscleral or pediculate, followed a few months later, when healing is complete, by a transfixing graft (**Figures 22–25**). If the cornea is perforated, a transfixing graft may be made straight away after repositioning the iris, either with a viscoelastic product or after iridectomy, if its condition prevents it from being reinstated.

Table 2 summarises the various therapeutic options.

Conclusion

Corneal ulcers are common in animals and may assume many forms. There is certainly no panacea, but the varying therapeutic methods available should make it possible to deal with most cases, providing the patient is still in a satisfactory condition when presented and the owner accepts the commitments necessitated by treatment, particularly the need for regular application of medication and frequent monitoring by the veterinarian.

Further Reading

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Table 2

Therapeutic approach to different ulcers

	Antibiotic	Cycloplegic	Anti-collagenase	Debridement	Third Eyelid Flap	Conjunctival covering	Plastic surgery
Superficial ulcer	+	+	+	+			
Ulcer with detached edges	+	+	+	+++	+		
Medium ulcer	+	+	++	++	++	+	
Evoluting ulcer	++	++	+++		++	+++	
Descemetocele	+++	++	+++		+	+++	+++
Staphyloma	+	+++	+			++	+++