Non-ulcerative corneal disorders in the dog and cat

Abstract:

Non-ulcerative corneal disorders include any conditions of the cornea which do not uptake fluorescein stain. Pathological changes result in some loss of corneal transparency, which is essential for normal vision. There are a limited number of ways in which the cornea can react to disease, and these include corneal oedema, neovascularisation, inflammatory cell infiltration, pigmentation, lipid or calcium deposition and fibrosis (scarring). Common non-ulcerative corneal diseases in dogs and cats include keratoconjunctivitis sicca (KCS), the inflammatory conditions pannus (dogs) and eosinophilic / proliferative keratitis (cats), and corneal sequestrum (cats).

The function of the eye is to receive light which is refracted and focused onto the photoreceptors of the retina. The cornea is the major organ of refraction (not the lens) and it must be transparent and maintain a normal curvature for perfect vision.

Corneal anatomy is important to review. The outer non-keratinised stratified squamous epithelium accounts for approximately 10% of corneal thickness. A basement membrane attaches this layer to the corneal stroma which constitutes approximately 90% of the corneal thickness and is made of mostly collagen. Descemet's membrane (DM) is the basement membrane of the innermost epithelium, which is one cell layer thick and contains an active ionic pump to remove fluid from the corneal stroma. The whole structure is 0.5-0.6mm thick in the dog and cat.

The cornea is transparent and it achieves this by the normal lack of blood vessels, the absence of pigment, the precise arrangement of the stromal collagen fibrils and by being in a state of dehydration. It is densely innervated which is why corneal ulcers (especially superficial ones) are so painful.

Corneal opacities can occur by a number of different mechanisms. Corneal oedema is over-hydration of the cornea, and can occur because of an epithelial defect (ulcer) or endothelial defect with failure to pump fluid out, for example in age-related corneal endothelial dystrophy. Scarring occurs as the replacement collagen fibrils are haphazard in orientation, and because of fibrosis. Neovascularisation may be superficial or deep, and is a normal part of corneal wound healing, but should regress when the healing is complete. The cornea may be infiltrated, most
commonly with inflammatory cells, as is seen in the immune-mediated condition episcleritis. Pigment comes from blood vessels and may remain after inflammation and is difficult or impossible to remove. Corneal foreign bodies cause opacity by their sheer presence.

Corneal disease may be congenital, e.g. dermoid; developmental, e.g. dystrophy; or acquired, e.g. ulceration. The approach to a case presenting with corneal disease involves history taking (for example, was there trauma involved), a thorough ocular examination, a Schirmer tear test, application of topical anaesthesia if the eye is painful, and fluorescein staining. An underlying cause is looked for; for example is it a breed-related problem, has it had previous treatment (e.g. grid keratotomy in a cat giving rise to a corneal sequestrum), trauma, eyelid conformation for trichiasis (rubbing hairs), corneal foreign bodies, inadequate tear production or nerve problems. Problems with the trigeminal or facial nerve may cause an inability to blink (lagophthalmos) which would cause corneal problems.

**Fluorescein stain** should be applied. This section is dealing with non-ulcerative keratitis, and by definition there should be no uptake of fluorescein stain. However many inflammatory lesions have diffuse faint fluorescein uptake e.g. eosinophilic (proliferative) keratitis and corneal sequestrum in cats. Therefore fluorescein should still be applied and used as part of the on-going monitoring of these cases. As mentioned previously, topical anaesthetic is very useful in these cases and allows for minor procedures to be done, for example corneal cytology or snip biopsy of the conjunctiva.

**Persistent pupillary membranes** are remnants of the embryonic vascular tissue which spanned the pupil in utero to provide nutrition to the underlying developing lens. The membrane usually regresses before the eyelids open but may leave behind some strands which arise from the iris colarette (centrally between the pupil margin and periphery) and may attach to another part of the iris, come forwards and attach to the cornea (where it may cause a white mark or corneal oedema) and backwards to attach to the lens capsule where it may form a focal cataract. They usually are of little consequence and require no treatment.

**Keratoconjunctivitis sicca** (KCS) is a common, serious blinding disease of animals, and most commonly affects dogs. It is a quantitative deficiency of the aqueous component of the tear film. This causes a drying of the ocular surface (the cornea and conjunctiva) which results in their inflammation. The tear film is composed of lipids and mucins as well as the aqueous portion, and it is also possible to suffer from the lack of mucins which would lead to premature evaporation of the tear film and qualitative deficiency. This may be diagnosed using the fluorescein break up time test.
The signs of keratoconjunctivitis include:

- Conjunctivitis
- Keratitis
- Purulent tenacious ocular discharge (often misinterpreted as pus / infection)
- Blepharospasm and general ocular discomfort
- Corneal neovascularisation
- Superficial corneal pigmentation

Causes of KCS include:

- Immune-mediated destruction of the lacrimal glands causing lacrimal adenitis
- Hereditary in some breeds
  - English Bulldog, West Highland white terrier, cocker spaniel, cavalier King Charles spaniel, shih tzu, Lhasa apso, pug, Pekingese
- Congenital hypoplasia of the lacrimal gland, especially in miniature breeds
- Iatrogenic
  - Drug-induced – topical atropine, general anaesthesia and sedation all lower tear production
  - Drug toxicity – sulphonamides, potassium bromide – withdraw drugs quickly
  - Surgical removal of protruding nictitans glands – cherry eye
- Neurogenic – damage to the parasympathetic portion of the facial nerve
- Infectious lacrimal adenitis, e.g. distemper, leishmaniasis
- Systemic metabolic disease e.g. diabetes mellitus, Cushings disease, hypothyroidism

Clinical examination should include a careful history taking, and thorough ocular examination as for other conditions with emphasis on the Schirmer tear test (STT).

<table>
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<th>STT reading:</th>
<th>Interpretation</th>
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<td>&gt;25mm/minute</td>
<td>Normal or the eye is irritated / painful</td>
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15-25mm/minute  Normal
10-14mm/minute  Sub-optimal
0-10mm/minute  Dry eye – keratoconjunctivitis sicca

Treatment of KCS should be started quickly before there are destructive permanent corneal changes. The owner should be instructed to clean the eyes well before application of treatment to reduce the mucoid ocular discharge, and therefore allow the medications more chance to work rather than getting de-natured by the mucoid discharge or not making sufficient contact with the conjunctiva. When tear levels are very marginally low and there are no supporting ocular signs of KCS, supplementation with artificial tears may be sufficient, although of course on-going monitoring will be required. Carbomer gel is normally used, although there are a wide variety of tear substitutes available. In more advanced KCS, artificial tears may still be used as an adjunct to treatment.

The appropriate and licensed treatment for KCS is Optimmune (Merck Animal Health) which contains 0.2% cyclosporine, a powerful immunosuppressant. Therefore it suppresses the immune-mediated attack on the lacrimal glands. There is a lag phase before the full benefit is seen, and it can take 4-6 weeks to reach maximum benefit. Therefore the treatment should not be stopped for at least this period of time, and artificial tears could be used to supplement it in the early days. It generally works very well, although it does have less of a benefit when the tear readings are really low, near zero. There are a variety of other unlicensed treatments. It is possible to make up a stronger solution of cyclosporine to 1 or 2% in corn oil when Optimmune fails. The use of this medication falls under the Cascade System. Pilocarpine eye drops may be used orally in the case of neurological dry eye at a dose of 2 drops of 2% solution twice daily for every 10kg. The dose may be increased by one drop once per week until systemic signs of toxicity such as vomiting occur and then reduced by one drop and kept at that dose. However if it is working at a lower dose, increasing is not necessary. Topical steroids could be considered to reduce neovascularisation and as an additional immunosuppressant. The potential danger is that dry eyes are more prone to corneal ulceration, and steroids are contraindicated in this situation. A course of topical antibiotics will reduce bacterial over-growth but are not required long-term. The purulent discharge is not due to bacteria but is due to the high levels of mucins and inflammatory cells. Tacrolimus is another immunosuppressant drug which is not yet available as an eye drop, but is showing very promising results for treatment of KCS. It is only available as a skin cream at present.
The condition is not treated but is managed, and it is important to communicate the life-long nature of the condition with the client. Merck Animal Health produce a client DVD which can help them to understand this. On-going monitoring is required, the frequency varies on a case by case basis. Optimmune treatment is a lot more successful early in the course of the disease than when tear levels have been allowed to reach zero.

Surgery is an alternative treatment which is carried out a lot less commonly than it used to be, due to the success of Optimmune. The duct of the parotid gland is re-routed to the conjunctival sac so that saliva will moisten the globe, called a **parotid duct transposition**. It is still an appropriate treatment in cases which are unresponsive to medical treatment, and in cases of congenital KCS (most common in Yorkies, Cavalier King Charles spaniels and small terriers).

**Pannus** (chronic superficial keratitis) is an immune-mediated condition which can affect any breed but principally affects the German shepherd, the greyhound and the border collie. It is a progressive, life-long disease which usually affects both eyes, although they may initially present with one eye more obviously affected. Like KCS, the condition is potentially blinding and therefore early management is key. Pannus usually affects the lateral cornea first, thought to be due to the fact the UV light (and high altitude) trigger the condition. It may progress to affect the rest of the cornea and the third eyelid. There is a stromal infiltrate with vascular cells, lymphocytes, plasma cells, pigment and lipid. Treatment of pannus involves immunosuppression using Optimmune, topical steroids, or a combination of the two. Optimmune is more desirable than topical steroids for long-term use. Typically more frequent treatment is required in the summer than in the winter. Treatment is applied until the condition is in remission and then slowly tapered to effect. Another form of treatment is to avoid the sunlight which can be achieved by the dog wearing UV-tinted Doggles, which many dogs do tolerate.

**Eosinophilic (or proliferative) keratitis** is a condition of cats (and horses) rather than dogs. It may affect one or both eyes. It is another inflammatory immune-mediated condition, similar to pannus. The cornea and conjunctiva are mainly infiltrated with eosinophils and mast cells. There may be an association with herpesvirus. Similar to pannus in dogs, the lateral cornea is often affected first, due to UV light exposure. The appearance varies, but typically is a raised white or pink cottage cheese-type adherent corneal exudate with a roughened surface. There may be some fluorescein retention over the area. Despite this, so long as the area is well vascularised, treatment is still either topical steroids or Optimmune. Oral immunosuppression may be provided if required. Oral famcyclovir (Famvir) could be used when the condition is first diagnosed, if feline herpesvirus is considered likely to be present. Oral megesterol acetate
(Ovarid) is useful for refractory cases but does have potentially serious side-effects. Usually the condition goes into remission but it can be recurrent so on-going management is required.

**Corneal sequestrum** is a condition almost unique to cats. It is focal, variably staining brown to black discrete plaque raised above the level of the corneal epithelium, representing an area of corneal degeneration and necrosis. Any breed may be affected, but there is a breed predisposition among the Persians, Siamese, Exotic short-hairs and Himalayans. It usually affects one eye but both eyes can be affected in some unlucky cats. It can affect young or old cats. The cause is unknown but it is most likely an inappropriate healing response to a chronic corneal ulcer or chronic irritation. There is thought to be an association with herpesvirus infection also. Treatment is either medical or surgical, although medical treatment is quite prolonged. This involves supporting the cornea with topical antibiotics and artificial tears until the lesion may eventually slough to leave a corneal ulcer which should heal with appropriate care. However this can take 6-12 months to occur, and the uncomfortable cat is a lot better off with surgical resection using a superficial keratectomy. Depending on the depth of the sequestrum, and therefore the depth of cornea which needed to be removed, a conjunctival pedicle graft or corneo-scleral transposition are the surgical treatments of choice. While a conjunctival pedicle graft may be resected in 6 weeks in an attempt to create a clear visual axis, leaving it in place permanently has been shown to reduce the likelihood of recurrence. A corneo-conjunctival transposition is preferable in some cases (especially if the sequestrum is in the centre of the cornea) as it transposes transparent cornea into the resected area. Thus the outcome is normally a clear cornea with better vision.