CPD article

# Canine keratoconjunctivitis sicca: an overview

Keratoconjunctivitis sicca (KCS) is a relatively common condition in dogs, which is caused by a deficiency of the aqueous component of the tear film. The most common cause is immune-mediated disease but other aetiologies include neurogenic, congenital, endocrine and infectious disease, drug-induced, iatrogenic, evisceration/prosthesis and irradiation. Diagnosis is made by performing a Schirmer Tear Test. Clinical signs include ocular discomfort, conjunctival hyperaemia, a tenacious mucopurulent ocular discharge and a lacklustre appearance to the corneal surface. Topical medication forms the mainstay of treatment but in refractory cases surgical intervention should be considered. This article gives an up-to-date overview into the management of canine KCS.

10.12968/coan.2014.19.7.336

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**Key words:** Keratoconjunctivitis sicca | Dry eye | Canine | Review | Management

Keratoconjunctivitis sicca (KCS) or 'dry eye' is a relatively common clinical disease encountered in general practice and arises as a result of a deficiency of the aqueous component of the tear film, characterised by desiccation of conjunctiva and the cornea (Barnett and Sansom, 1985; Barnett Sansom, 1987; Helper, 1996). Immune-mediated KCS is the most common form of the condition in dogs and is a bilateral disease (Kaswan, 1985).

Since the introduction of topical cyclosporine in 1987, medical management has formed the mainstay of treatment for canine KCS and generally offers a good response in the majority of cases if the condition is caught early (Kaswan, 1990; Olivero et al, 1991; Bounous et al, 1995; Sansom and Barnett, 1995; Izci et al, 2002).

However, some immune-mediated cases or cases of differing aetiologies fail to respond to this approach and alternative medical and even surgical options need to be considered.

This article gives an overview on how to diagnose and successfully manage canine KCS, including the more challenging, atypical cases. The author will also review the latest literature referring to canine KCS, focusing specifically on the most up-to-date treatment options available.

## Aetiologies

### Immune-mediated

As already mentioned, immune-mediated destruction of the lacrimal glands is by far the most common aetiology of KCS in our canine patients, and certain breeds are over represented, including the West Highland White Terrier, Cavalier King Charles Spaniel, English Cocker Spaniel and the Shih Tzu (Sanchez et al, 2007). A sex predisposition in West Highland White Terriers has also been identified with females being more likely to be affected (Barnett, 1988).

### Neurogenic

Neurogenic dry eye, whereby the parasympathetic innervation to the lacrimal glands is lost, is not uncommon, and in a recent retrospective review of 11 cases the majority were presumed to be idiopathic (Mathies et al, 2012). However, no diagnostic imaging was reported in this study to specifically rule out other aetiologies of neurogenic KCS. Possible pre-ganglionic lesions affecting the parasympathetic fibres include otitis (media or interna), petrositis, and erosive lesions involving the floor of the middle fossa of the skull. In cases of otitis and petrositis the KCS may be accompanied by signs of facial nerve paralysis, Horner's syndrome or vestibular disease. In cases of erosive

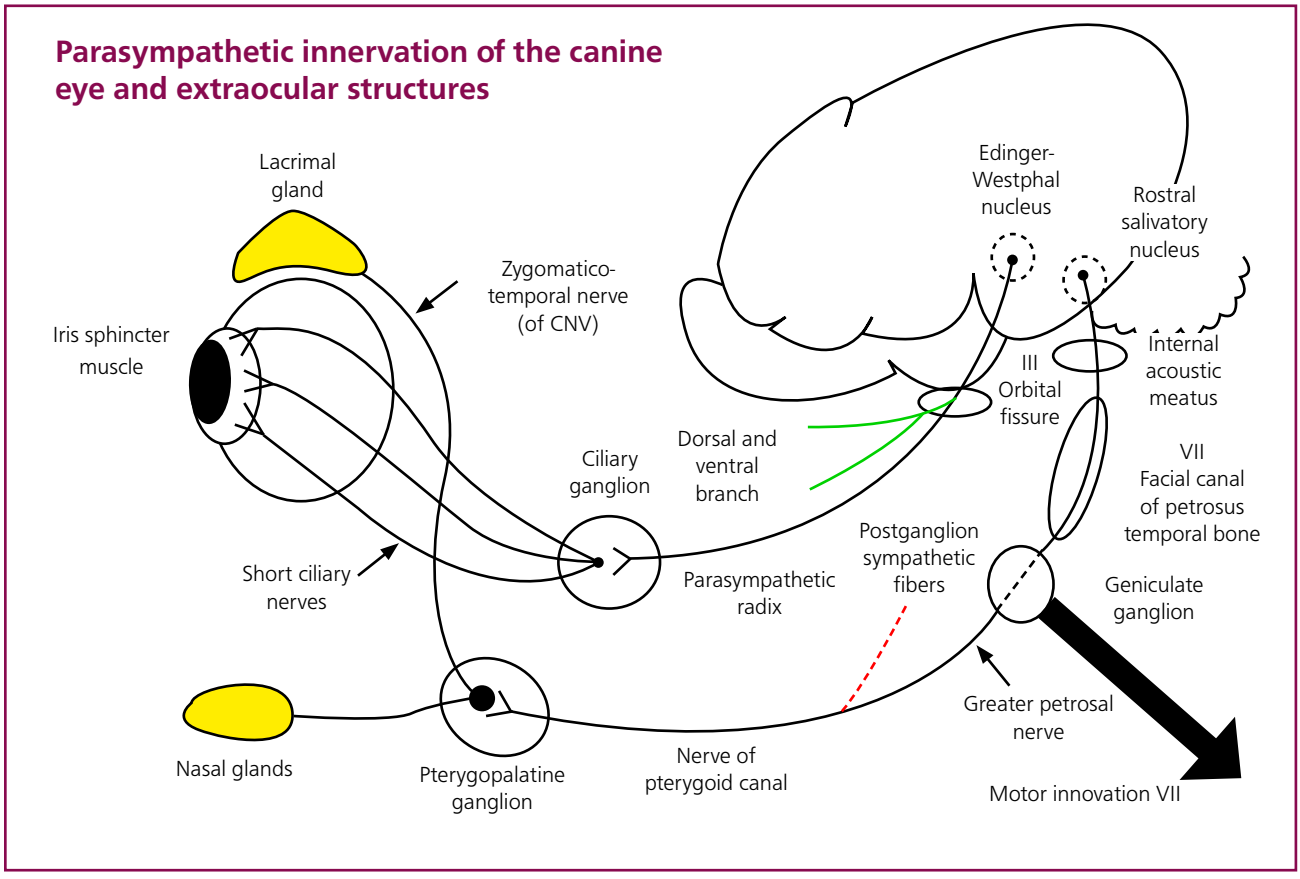


*Figure 1. A diagram showing the parasympathetic innervation to the eye, extraocular muscles and nose in a dog*

lesions involving the floor of the middle fossa of the skull, there may be concurrent signs of trigeminal nerve dysfunction including facial anaesthesia. Lesions involving the pterygopalatine fossa itself could include periorbital myositis, cellulitis and dental abscessation. Postganglionic parasympathetic lesions are most commonly associated with orbital trauma (Mathies et al, 2012; Webb and Cullen, 2013) (*Figure 1*).

### Other causes

Other causes of KCS include: endocrine disease (diabetes mellitus, hypothyroidism and hyperadrenocorticism) (Williams et al, 2007),; drug-induced causes (systemic sulphonamides and etodolac, topical atropine and topical/general anaesthetic) (Wilkie and Wolf, 1990; Klaus et al, 2007; Giuliano, 2013); surgical removal of the nictitans gland (Helper et al, 1974); infectious disease (e.g. distemper, leishmaniasis); and evisceration/prosthesis and irradiation (Giuliano, 2013). Although anecdotally congenital KCS may occur in the English Cocker Spaniel, two relatively new breed-related congenital dry eye syndromes have been described in the Yorkshire Terrier (Herrera, 2007) and Cavalier King Charles Spaniel (also known as ichthyosiform dermatosis) (Hartley et al, 2012).

## Clinical presentation

### General signs

Canine KCS can present acutely or chronically and the associated clinical signs can vary. Ocular discomfort, conjunctival hyperaemia, a tenacious mucopurulent ocular discharge and a lack-lustre appearance to the corneal surface are the most common signs (*Figure 3*). Sequelae to KCS may include corneal neovascularisation, corneal pigmentation and progressive corneal ulceration, all which can result in blindness.

### Neurogenic signs

An ipsilateral dry nose (*Figure 4*) is considered pathognomonic for neurogenic KCS but any acute-onset unilateral KCS or KCS not responding to conventional treatment could be considered to be neurogenic in origin. The dry nose is due to the shared pre-ganglionic parasympathetic fibres up to the point of the synapse in the pterygopalatine ganglion of the lateral nasal gland and the lacrimal glands (*Figure 1*). As already discussed, the presence of other neurologic deficits (Horner's syndrome, facial paralysis, signs of vestibular disease or trigeminal dysfunction) may help in localisation of lesions. If neurogenic KCS is present without signs of facial paralysis, the lesion is likely affecting the greater petrosal nerve distal to the geniculate ganglion (Mathies et al, 2012).

### Laterality

Immune-mediated, drug-induced, congenital ichthyosiform dermatosis-related, infectious and endocrine disease-associated KCS are always bilateral, whereas the other causes discussed are usually unilateral.

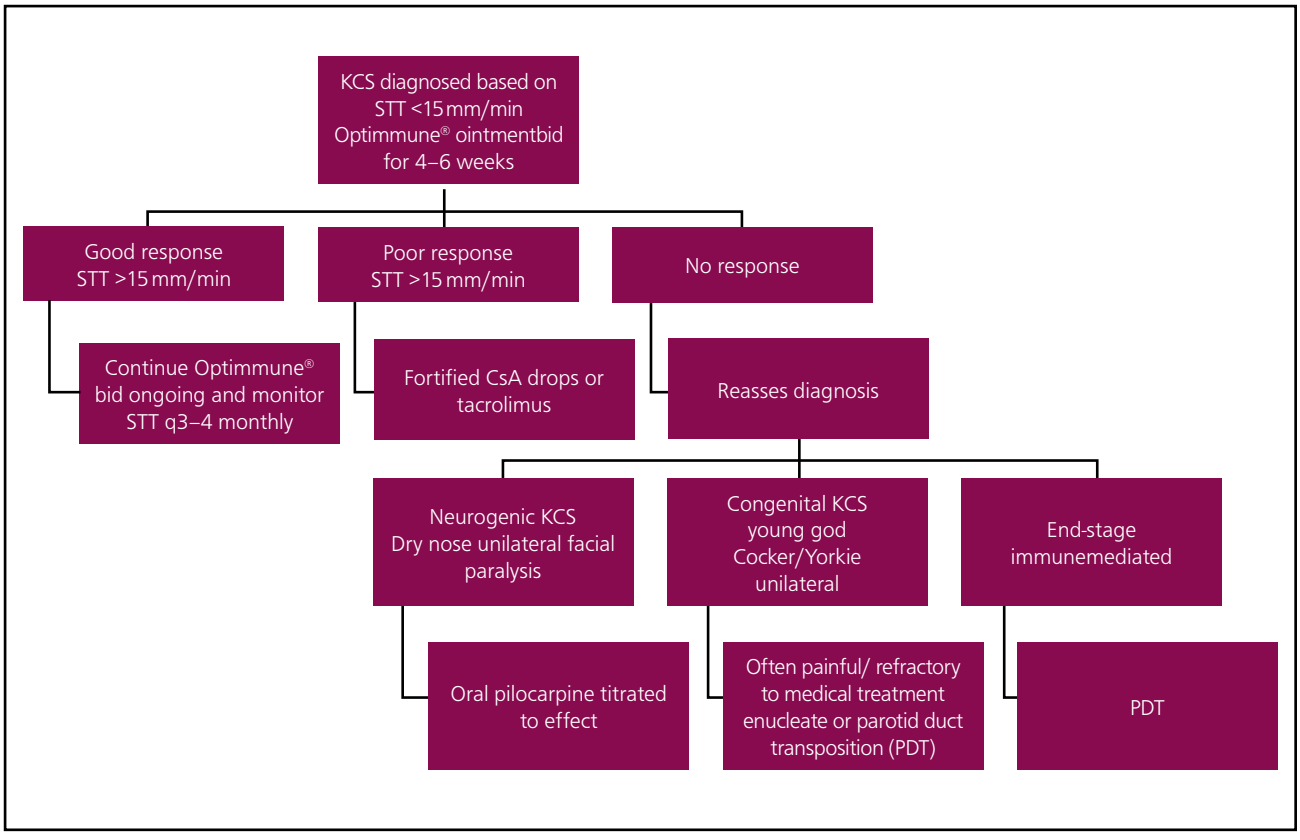


*Figure 2. A flow chart summarising the treatment of canine keratoconjunctivitis sicca*

## Diagnosis

Any dog that presents with a red, irritated eye and ocular discharge, or has a history of chronic conjunctivitis, should undergo a Schirmer Tear Test (STT). The STT (type 1) remains the standard means to assess both the reflex and basal aqueous tear production in dogs. It is important to perform this test early on in the examination to minimise the effect of reflex tearing due to eyelid manipulation and before topical treatments (e.g. fluorescein) have been applied. The distal tip of the STT strip contacts the corneal surface. A STT (type 2) can be performed following the application of topical local anaesthetic and measures only basal tearing.

In the clinical setting canine STT 1 readings are interpreted as in *Table 1*.

**Table 1. STT1 readings and interpretation**

| Schirmer Tear Test 1 (STT1) reading (mm/min) | Interpretation |
|---|---|
| ≥15 | Normal production |
| 11–14** | Early KCS |
| 6–10 | Moderate KCS |
| <5 | Severe KCS |
| 0 | Absolute KCS |

**Borderline results should be interpreted with caution and considered in conjunction with other clinical signs, as other factors (e.g. topical atropine) may reduce the STT1 in the absence of true KCS

It is important to note that in cases of ulcerative keratitis the STT1 reading may be falsely elevated due to pain in the affected eye, causing increased levels of reflex tearing.

Although not a subject for discussion in this article, there are a subset of dogs that present with a qualitative tear film abnormality: these cases may show clinical signs similar to KCS but have normal STT1 values. A tear film break-up time in such individuals will be significantly decreased (<5 seconds) (Giuliano, 2013).

Cases of neurogenic KCS should undergo a neuro-ophthalmic examination including palpebral, corneal and vestibulo-ocular reflexes on top of the routine ophthalmic examination. Further diagnostic imaging, such as an MRI, scan should be considered if there are concurrent neurological deficits.

## Treatment

Treatment of canine KCS requires first an accurate diagnosis as to the underlying cause of the aqueous tear film deficiency. For the majority of causes, topical lacrimostimulants and lacrimomimetics +/- temporary use of antimicrobial agents make the mainstay of treatment.

### Lacrimostimulants

Topically applied cyclosporine A (Optimmune®, MSD Animal Health) achieves its action through both immunomodulating and tear-stimulating properties. This calcineurin inhibitor blocks the activation and proliferation of T lymphocytes involved in immune-mediated lacrimal gland dysfunction. It also has an additional mucino-

genic effect, which also helps to improve the quality of the pre-ocular tear film (Olivero, 1991; Sansom et al, 1995; Izci, 2002). A small amount of the drug should be applied to both eyes twice daily and it may take up to six weeks to exert its maximal beneficiary effects. Stronger concentrations of the drug can be compounded 'in-house' with corn oil but concentrations greater than 1% tend to cause local irritation in the author's experience.

Recently, another topically applied immunomodulatory agent has become more widely used in the treatment of KCS: tacrolimus (Protopic, Astellas). Tacrolimus is a macrolide antibiotic that achieves its action in a similar way to cyclosporine A (Berdoulay, 2005). The use of this drug is currently off-licence in the UK and should therefore be reserved for use in cases that are refractory to treatment with cyclosporine A (ideally in conjunction with an off-licence consent form signed by the owner). It is also important that owners are instructed to wear gloves to prevent percutaneous absorption of the drug. A small amount can be applied to the eye using a cotton bud or 1 ml syringe twice daily (the plunger is temporarily removed and the syringe is partly filled with the ointment—the syringe is then reconstructed and used to apply a small amount of the ointment directly into the eye).

A recent study has shown that another calcineurin inhibitor, SCY-641 when applied topically in an aqueous solution to dogs suffering naturally occurring KCS was well tolerated and efficacious. However, further trials are required before this drug becomes available to be used in a clinical setting (Gilger et al, 2013).

Neurogenic and some congenital KCS cases may benefit from treatment with the parasympathomimetic agent pilocarpine (Alcon). Traditionally, a 1% solution is given orally at an initial dose of 1 drop/10kg 2–3 times daily and titrated to effect. The dose is gradually increased until there is a beneficial clinical effect noted, i.e. increased tear production. However, in poorly responsive cases the dose may have to be increased until signs of systemic toxicity are noted (hyper salivation, vomiting, diarrhoea and cardiac arrhythmias), at which point it is discontinued and restarted at a lower dose. If applied topically, pilocarpine is irritant but has been used as a diluted 0.1% solution by the author to some effect. Ongoing lifelong therapy is usually required in cases of neurogenic KCS but some cases (50% of cases in one study) (Mathies, 2012) may spontaneously recover and so no longer require treatment.

## Lacrimomimetics

Topical lacrimomimetic therapy is very important especially early on in the management of KCS, i.e. until the aqueous component of the tear film normalises. Lacri-Lube® (Allergan), ViscoTears® (Novartis) and Lubrithal (Dechra) are all examples of commonly used tear replacement therapies, although the former is of preference due to the viscous nature of the product and can be applied three times daily (as opposed to the other less viscous options, which require higher frequencies of application). A relatively new cross-linked hyaluronic acid based hydrogel (Remend®, Bayer Animal Health) has shown to improve the clinical signs associated with KCS within two weeks when applied topically twice daily and may be a useful adjuvant in the medical treatment of KCS (Williams and Mann, 2013).

*Figure 3. The right eye of a Cavaliar King Charles Spaniel showing clinical signs of keratoconjunctivitis sicca, including conjunctival hyperaemia, a tenacious mucopurulent ocular discharge and a lack-lustre appearance to the corneal surface*

*Figure 4: An ipsilateral dry nose in a dog suffering from unilateral neurogenic keratoconjunctivitis sicca*

## Topical antibiotics

Topical antibiotics with a broad spectrum of activity (e.g. chloramphenicol) may also be of benefit early on in the treatment course of canine KCS. Secondary bacterial infections are not infrequent in KCS due to inadequate cleansing of the ocular surface (Petersen-Jones, 1997). In cases of a persistent mucopurulent ocular discharge despite treatment, bacterial culture and sensitivity testing may be required.

## Surgical intervention

In medically refractive cases of canine KCS surgical intervention should be considered. Although permanent partial tarsorrhaphy and punctal occlusion have been described, these techniques have shown limited benefit, and parotid duct transposition (PDT) is the surgical option of choice for cases in which medical management has proven unsuccessful. However, dogs with xerostomia (dry mouth) are not good candidates and testing for saliva production prior to surgery is essential. This can be done by applying a small amount of lemon juice to the tongue and observing the area of the parotid papilla (the

## KEY POINTS

- Immune-mediated destruction of the lacrimal glands is the most common aetiology of canine keratoconjunctivitis sicca (KCS), and certain breeds are over represented
- Early diagnosis and treatment with topical cyclosporine generally offers a good response in the majority of cases of dogs with KCS
- In cases that prove refractory to standard medical therapy, reconsider the underlying aetiology (e.g. neurogenic) and/or modify the treatment
- Surgical intervention in the form of parotid duct transposition can be successful in medically refractive patients but case selection and appropriate microsurgical equipment and training are important to maximise a successful outcome
- In neurogenic KCS, a neurological examination is important to ensure no other neurological deficits are present

buccal mucosa, dorsal to the caudal aspect of the maxillary carnasial tooth). A PDT can be performed via the oral or facial approach and appropriate microsurgical equipment and training are important to prevent serious intra-operative complications. A recent retrospective published review carried out by the author showed that although the procedure carries a relatively high complication rate (51%: of which the majority could be managed conservatively) the overall success rate was very high (93%). The study also highlighted that dogs post PDT were generally more comfortable, had improved vision and required less ongoing maintenance (Rhodes et al, 2012).

The placement of episcleral silicone matrix cyclosporine implants in dogs with KCS has just been described in 15 dogs in a pilot study. The results showed that the implants were well tolerated and effective in dogs with KCS responsive to topical cyclosporine as well as dogs with a poor response to topical treatment. However, further study is required to evaluate the duration of efficacy and optimal dose of drug (Barachetti et al, 2014).

## Summary

Canine KCS is a relatively common condition encountered in general practice that can be readily diagnosed. Although the majority of cases can be managed with standard medical therapies, a sub-group of dogs with KCS prove to be very challenging. In such cases. the underlying aetiology should be reviewed and alternative medical or surgical options considered. In cases of neurogenic aetiology the presence of other neurological signs may assist the clinician in localising the exact position of the lesion(s) and prompt the possible need for diagnostic imaging. Referral to a specialist ophthalmologist can be beneficial especially if the dog would benefit from PDT surgery. Brand new treatments undergoing clinical trials may prove useful in the future to manage canine KCS refractory to current medical management options. CA

*Conflict of interest: none*

*Acknowledgement: The author would like to thank Carolin Chiwitt MRCVS for her contribution to Figure 1.*

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