Keratoconjunctivitis sicca in dogs: causes, diagnosis and treatment

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ANDREW LEWIN BVM&S, MRCVS examines causes of the condition, diagnosis and medical treatment of KCS, which, he says, has led to a reduction in the need for surgical intervention

THE pre-ocular tear film (PTF) is composed of lipid, mucus and aqueous secretions. The function of the PTF is to maintain ocular surface health by facilitating lubrication, removal of foreign material and provision of antimicrobial components.

Keratoconjunctivitis sicca (KCS) is caused by a deficiency in the aqueous portion of this tear film, which is produced by the nictitans and lacrimal glands. In one study (Helper, 1996), KCS was estimated as the underlying condition in one per cent of all canine patients seen at a group of referral centres. If left untreated or poorly controlled, it can result in severe pain and, ultimately, blindness for the patient. The condition can generally be readily diagnosed in the consulting room, and in most cases, be managed effectively with diligent monitoring by the veterinarian and owner. Some cases may prove difficult to control with medical treatment alone and so surgery, in the form of a parotid duct transposition (PDT), should be considered for those patients that prove refractory to medical therapy.

Causes of canine KCS

There are many causes of KCS in dogs (Table 1), with some breeds more likely to be affected in the UK (Table 2).

The local, immune-mediated form is the most common type of KCS in dogs, although systemic immune-mediated diseases may also affect tear production (Giuliano and Moore, 2007). In both of these forms, the function of the nictitans and lacrimal glands is compromised as a result of immune-mediated adenitis. Systemic conditions including hypothyroidism, diabetes mellitus and hyperadrenocorticism can all lead to reduced tear production (Williams, 2007).

Drug therapy, such as topical atropine and systemic sulphonamides, can both result in reduced tear production, and these effects can be either temporary or permanent. It has been suggested dogs of less than 12kg bodyweight undergoing treatment with oral trimethoprim-sulfadiazine are at an increased risk of developing KCS (Berger et al, 1995). Infectious conditions, such as distemper virus and chronic blepharoconjunctivitis, can lead to KCS.

Iatrogenic KCS can result from the removal of the nictitans gland – this was historically suggested to be the preferred treatment for nictitans gland prolapse before the gland's role in tear production was properly understood (Saito et al, 2001).

The uncommon congenital condition acinar hypoplasia is sometimes seen in miniature breeds of dogs that can present with unilateral severe ocular dryness (Herrera et al, 2007).

Neurogenic KCS can be caused by a loss of parasympathetic innervation to the lacrimal gland (CN VII) or a loss of sensory innervation to the cornea (CN V). Loss of parasympathetic innervation can be idiopathic or develop as a result of inner ear disease, trauma or neoplasia.

Clinical presentation

Canine KCS may present as either an acute or chronic condition. In the acute form, the affected eye(s) may be extremely painful, and there may also be resultant corneal ulceration, which is generally axial in position (Figure 1). These cases can progress very quickly to full thickness ulceration and globe rupture if not treated effectively. Another possible sequel of acute KCS is stromal malacia (melting ulceration), which requires intensive management.

In the early stages of the chronic form of KCS the only clinical signs may be conjunctival hyperaemia, mild chemosis and an intermittent mucoid to mucopurulent discharge. At this stage the condition may be misdiagnosed as a bacterial conjunctivitis if a Schirmer tear test one (STT 1; see later) is not performed. The condition will progress without treatment, with increasing amounts of tenacious mucopurulent discharge as well as worsening conjunctival hyperaemia and discomfort. The cornea develops a lacklustre appearance and disruption of Purkinje image becomes evident as the disease increases in severity. Eventually, corneal neovascularisation and pigmentary keratitis may develop, along with blepharitis or periocular dermatitis. Many of these advanced clinical signs can be seen in Figure 2.

One possible finding on physical examination in cases of neurogenic KCS is ipsilateral nasal

crusting (Figure 3). A common misconception is that the nasal crusting is due to a lack of tears flowing down the nasolacrimal canal, instead, the nasal mucosa is moistened by the lateral nasal gland. Nasal dryness tends to be a feature of neurogenic KCS; it occurs because both the lacrimal gland and the lateral nasal gland share common innervation by the preganglionic fibres of the nerve of the pterygoid canal. Other clinical signs that are occasionally observed in cases with neurogenic KCS include Horner's syndrome, facial paralysis and trigeminal nerve deficits (Mateis et al, 2012).

Diagnosis

The diagnosis of KCS depends first and foremost on consideration of the signalment, history and clinical findings. These may raise the index of suspicion of the presence of KCS, but confirmation of the diagnosis depends on the results of ancillary tests.

Schirmer tear test

The most common method of measuring tear production in dogs is the Schirmer tear test (STT). Both type one (STT 1) and type two (STT 2) tests can be performed. STT 1 measures both the reflex and basal tear production, as no topical anaesthetic is applied prior to the start of the test. STT 2 measures only the basal tear production, as topical local anaesthetic (for example, proxymetacaine) is applied to the cornea prior to applying the test strip. The STT strips are bent at the notch while still in the packaging, to avoid contact with the clinician's fingers (Figure 4). If the strips are touched at the corneal contact site, sterility will be compromised and any grease transferred from the clinician's hand on to the paper strip may interfere with aqueous tear absorption. The short section of the bent strip is placed in the lateral half of the lower conjunctival sac and then, if necessary, the eyelids are held closed to retain the strip in position (the strip should contact the corneal surface to provoke reflex tear production). It is necessary to measure the production of tears for a full minute as it has been shown the value will not rise in a linear fashion during this time (Williams, 2005). In dogs, an STT value of more than 15mm/ min is considered normal.

The mean normal value of the STT 1 is 20mm/min in dogs and 17mm/min in cats (Bexfield and Lee, 2010). An STT 2 will produce slightly lower values in normal eyes than the STT 1 and should be interpreted accordingly. In combination with clinical signs consistent with a diagnosis of KCS, an STT 1 value between 6mm/ min and 14mm/min in dogs is indicative of mild to moderate KCS and a value lower than 5mm/min is consistent with the presence of severe KCS. It is important to remember that occasionally qualitative tear deficiencies may be present, and such cases can present with a normal STT value. Other measures of tear production, such as the phenol red thread test, are available, but these are not widely used in non-exotic species.

Fluorescein staining

In any case where KCS is suspected, it is very important to assess both eyes for possible signs of

corneal ulceration, including the use of fluorescein stain.

In early cases of KCS, frank fluorescein staining may be absent, but the retention of very small areas of fluorescein on the roughened corneal surface can often be seen in such patients as fluorescein stippling. Identification of subtle fluorescein staining is aided by illumination with ultraviolet or cobalt blue light. Fluorescein may also be used to assess the tear break-up time (TBUT). In this test, a small amount of fluorescein is applied to the eye and the patient is allowed to blink. The eyelids are then held open and the corneal surface observed with the aid of a blue light source (for example, a Wood's lamp or slit lamp biomicroscope). The time taken for the first dark dry spot to appear is noted and compared against normal values. A normal TBUT time is between 15 and 25 seconds whereas a value of 10 seconds or less is indicative of tear film instability, which is a feature of a qualitative tear film abnormality (Giuliano and Moore, 2007). Rose Bengal is another vital stain that may be used in the eye; however, it is not widely available in the UK and can cause quite marked irritation. Rose Bengal adheres to devitalised cells and epithelial defects, and it can be useful to highlight more subtle corneal pathology such as that seen in some early cases of KCS.

If clinical signs consistent with the presence of KCS are present, but the STT value is within normal limits, a qualitative tear abnormality should be considered. In cases such as this particular attention should be paid to the health of the eyelid margins and of the meibomian glands in particular, as these secrete the lipid portion of tears. Diseases such as meibomianitis or chalazion will impair the function of these glands. A reduction in the number of conjunctival goblet cells can also result in an unstable tear film due to a deficiency in tear film mucins.

Treatment

The majority of patients with KCS can be successfully managed medically, with surgery being reserved for cases that are refractory to medical therapy. The treatment of choice depends on the primary cause of the KCS, if one is identified.

A commonly used drug for treatment of KCS is topically applied ciclosporin A 0.2 per cent, which is believed to act through the inhibition of T lymphocytes. This preparation should be applied twice daily, and tear production should be regularly monitored using STT 1. In severe cases, application of the drug every eight hours should be considered. Up to 12 weeks of treatment may be required before a clinical improvement is seen, but the majority of dogs show a good response within six weeks.

In dogs that present initially with a STT value of zero to 1mm/min, there is a 50 per cent chance of regaining normal levels of tear production using treatment with ciclosporin A. This rises to 80 per cent in dogs with an STT value of 2mm/min to 14mm/min (Kaswan and Salisbury, 1990). The cost of ciclosporin A 0.2 per cent may be prohibitive in some cases, although owners should be made aware that one tube should last slightly longer than four weeks if the correct amount (5mm strip) is

applied to each eye twice daily. In refractory cases, other “home-made” preparations of ciclosporin A are occasionally used at higher concentrations (half, one or two per cent w/v) than the commercially available product. These more concentrated preparations may cause local irritation when applied topically.

Tacrolimus ointment is another topically applied immunomodulatory agent that has become more widely used (0.1 per cent and 0.03 per cent). Tacrolimus is a macrolide antibiotic that achieves its effect through an action similar to that of ciclosporin A. Use in the UK is off licence and should be reserved for cases refractory to treatment with the licensed form of ciclosporin A. Preliminary data on the use of tacrolimus suggests it can be effective in dogs shown to have a poor response to topical ciclosporin A (Hendrix et al, 2011).

Tear replacement therapy is an essential component in the treatment of KCS and should be tailored to each individual patient’s requirements. An application frequency of once every two to six hours is desirable with most products and many tear replacement therapies are available to veterinary practitioners. They vary in composition and viscosity, with the more viscous preparations more suitable for overnight use as they may remain in the eye for longer. Tear replacement therapy is only ever supplemental and should not replace treatment aimed at any underlying cause, especially as early therapy in cases of immune-mediated KCS has a much higher success rate.

A broad-spectrum topical antibiotic is often useful in management of cases where a secondary bacterial infection is present. Initially, this should be applied four times daily, reducing to twice daily as the condition improves. The use of a combination antibiotic/corticosteroid drop is best avoided in KCS due to the potential risk of associated corneal ulceration.

In cases of neurogenic KCS, the use of the parasympathomimetic drug pilocarpine may be warranted. Pilocarpine is available as drops in various concentrations and it is occasionally used for the treatment of human glaucoma. Pilocarpine is irritating when applied topically, but there have been anecdotal reports of its topical use at a 0.1 per cent dilution for the treatment of neurogenic KCS, or it may be used orally as a one per cent preparation, mixed with food (one drop/10kg orally, twice daily). The oral dose should be increased until early signs of toxicity are observed (hypersalivation, vomiting, diarrhoea or cardiac arrhythmias). Owners should be carefully advised how to monitor for these adverse signs and to stop treatment when they are seen. Once the side effects have resolved, treatment can be reinstituted at a slightly lower dose than that which induced signs of toxicity. In some cases, treatment can be stopped altogether after around six months, but in others it may need to continue as a lifelong therapy.

If medical management of KCS is unsuccessful, surgical intervention should be considered. The options for surgical management are quite limited, with PDT being the most suitable choice in the majority of cases. Other techniques, such as punctual duct occlusion and permanent partial tarsorrhaphy, have been shown to have limited usefulness in severe KCS cases (Williams, 2002; Giuliano and Moore, 2007).

PDT can be performed either via an oral or facial approach. A study by Rhodes et al (2012) showed PDT has a 92 per cent success rate – as judged postoperatively by the ophthalmologist and by an owner satisfaction survey (Figures 5 and 6). Complications of the procedure vary in severity and although they can occur quite frequently, in most cases they are transient (Table 3). Dogs that have a dry mouth are not surgical candidates, and testing for this by stimulating salivation with a few drops of lemon juice applied to the patient's mouth prior to surgery is essential. In brief outline, the parotid duct is first cannulated using suture material and the duct and its papilla are subsequently freed from the surrounding tissues. Once mobile, the papilla is repositioned and sutured in place in the ventrolateral conjunctival fornix. The composition of salivary fluid and tears is markedly different, with the result that saliva is a suboptimal replacement that often results in calcium deposition on the cornea and eyelids. Rhodes et al (2012) showed approximately onethird of patients will require some ongoing medical management after PDT.

Conclusion

While the diagnosis of most cases of KCS may not present many difficulties to the small animal practitioner, management of the condition can be challenging. A thorough history and clinical examination will help to avoid missing treatable cases of KCS. To achieve good owner compliance, the regimen used in each case should be tailored to meet both the animal's and the owner's requirements. The emergence of medical treatments for the condition has led to a reduction in the need for surgical intervention, but this is still essential in selected cases. A good understanding of the condition should help the practitioner to choose the most effective treatments available, to refer when necessary and to achieve successful outcomes in the majority of cases.

• Note some drugs mentioned in this article are not licensed for use in dogs.

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New developments in the treatment of immune-mediated KCS

A published pilot study (Gilger et al, 2013) in a small number of dogs (n=20) demonstrated the effectiveness of SCY-641, a topical calcineurin inhibitor. To date, this drug has no recorded adverse reactions and it can be formulated in an aqueous solution (unlike ciclosporin A and tacrolimus), which may facilitate easier application in some dogs. It may be at least as efficacious at increasing STT values as ciclosporin A and tacrolimus. The authors acknowledged the limitations of the study and called for further testing to be performed. SCY-641 may be available in the future as an option for treating KCS in canine and feline patients.

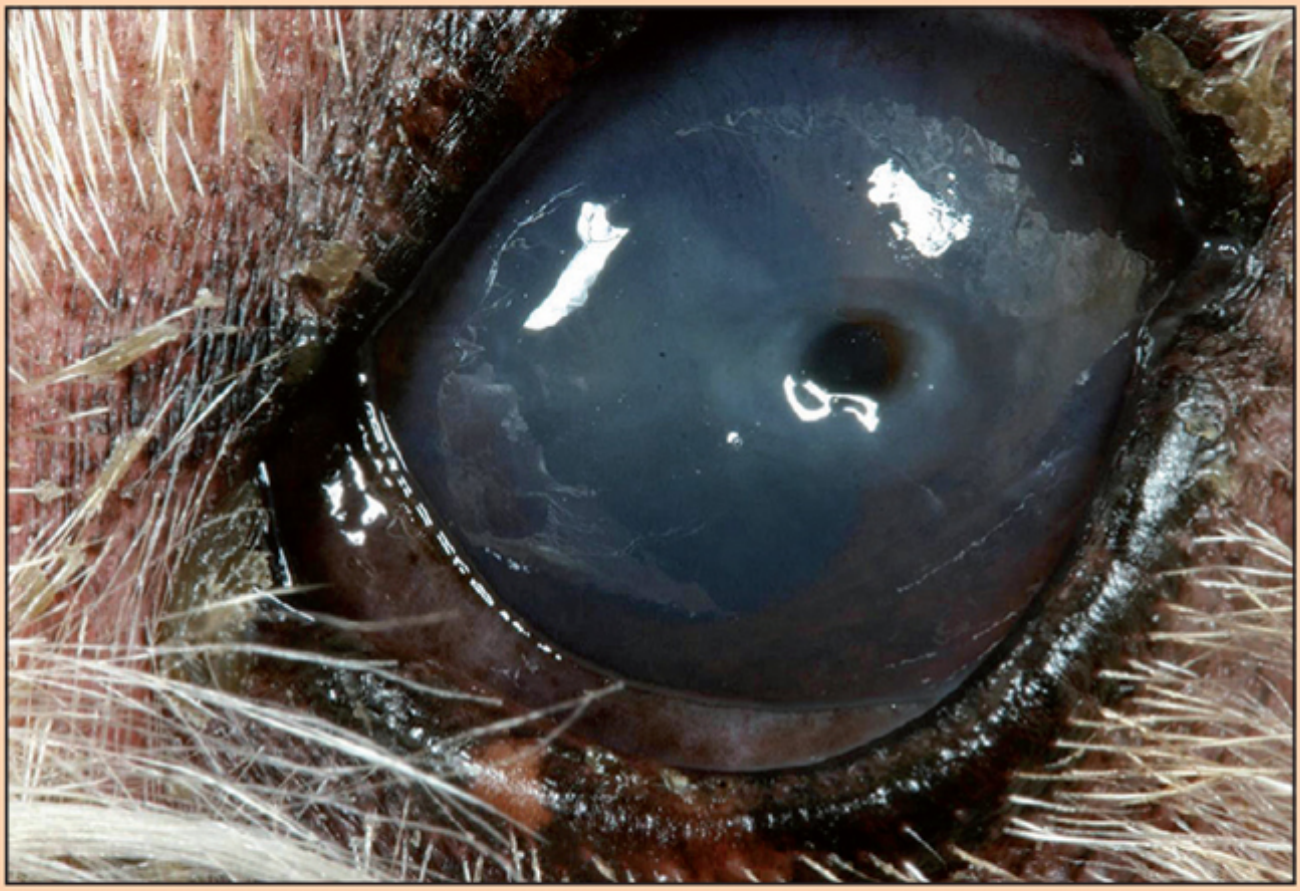


Figure 1. Keratoconjunctivitis sicca (KCS) with associated stromal ulceration in an eight-year-old neutered female West Highland white terrier. This is a serious potential complication of poorly managed KCS.

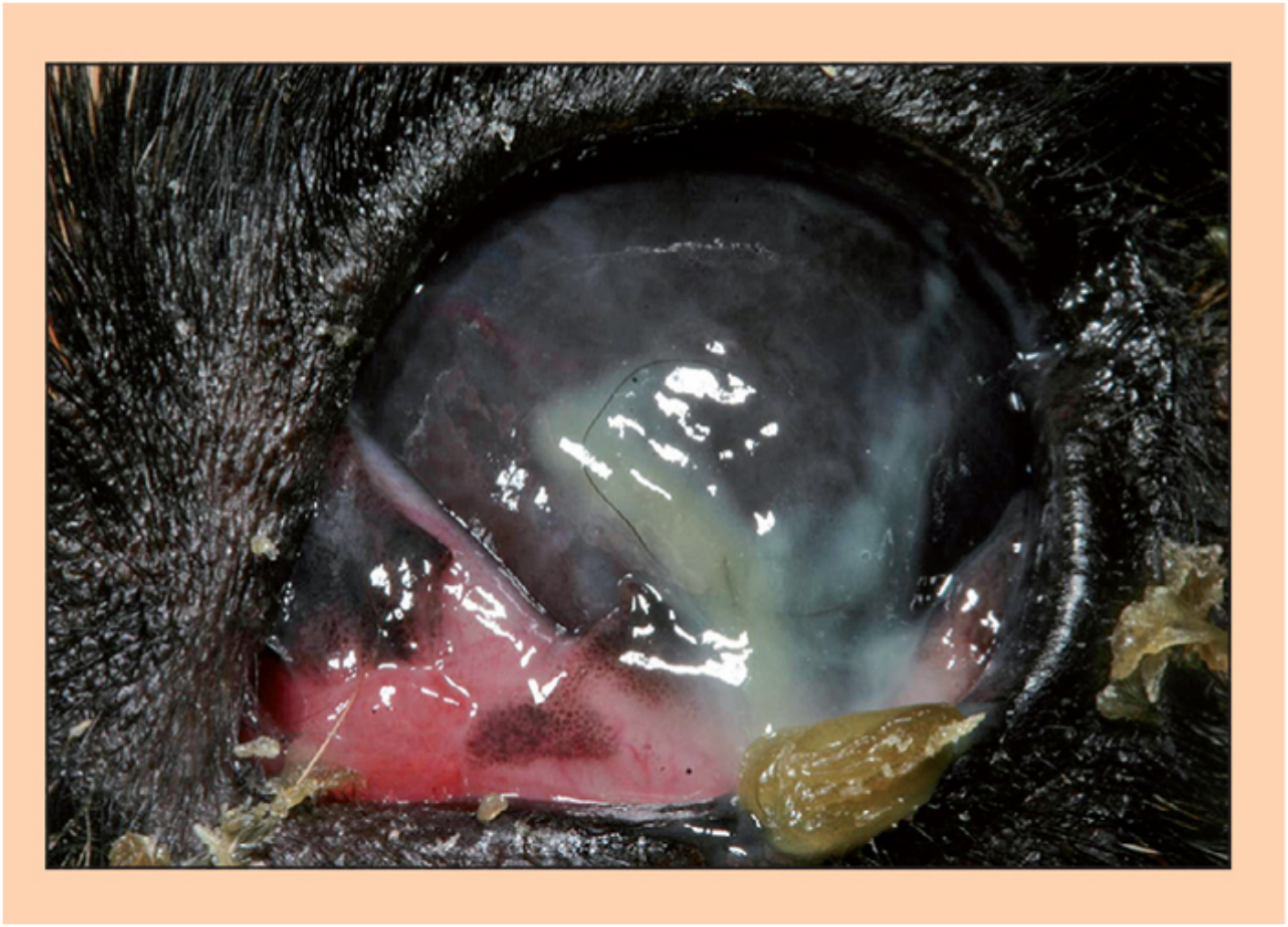
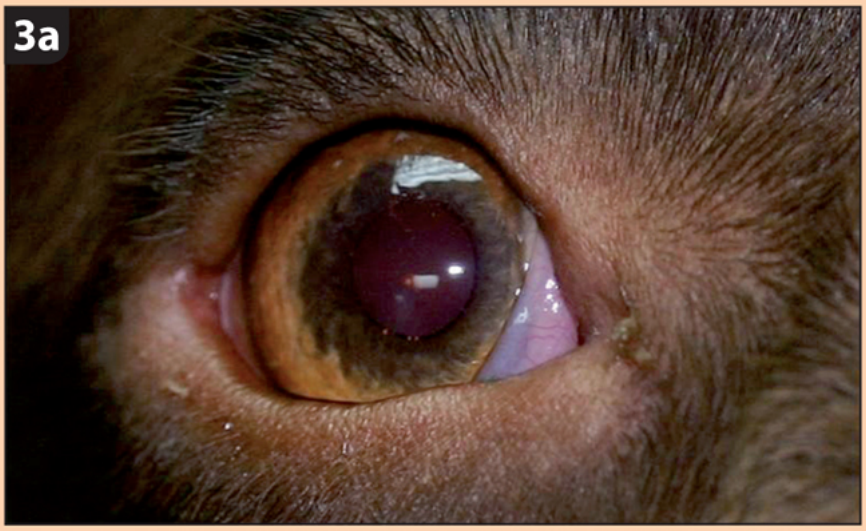


Figure 2. KCS in a four-year-old female cavalier King Charles spaniel. Note the lack of corneal lustre, mucopurulent discharge and hyperaemia of the third eyelid.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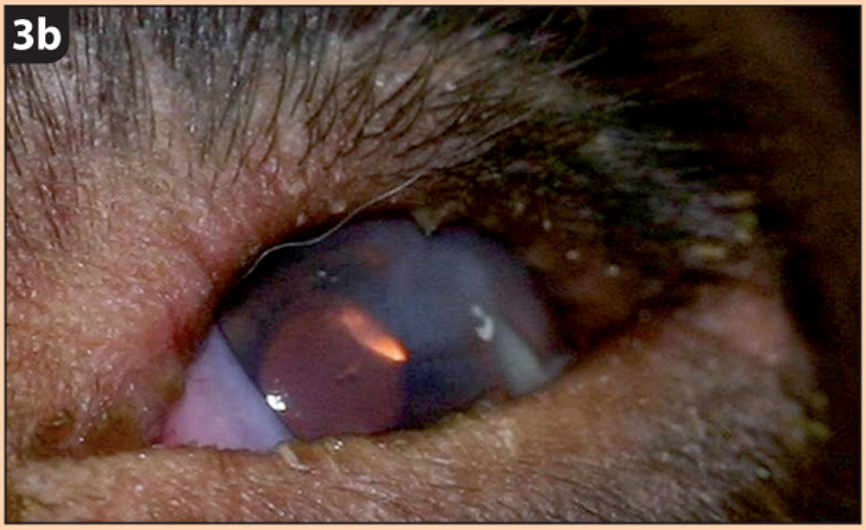
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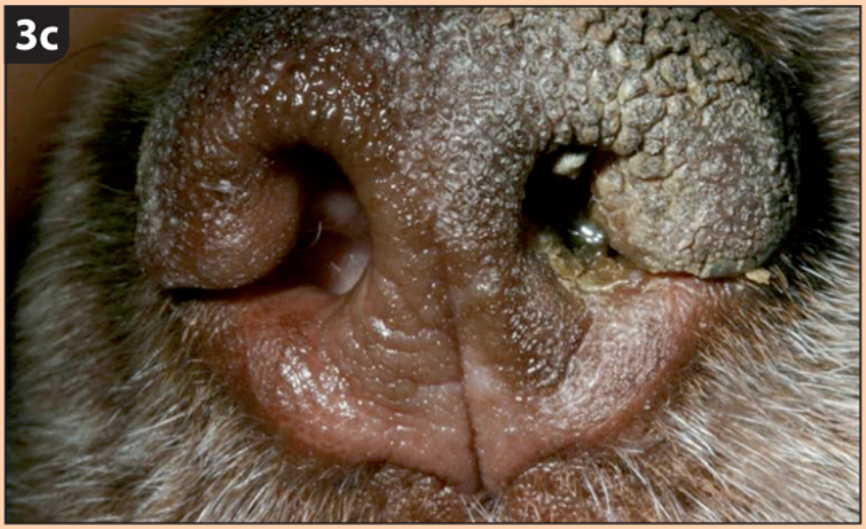
3c

Figure 3a-c. Ipsilateral nasal crusting in a one-year-old male entire crossbreed dog with unilateral idiopathic neurogenic KCS. The dog's unaffected right eye (3a), the left eye (STT 1, 0mm/min; 3b) and nose dry on its left side (3c).

Figure 4. How to prepare STT strips correctly. Note the strips have been folded at the notch while still in the protective packaging.

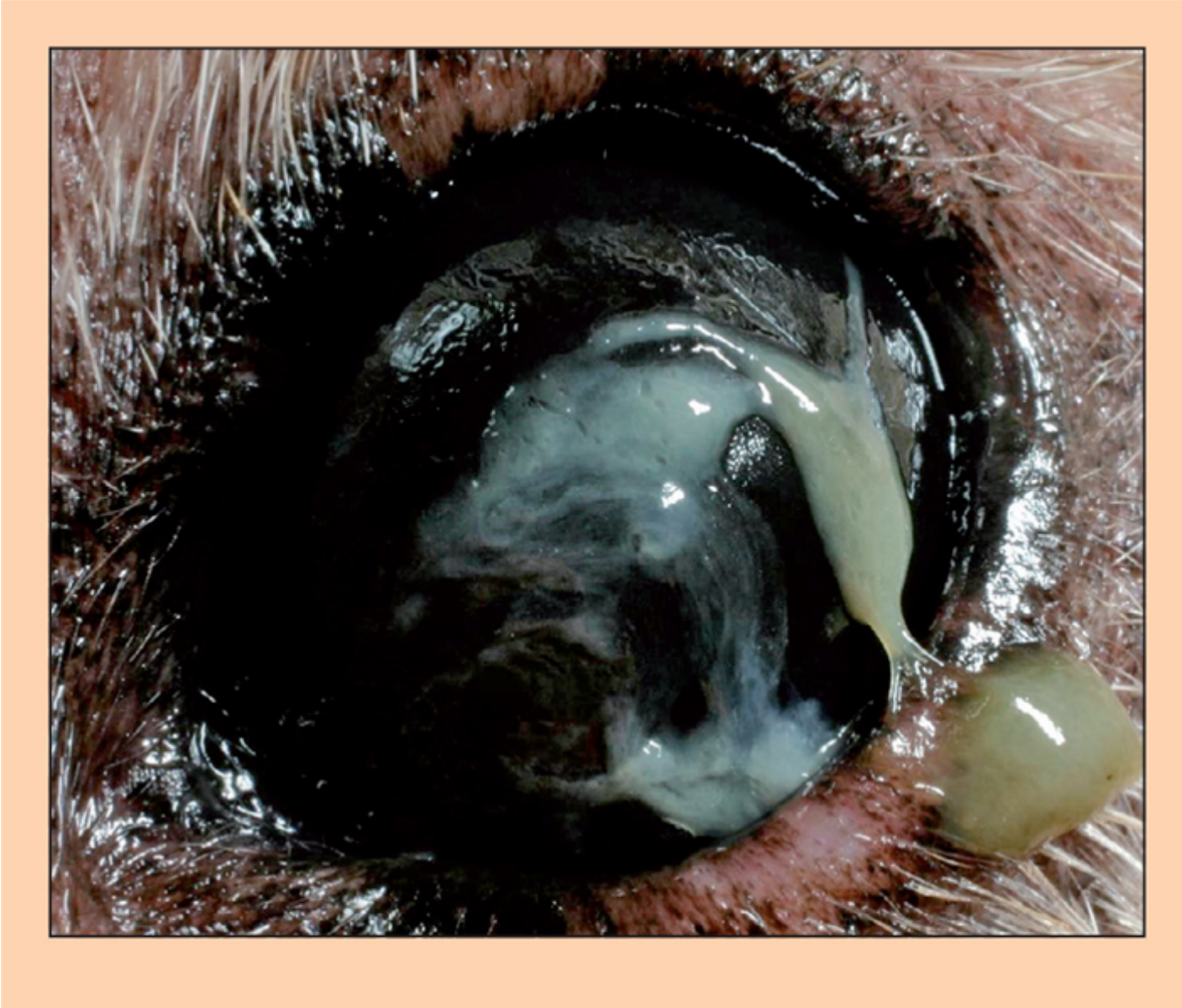

Figure 5. Tenacious mucoid discharge and total corneal pigmentation in a West Highland white terrier with chronic, absolute KCS, prior to parotid duct transposition.

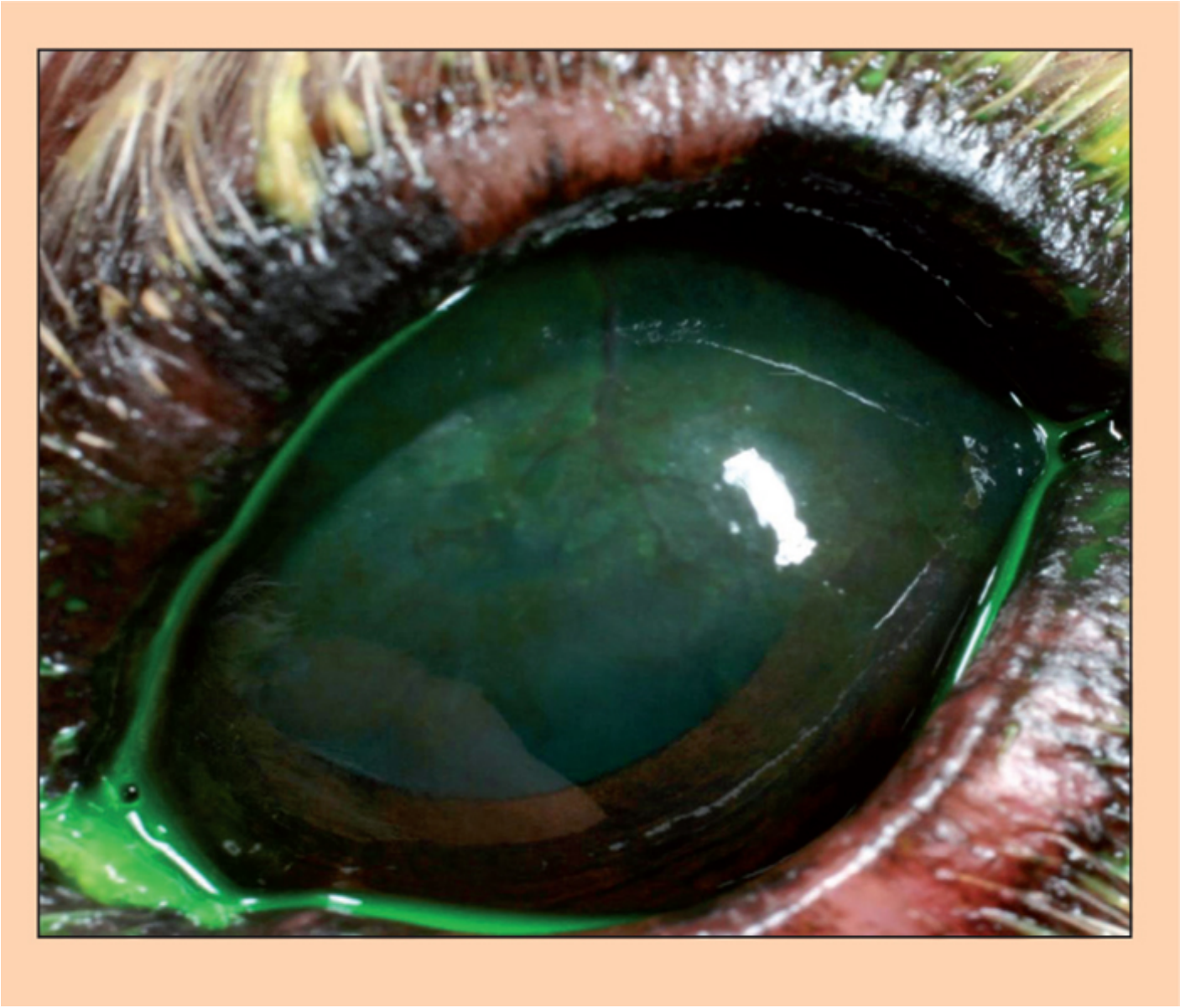

Figure 6. Improvement in corneal clarity in the same dog as Figure 5 four weeks post-parotid duct transposition surgery (note fluorescein has been applied).

Immune-mediated
Drug therapy: topical atropine, sulphonamides.
Infectious: distemper, chronic blepharoconjunctivitis.
Congenital: acinar hypoplasia.
Iatrogenic: nictitans gland removal.
Systemic conditions: hypothyroidism, diabetes mellitus, hyperadrenocorticism.
Neurogenic.
Trauma to eye and orbit.

Table 1. Causes of keratoconjunctivitis sicca in dogs

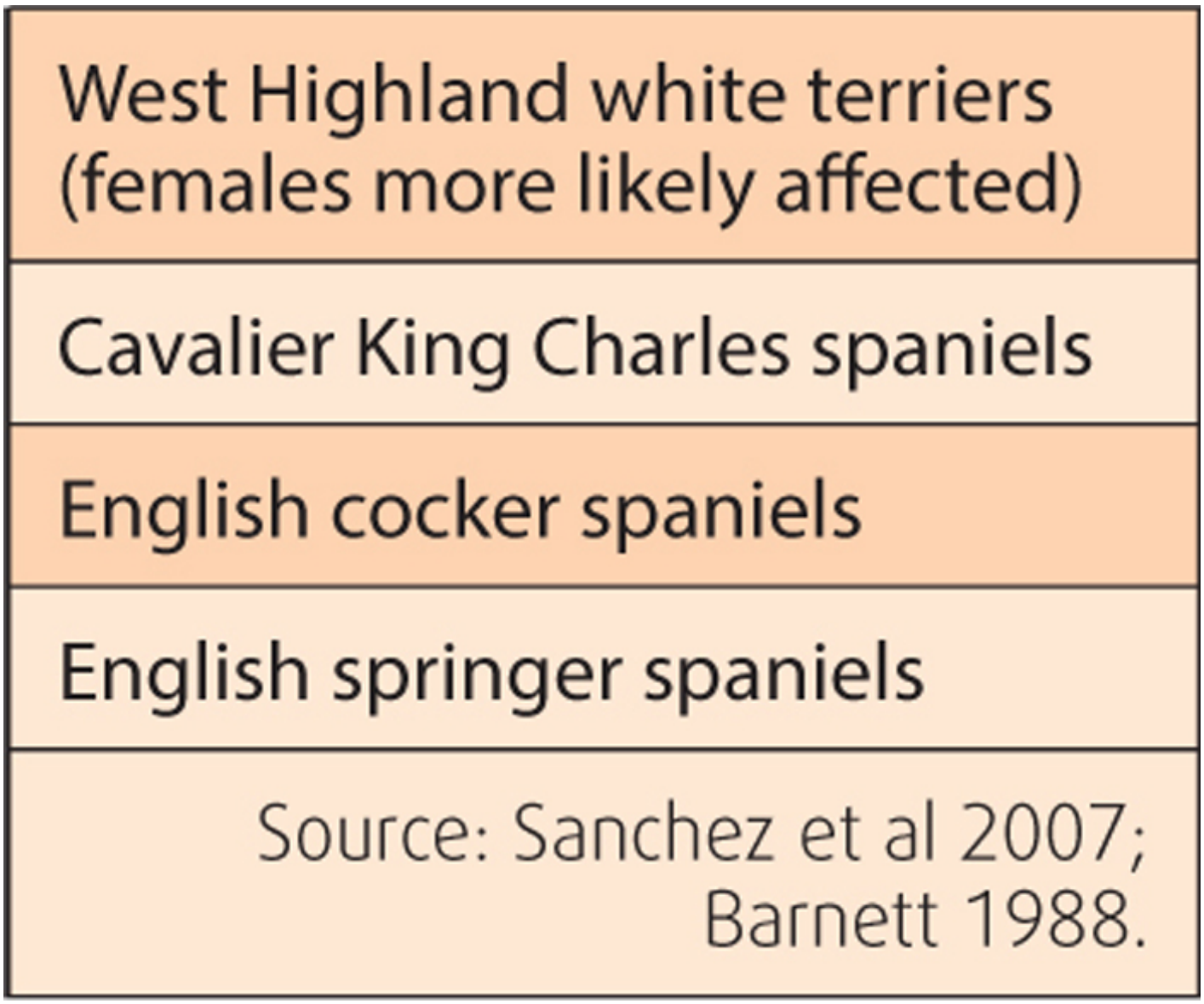

Table 2. Dog breeds more likely to be affected by KCS in the UK

Surgical complications
Intraoperative duct trauma
Facial swelling
Temporary/permanent duct failure
Wound dehiscence
Iatrogenic corneal ulceration
Lower lid entropion
Long-term complications
Corneal and eyelid calcium deposition
Salivary epiphora and discomfort
Mucoid ocular discharge
Salivary epiphora and discomfort
Mucoid ocular discharge
Conjunctival hyperaemia
Progressive corneal pigmentation
Blepharitis
Facial dermatitis
Parotid duct sialolithiasis
Parotid duct dilation
Orbital sialocoele
Bullous keratopathy
Recurrent epithelial erosion
Stromal abscessation

Table 3. Complications associated with parotid duct transposition