Keratoconjunctivitis sicca ("Dry Eye")

By Stephanie Shrader, DVM and John Robertson, VMD, PhD

Introduction and Overview

Keratoconjunctivitis sicca (KCS) is a disease of the eyes, characterized by inflammation of the cornea and conjunctiva. This condition occurs secondary to a deficiency in formation of the tear film that normally protects the cornea (Best et al, 2014), which leads to dry, irritated eyes. As a result, KCS is commonly known as "dry eye" or in veterinary terminology, xerophthalmia. This disease occurs often in West Highland White Terriers, but is also common in many other breeds, including Lhasa Apso, English Bulldog, American Cocker Spaniel, English Springer Spaniel, Pekingese, Pug, Chinese Shar Pei, Yorkshire Terrier, Shih Tzu, Miniature Schnauzer, German Shepherd, Doberman Pinscher, and Boston Terrier. While the reported incidence of KCS across all dog breeds ranges from 1% to 2%, there appears to be an increased predisposition reported for both neutered male and female dogs, and for female West Highland White Terriers, in particular.

Relevant Anatomy of the Eye

To understand how KCS develops and ultimately how it is treated, if is important to have a good appreciation of the relevant anatomy of the eye and the glands that produce tears. The relevant components of the eye are the clear outer cornea, the conjunctiva, the eyelids, and the Meibomian and lacrimal glands *(Figure 1A, 1B)*. The Meibomian glands are located along the edge of the eyelid. There are two lacrimal glands associated with each eye. One lacrimal gland is located slightly above and lateral to the eye, and the other is located medially by the third eyelid (also called the nictitating membrane.

How Tears Are Produced

The tear film that covers the eyes is made up of three distinct layers. The outermost layer is made up of oils, which are secreted by the Meibomian glands. This lipid layer provides protection against evaporation, binds the tear film to the cornea, and prevents tears from simply pouring out over the lower eyelid onto the face. The middle layer of the tear film is the aqueous layer, which is produced by the lacrimal glands. As its name would suggest, the aqueous layer consists primarily of water, along with important proteins and enzymes that help remove bacteria and cellular waste material, and lubricate the surface of the cornea. The innermost layer of the tear film is the mucin layer, which is is produced by tiny secretory cells in the conjunctiva known as goblet cells. The mucin layer facilitates the spread of the tear film over the cornea.

What Causes Keratoconjunctivitis sicca?

There are several potential causes of KCS in dogs, which include immune disorders that destroy the lacrimal tissue, diseases that affect the conjunctiva and lacrimal tissue, congenital conditions in which the lacrimal tissue fails to develop, medications, traumatic incidents and treatments. The common feature among these causes is that they impair the ability of the tear-secreting tissues in the eye to perform their basic functions, with the end result being the development of "dry eye".

Immune-Mediated Adenitis: The most common cause of KCS is immune-mediated lacrimal adenitis, which means that the body's own immune system is causing abnormal inflammation of the lacrimal glands. The underlying reason why the immune system targets the lacrimal glands for destruction is unknown, but the end result is infiltration of the glands with lymphocytes and the inability to produce the aqueous layer of the term film. There does not appear to be a specific breed predisposition to this condition.

Common Clinical Findings
West Highland White Terriers at Risk
Red, Irritated Eyes
Pawing at Eyes
Ocular Discharge

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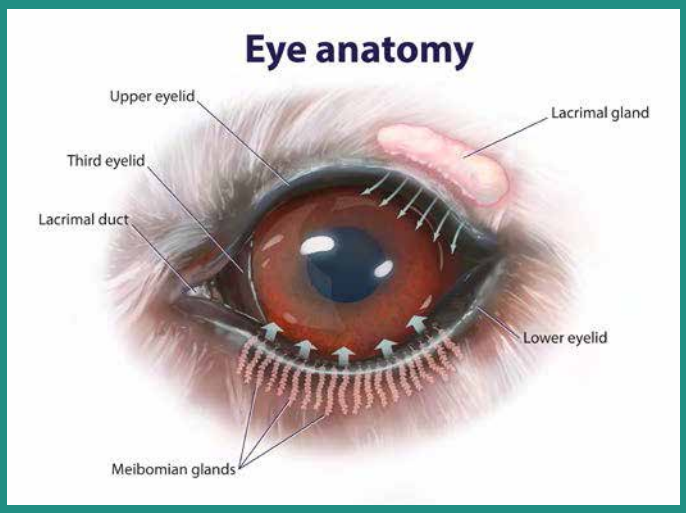

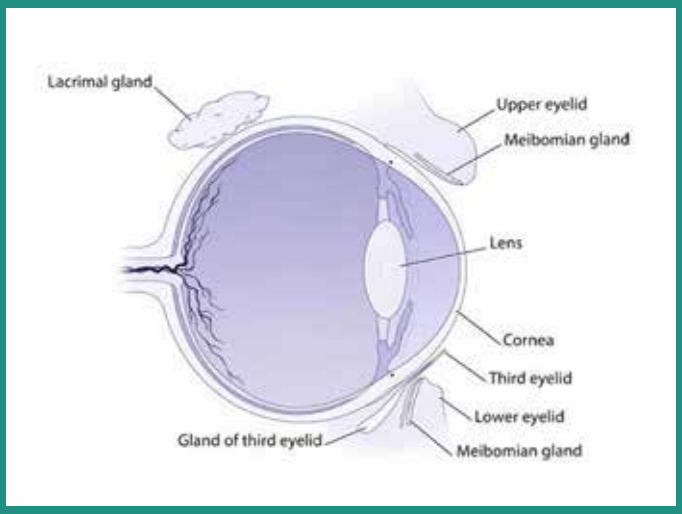

Figure 1A and B - *Two illustrations depicting the important anatomical features of the dog, particularly the locations of the lacrimal and Meibomian glands that are critical to the secretion of the tear film.*

Congenital Acinar Hypoplasia (Congenital Alacrima): As its name implies, this condition is genetic in origin and the term 'alacrima' literally means "no tears." This is an autosomal recessive trait in which the responsible allele is carried on the non-sex determining chromosomes. Thus, if two animals having the recessive trait for alacrima mate, there is a 25% chance that the offspring will inherit the disorder. Breeding dogs that have congenital disorders is problematic, as this practice continues the disease in future offspring. Most breeders monitor the health of litters they have sold, in order to detect the emergence of congenital disorders such as this in litters or breeding stock. Therefore, it is critical that the history and health records of potential breeding pairs are obtained and examined before a puppy at risk of conditions such as this are purchased. There is evidence that Yorkshire Terriers and Bedlington Terriers are overrepresented when compared to reference populations of dogs (Westermeyer et al, 2009).

Drug and anesthesia induced decreases in tear production: Certain drugs/anesthetics can produce either temporary or permanent KCS. A decrease in tear production for up to 24 hours is sometimes noted to occur after anesthesia and surgery, but the inciting cause is unknown. Consequently, it is important for all veterinarians to use a lubricating ointment or fluid to protect eyes during surgery to prevent this temporary decrease in tear production.

There are other drugs whose use have been associated with the development of KCS. These include some of the sulfonamide antibiotics and etodolac, an orally administered nonsteroidal anti-inflammatory drugs that has been used to help relieve pain and inflammation in dogs with osteoarthritis (Klauss et al, 2007). In the latter study, dogs that had received the drug for less than 6 months had a much better chance to complete remission of clinical signs. The investigators advised veterinarians to monitor tear production before and during administration of this drug to ensure that problems can be identified early and drug administration discontinued, if necessary.

Iatrogenic KCS: The term 'iatrogenic' refers to a problem that develops as a result of or associated with a treatment. Consider, for example, a dog that has an abnormal growth involving the gland of the third eyelid (nictitans gland). If this abnormal growth were removed, it could increase the risk that the dog will develop KCS, because that gland is responsible for production of part of the tear film. In fact, this is what happened years ago when a condition caused by inflammation and proliferation of lymphoid tissue near the third eyelid (i.e., "Cherry Eye") was treated by removal the gland. Today, this condition is treated using a combination of medical and surgical treatments instead of removal.

Infectious Diseases: A common viral disease in dogs, canine distemper, is often associated with KCS. Canine distemper is a highly contagious disease that is typically spread via aerosolized respiratory secretions. In most cases, the virus first attacks the respiratory system, and then spreads to the gastrointestinal and nervous systems. When the virus colonizes components of the eye, including the cornea, conjunctiva and the lacrimal glands,

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"The common feature among these causes is that they impair the ability of the tear-secreting tissues in the eye to perform their basic functions."

KCS can develop (Gilger, 2009). Consequently, it is extremely important to have all dogs vaccinated against the canine distemper virus.

Metabolic Diseases/Disorders: Tear production has been reported to be reduced in a small number of patients being evaluated for endocrine abnormalities commonly encountered in dogs (Williams et al, 2007). These three conditions were hypothyroidism, diabetes mellitus and hyperadrenocorticism (Cushing's disease). Although the underlying cause or causes for the reduction in tear production were not identified in that clinical study, the investigators suggested that tear production should be measured in dogs with any of these conditions to reduce the chances the damage to the cornea could occur.

Figure 2 - *xamination of a dog's eye using a specialized ophthalmoscope.*

Figure 3 - *An affected eye in a dog with keratoconjunctivitis sicca, characterized by a cloudy cornea and thick ocular discharge.*

Neurologic: Parasympathetic innervation to the lacrimal glands is provided by one of the 12 cranial nerves, namely the facial nerve. Damage to this nerve, either due to disease or trauma, can result in KCS by decreasing the amount of tear film produced. Similarly, damage to the ophthalmic branch of the trigeminal nerve could result in loss of innervation to the lacrimal gland, conjunctiva, and upper eyelids, with the end result being the development of KCS.

How Is Keratoconjunctivitis sicca Diagnosed?

Dogs with KCS are often presented to the veterinarian because they have red/irritated eyes, are pawing at their eyes because they itch and/or hurt, and may have a thick ocular discharge that can range from off-white to green in color. The veterinarian also may notice that the third eyelid is protruded, and that the cornea no longer has its normal shiny appearance *(Figures 2 and 3)*. This latter finding is due to inflammation of the cornea. In advanced cases of disease, there may be evidence of corneal ulceration and pigmentation; corneal scarring may lead to vision loss.

To differentiate KCS from other ocular disorders, the veterinarian will do a comprehensive eye exam that will include a Schirmer tear test, staining of the cornea with fluorescein dye, and evaluation of pressures within the eye for evidence of glaucoma.

Schirmer Tear Test: The Schirmer tear test is a painless diagnostic procedure designed to quantify the amount of tear film produced by the eye. To perform this test, the veterinarian places a thin strip of paper (about an inch long and quarter of an inch wide) just under the dog's eyelid for one minute. This piece of paper has a small scale on it *(Figure 4)*. During the minute, the tear film "wicks" up the paper. At the end of one minute, tear production is quantified by measuring the distance the tear film travelled in the paper. The result is reported in mm/min, with values for normal dogs being >15 mm/min.

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Figure 4 - *A packet of standardized Shirmer Tear Test strips that are used to measure tear production.*

Figure 5 - *The eye of a dog with keratoconjunctivitis sicca in which the green fluorescein stain identifies a damaged area of the cornea.*

Application of Fluorescein Stain: Fluorescein is a bright yellow/orange stain that is used to detect corneal ulceration. The veterinarian will place a few drops of the stain in the eye, turn off the exam room lights, and use the ophthalmoscope to determine if corneal ulcers are present *(Figure 5)*. In dogs with KCS, it is not uncommon to also find corneal ulceration because of the chronic irritation.

Examination of Intraocular Pressure: Although changes in intraocular pressure generally do not occur in dogs with KCS, most veterinarians will measure intraocular pressure to rule out another relatively common eye disease, namely glaucoma. Measurement of intraocular pressure is performed in a quick, painless manner using a special handheld device known as a tonometer. Normal intraocular pressure in dogs ranges from 15 to 25 mmHg.

Treatment of Keratoconjunctivitis sicca

There are a variety of treatments for KCS that can be used. These include stimulating the production of tears, replacing the tears, reducing inflammation and controlling bacterial infections. For most dogs with KCS, topical treatments will be required for the life of the animal. Initially, application of topical medications to the eye can be challenging, as some dogs with KCS are painful. Fortunately, with effective management, the level of pain decreases and putting medications in the eyes becomes a routine practice for both dog and owner. Providing rewards as positive reinforcement may help. The following guidelines for deciding when to initiate therapy appear to be reasonable (Best, 2014):

1. Initiate therapy for KCS in all dogs presented with clinical signs of the disease and Schirmer tear test results <5 mm/min.
2. Either initiate therapy for KCS or repeat the Schirmer tear test in one month in breeds predisposed to the disease that have clinical signs of the disease and Schirmer tear test results of 10-15 mm/min.
3. Consider other causes for reduced tear production in dogs presented with clinical signs of the disease and normal Schirmer tear test results.

Stimulating Tear Production: Three drugs are commonly used in an effort to restore tear production in dogs with KCS. Two of these compounds, cyclosporine A and tacrolimus, modulate the immune response that appears to be responsible for the condition in a large number of dogs. They also reduce inflammation, restore production of mucin by goblet cells, and stimulate tear production. These drugs appear to be very effective, positive responses being reported for more than 80% of affected animals (Kaswan et al, 1990; Hendrix et al, 2011). The third compound, pilocarpine, stimulates tear production by interacting with receptors in the lacrimal system. This drug is used when the cause of the condition is determined to be neurogenic in origin (i.e., damage to the nerves involved in tear production).

Replacing Tears: Tear replacement solutions are typically a combination of ingredients that replace one or more components of the tear film. There are three types of solutions, gels and

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ointments that are used for this purpose. These include artificial tear solutions that help remove debris and mucus from the surface of the eye. Artificial tear solutions have a relatively short duration of activity, must be reapplied several times a day and are not effective as the sole treatment. Another approach is to use cellulose-based solution and gels that are thicker, last longer and can be applied less often. The most viscous formations, which include lanolin, mineral oil or petrolatum, are used most often for dogs that produce tear film deficient in lipids.

Topical Anti-Bacterial and Anti-Inflammatory Drugs: In some affected animals, there may be a secondary bacterial infection causing the thick, mucopurulent discharge. In these cases, topical ophthalmic anti-bacterial drugs will need to be applied to the eyes 3-4 times daily. These drugs typically include a combination of bacitracin, neomycin and polymyxin. If the conjunctiva are inflamed, many veterinarians also will use topic corticosteroids, such as prednisolone or dexamethasone, to reduce the inflammation. These medications are manufactured as ointments and solutions; your veterinarian will determine which medication is best for your dog.

Surgical Intervention (Parotid Duct Transposition): Some dogs with severe KCS that is unresponsive to medical therapy, may require surgery. To understand the rationale for the surgical procedure used, it first is important to know a bit about the parotid salivary gland that is located behind the jaw and just below the base of the ear. This is the largest salivary gland in the body and produces secretions that aid in chewing and lubricating food and swallowing. Because tears and saliva share similar properties, saliva can be used successfully to treat dogs with severe KCS. The surgical procedure that is performed moves the duct that normally connects the gland with the mouth to a position near the conjunctiva (Figure 6). When this is done, the lubricating and antibacterial secretions from the salivary gland flow onto the surface of the eye. This flow of saliva is intermittent, and increases in response to eating. Veterinarians with experience performing this procedure routinely are most likely to have a successful outcome.

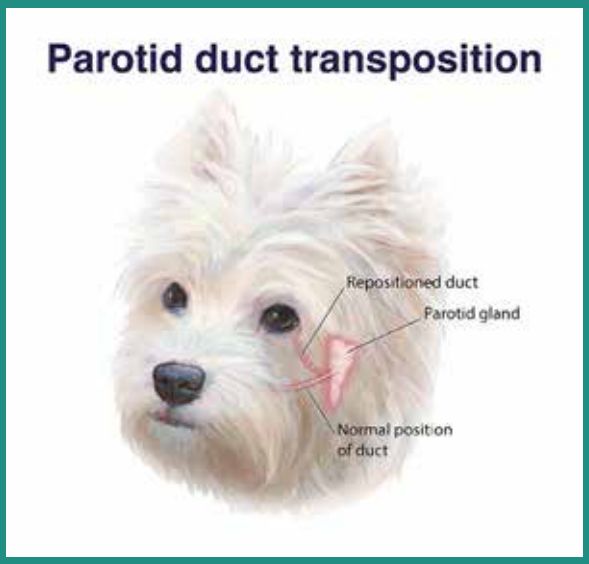

Figure 6 - *An illustration depicting the normal position of the parotid duct where it enters the mouth and its new location adjacent to the eye after the parotid duct transposition surgery has been performed.*

Current Research About Keratoconjunctivitis sicca

The majority of the published studies regarding KCS have centered on its association with other concurrent diseases and on the effectiveness of different treatments. With the increased interest in the effects of diabetes in dogs, the results of a recent study comparing the prevalence of KCS in dogs after treatment of cataracts in dogs with and without diabetes are summarized below. The other two studies selected for review compare the effectiveness of different treatments for the KCS.

Gemensky-Metzler AJ, Sheahan JE, Rajala-Schultz PJ, Wilkie DA, Harrington J. Retrospective study of the prevalence of keratoconjunctivitis sicca in diabetic and nondiabetic dogs after phacoemulsification. Vet Ophthalmol. 2015 Nov;18(6):472-80.

In this study, the occurrence of KCS was compared for 118 diabetic dogs and 117 nondiabetic dogs undergoing a procedure called phacoemulsification for treatment of cataracts. The Schirmer tear test was performed before surgery and several times after surgery for up to one year; a diagnosis of KCS was based on the presence of clinical signs consistent with the disease and Schirmer tear test results < 15 mm/min. The investigators determined that the greatest risk for developing KCS was during the first 2 weeks after surgery, and the animals at greatest risk were small dogs, small diabetic dogs and large dogs with preoperative Schirmer tear test results <22 mm/min. Based on their findings, the investigators suggested that monitoring of tear production and the use of artificial tear supplements immediately after cataract surgery may be warranted for all dogs, but especially for small diabetic dogs.

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Chen T, Powell CC. Effect of once daily topical 0.3% naltrexone on tear parameters and corneal sensitivity in dogs with uncontrolled keratoconjunctivitis sicca: a double-masked randomized placebo-controlled clinical trial. Vet Ophthalmol. 2015 Nov;18(6):497-501.

In this study, the investigators evaluated the effectiveness of naltrexone, a drug that normally is given to antagonize the effects of opioids, on tear production and corneal sensitivity in dogs with KCS. The study was based on a previous small study in which two animals had increases in their Schirmer tear test results after being treated with the drug. To eliminate the chance that people involved in the study might be biased if they knew whether or not the drug was being given, they performed this study as a double-masked placebo-controlled trial. This means that the animals either received naltrexone or a commercial saline solution eye wash once daily, without the people involved knowing which was being used until after the study had ended. Sixteen dogs with KCS were involved in the study, and corneal sensitivity and Schirmer tear test results were recorded over 5 weeks. They found no evidence of an increase in tear production or a change in corneal sensitivity, and speculated that this lack of effect may have been due to the chronic nature of the disease in the dogs or the relatively short duration of treatment.

Rhodes M, Heinrich C, Featherstone H, Braus B, Manning S, Cripps PJ, Renwick P. Parotid duct transposition in dogs: a retrospective review of 92 eyes from 1999 to 2009. Vet Ophthalmol. 2012 Jul;15(4):213-22.

Some dogs with KCS fail to respond to medical therapy and develop chronic ocular pain or blindness. In an effort to treat these severely affected dogs, fifty years ago veterinary surgeons began surgically moving the parotid duct to bathe the cornea in saliva. This procedure was widely used until it was determined that cyclosporine was effective in the treatment of KCS. Because relatively few veterinary ophthalmologists now have the training and experience needed to successfully perform the procedure. The investigators in this study consider transposition of the parotid duct a viable technique in the treatment of dogs with severe KCS. The aim of this study was to critically assess the success of this procedure in dogs over a 10-year period. Although there was a 50% complication rate, the overall surgical success rate was 92%, and 90% of owners were satisfied with the outcome.

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Lead, guide and advocate on behalf of Westies.

Develop and communicate to Westie owners, Westie breeders, veterinarians and others who share our challenges.

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