

## **DRY EYE DISEASE: WHERE ARE WE?**

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### **INTRODUCTION**

As veterinarians, we not only should understand the Schirmer tear test, but understand the tear film and its importance. There are times in which keratitis and conjunctivitis may seem like dry eye, but the STT is normal.

#### **The Tear Film**

The tear film is composed of three parts- mucin, aqueous, and lipid. Mucin, which sticks the tear film to the cornea and fills any corneal epithelial irregularities, is mixed with the aqueous portion of the tear film. The aqueous portion of the tear film contains many nutrients that are required by the superficial cornea and provides a flushing action. The lipid layer that is produced from the meibomian glands prevents evaporation of the tear film. Deficiencies in any of these components lead to types of dryness and irritation. If the tear film is healthy, many other ocular problems, such as corneal pigmentation, vascularization, and scarring, corneal ulcers, and discomfort can be avoided.

#### **Blinking and Corneal Sensitivity**

Tear distribution is initiated by a complete blinking action which moves lateral to medial “squeegeeing” the tear film towards the nasolacrimal punctae. If the eyelid remains open long enough or the tearfilm evaporates too quickly, the epithelium is exposed and the nerve endings detect the drying and trigger another blink. If a patient is brachycephalic, has facial nerve paralysis, or is exophthalmic, this reflex is incomplete. If corneal sensitivity is decreased due to trigeminal nerve dysfunction or breed (brachycephalic), tear production can decrease leading to keratitis.

### **CANINE DRY EYE DISEASE**

#### **Quantitative**

When the aqueous layer of the tear film is decreased, mucus and lipid accumulate on the surface of the eye. Patients often present with excessive white or ropy discharge on their eyelids. Clinical signs of decreased aqueous tear production include conjunctival hyperemia, corneal edema, lackluster surface of cornea, corneal vessel ingrowth, corneal pigmentation, and corneal ulceration. In chronic KCS cases, the corneal epithelium becomes thickened and keratinized. If left untreated, these clinical signs of KCS can result in loss of vision. Diagnosis of quantitative tear film disorders is made based on clinical signs and a Schirmer tear test <15 mm/min.

#### **Etiologies**

There are several etiologies of dry eye disease in dogs with the most common being immune-mediated and breed-related. For this presentation, we will focus on lesser-known causes of dry eye disease in dogs.

#### **Neurogenic KCS**

Damage to the parasympathetic innervation of the lacrimal glands (runs with CV VII) results in neurogenic KCS. Neurogenic KCS is often unilateral and has a severe/acute onset. The nares on the unilateral side will appear dry if the parasympathetic innervation is damaged proximal to the pterygopalatine ganglion (xeromycteria). Neurogenic KCS can occur following trauma to the nerve (blunt trauma, proptosis, or ear canal surgery). It can also be idiopathic and is seen in middle-aged female dogs more often. Sometimes this disease is permanent, but neurogenic KCS can improve if the underlying cause is addressed, and the tear film is supported. This disease has recently been associated with long-lasting otic medication like osurnia. In these cases, the onset of absolute dry eye is within 24 hours and the recommendation is to flush the ear, support the

eye with tear supplements and most will resolve within 3 months. Idiopathic neurogenic KCS has been reported to often resolve within a couple of months and sometimes medications can be stopped.

## **Endocrine Diseases**

Three endocrine diseases have been associated with dry eye signs in dogs. These are hyperadrenocorticism, hypothyroidism and diabetes mellitus. The underlying cause is unknown for hypothyroid and Cushing's disease, but is thought to be due to decreased corneal sensitivity in diabetes mellitus.

## **Congenital (lacrimal gland aplasia/hypoplasia)**

Congenital lacrimal gland hypoplasia is often the cause of KCS in young dogs with severe clinical signs. Miniature breed dogs are predisposed, including Yorkshire terrier, miniature pinscher, pug, and Chihuahua. This type of dry eye can be difficult to treat and often is non-responsive to medical therapy. A parotid duct transposition may be necessary to improve ocular lubrication in these dogs.

## **Qualitative**

Qualitative tear film dysfunction is caused by a decrease in lipid or mucin and is not completely understood. Sometimes when the STT is performed, it is normal or elevated even if tear quality is poor as the aqueous production isn't affected. These cases usually have red, itchy eyes or have mild non-ulcerative keratitis. It can affect one or both eyes.

## **Tear Film Break Up Time (TFBUT)**

TFBUT is an indirect evaluation of the mucin or lipid layers of the tear film. It measures the time it takes for the tears to evaporate from the corneal surface. To perform, wet the fluorescein strip with 1 drop of eyewash, touch to the bulbar conjunctivae of each eye. Do not rinse. Manually blink the eye and hold open while observing the dorsolateral portion of the cornea with magnification and the cobalt filter for dark spots to appear in the fluorescein stain, indicating drying. The TFBUT is the time it takes for the drying to occur. Reports of normal values for dogs and cats vary, but most texts agree that normal is between 10-20 seconds. This is a notoriously difficult test to interpret or repeat with accuracy. The presence of red eyes and keratitis in the absence of other clinical causes can be adequate for a presumptive diagnosis of qualitative KCS and treatment with artificial tears or tear stimulants.

## **TREATMENT OF DRY EYE DISEASE-GENERAL**

### **Tear Stimulants**

There are two main categories of tear stimulants: T-cell modulators increase tear production by controlling glandular inflammation and dysfunction, and cholinergic agents stimulate the glands via parasympathetic fibers for the treatment of neurogenic KCS.

Treatment (Immune-mediated)-T-cell modulators

Cyclosporine A (topical)- available commercially as Optimmune (cyclosporine 0.2%) and can be compounded into a 1-2% oil or aqueous-based solution. The oil formulations are more bioavailable than the aqueous-based solutions

Tacrolimus (topical)- must be compounded into a solution for use in the eyes. It can be compounded from 0.02%-1% solutions, but the author is most familiar with 0.02-0.03%. Tacrolimus has been shown to be effective in some cases that are non-responsive to cyclosporine. It has also been thought anecdotally to decrease corneal pigmentation better than cyclosporine.

Treatment with either drug is usually 2-3 times per day. These drugs are the mainstay of immune-mediated dry eye therapy but are also used for other types of dry eye disease (including qualitative) because they improve mucin quality and increase tear production locally at the lacrimal glands. In most cases, tear production improves within 30-45 days.

Cyclosporine episcleral implants have recently been evaluated for control of immune mediated dry eye disease. They have been found to be useful and can last up to 8 months. This implant would be a good choice for dogs that are difficult to treat topically. These can be purchased from the NCSU pharmacy. They have not been used in cats.

### **Treatment (neurogenic)-cholinergic agents**

Neurogenic KCS may not respond well to tacrolimus or cyclosporine alone. This lack of response could even be the reason you are suspecting neurogenic KCS. Most of the time, these medications are still given as adjunctive therapy for their local effects on the tear gland.

The mainstay of treating neurogenic KCS is a direct acting parasympathomimetic drug-pilocarpine. This is an eye drop but is usually used systemically for the effects on the tear gland and nasal mucosa. It is given on the food to decrease side effect and taste aversion. At the 1-2% commercially available concentration, it usually causes uveitis when used topically.

Pilocarpine 1-2% drops: 1 drop/10 kg PO q 12 h in food (it tastes bitter). After 2 weeks, if the initial dose is insufficient, I increase by 1 drop/day every 5 days, watching for toxicity. (i.e., salivation, vomiting, diarrhea, bradycardia). Depending on size of patient, I usually stop increasing if I reach 5-7 drops BID or if toxicity seen. If gastrointestinal signs occur, decrease dose back to level where medication was tolerated.

Another option is compounded Pilocarpine 0.1 % eye drops into affected eye 1-2 times daily. Systemic side effects are less and because it is diluted, topical side effects are minimal.

### **Tear Substitutes**

Ointments, gels, and viscous drops are available, and some are preservative free. The viscosity of a drop/gel is the most important factor when choosing a tear replacement.

Of the tear replacement agents, hyaluronate is particularly useful. Hyaluronic acid is present in normal tears, and it becomes less viscous during blinking to aid tear dispersion and more viscous between blinks to provide good lubrication. Hyaluronates are also helpful for chronic conjunctivitis, corneal ulceration, and corneal sequestration in cats (thought to possibly be related to feline dry eye disease) because they support mucin and may help with goblet cell regeneration. Hyaluronic acid is a common ingredient in many artificial tears (veterinary and human products; preservative and preservative-free).

### **Anti-inflammatories**

Dry eye disease is inflammatory in dogs. Topical and oral anti-inflammatories are useful in reducing ocular surface inflammation, improving comfort, and diminishing corneal opacities and vascularization. Due to the propensity for corneal ulceration formation with KCS. Topical NSAIDs may be useful to help with inflammation if an ulcer is not present.

### **FELINE DRY EYE DISEASE**

KCS is rare in cats and for a long time was thought not to exist. Recent studies and case reports have suggested that cats do suffer from dry eye disease, but their clinical signs can be different than dogs. Decreased tear production can occur temporarily in patients with chronic infectious conjunctivitis or keratitis. In contrast to canine KCS with marked corneal vascularization, pigmentation, and ocular discharge, feline KCS is characterized by variable conjunctival hyperemia, non-healing corneal ulceration, corneal sequestra formation and mild diffuse corneal opacification resulting from epithelial hyperplasia. Excessive mucus discharge is rarely a component. It may affect one or both eyes. Dry eye in cats is thought to commonly be neurogenic in origin.

### **Treatment**

Response to cyclosporine is usually poor owing to the underlying causes of tear film dysfunction in cats. Supportive care with hyaluronic acid artificial tears, possible treatment with anti-viral medications, has been advocated in the few case studies that are published.