GIVE THEM SOMETHING TO CRY ABOUT! DRY EYE IN DOGS

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THE TEAR FILM

The tear film plays a very important role in maintaining the health of the ocular surface. The main functions of the tear film include maintaining lubrication between the eyelids and surface, delivering nutrients to the cornea, providing antimicrobial surface proteins, and washing away debris from the surface. There are 3 layers to the tear film: mucin, aqueous, and lipid. The mucin layer is the innermost layer and is produced by the goblet cells in the conjunctiva. This layer binds the tear film to the ocular surface, preventing dehydration of the cells and reducing the ability of bacteria to adhere to the cornea. The aqueous layer is the thickest layer, produced by the lacrimal gland and gland of the 3rd eyelid. This layer contains the oxygen, glucose, water and electrolytes required for corneal health, since this tissue lacks a blood supply. In addition, the aqueous layer possesses immune proteins, such as lactoferrin, lysozyme, and IgA, which help combat infection of the ocular surface. The lipid layer is the most superficial layer and is secreted by the meibomian glands. This layer forms a thin, oily covering that allows the tear film to spread evenly over the surface and prevents evaporation. Normal eyelid function is also a crucial factor in maintaining a normal tear film. A normal blink mechanism is vital to spread the tears over the surface of the eye, wash away debris, and propel the tears and debris into the medial canthus where drainage occurs through the nasolacrimal system.

Pathogenesis of Tear Film Disease

Abnormalities in the quantity or quality of the tears will result in ocular surface pathology. The conjunctival and corneal epithelial cells suffer from hypoxia and desiccation, with further injury occurring as frictional irritation ensues. Debris that would normally be flushed from the ocular surface (dead cells, mucus, particulates) accumulates, and bacteria more easily colonize the compromised surface. These consequences of tear film disease culminate in inflammation of the ocular surface, leading to cell damage and progressive disease.

Tear Deficiency

There are multiple mechanisms by which tear film disease develops. A decreased secretion of tears may be the result of glandular dysfunction, or from interruption of the nerve supply to the glands. Insufficient aqueous tear production is known as a quantitative tear deficiency and results in the clinical syndrome of keratoconjunctivitis sicca (KCS, dry eye). Deficiencies in either the lipid or mucin tear layers are known as a qualitative tear deficiency, which can also result in symptoms of ocular surface inflammation. Lastly, disorders that result in poor tear film coverage, such as lagophthalmos, facial nerve palsy, or other eyelid disorders, are termed distributional tear deficiencies.
Quantitative Tear Deficiency
KCS is the most common form of tear deficiency in dogs. Compromise to the glandular secretion can be caused by a variety of diseases affecting the lacrimal gland, 3rd eyelid gland, or both. Infectious diseases, such as canine distemper virus and blepharoconjunctivitis, can induce a lacrimal adenitis with subsequent KCS. Certain breeds, such as Pugs and Yorkshire Terriers, are predisposed to lacrimal aplasia leading to clinical KCS at a very young age. Certain drugs are known to reduce tear secretion (atropine, general anesthesia), while others may be toxic to the lacrimal gland (sulfasalazine, trimethoprim sulfa, etodolac). Trauma to the eye or the orbit as well as radiation therapy may damage the lacrimal gland and lead to KCS. Certain metabolic conditions are associated with decreases in tear production, including diabetes mellitus, hyperadrenocorticism, and hypothyroidism. However, the majority of KCS cases in dogs are the result of idiopathic, lymphoplasmacytic inflammation with secondary glandular atrophy. Certain breeds have a much greater incidence as compared to the general population suggesting a genetic component. English Bulldogs, Cavalier King Charles Spaniels, West Highland White Terriers, Shih Tzus, and Pugs are some of the most commonly affected breeds. Loss of the parasympathetic innervation to the lacrimal gland is known as neurogenic KCS, and can occur with chronic otitis, peripheral neuropathies, idiopathic disease, or primary neurologic diseases.

Qualitative Tear Deficiency
Diseases that affect the eyelid margins can result in abnormal secretions by the meibomian glands and subsequent instability to the tear film. The lack of a functional oily surface layer leads to premature evaporation of the tears and surface irritation. Inflammation of the eyelid margin, known as marginal blepharitis or meibomianitis, causes swelling of the eyelid margins and abnormal lipid secretion. Certain autoimmune conditions that affect the eyelids, such as lupus erythematosus and bullous pemphigoid, may also result in abnormal meibomian gland secretions. Chronic conjunctivitis can lead to a deficiency in the mucin production by the conjunctival goblet cells and also lead to an unstable tear film.

Distributional Tear Deficiency
Poor eyelid conformation or function will result in abnormal tear coverage over the ocular surface. Lagophthalmos (incomplete blinking) caused by buphthalmos, exophthalmos, or facial nerve paralysis will result is axial (central) corneal disease secondary to poor tear distribution. Diseases that affect the sensory innervation to the cornea will reduce the reflexive blink rate, reduce tear distribution, and result in corneal desiccation.

Clinical Signs of Dry Eye
Quantitative tear deficiency, or KCS, may develop acutely, however more often occurs over a period of weeks to months. Acute KCS will produce significant pain and often severe central corneal disease. Corneal ulceration can become severe, associated with bacterial infection, melting, and even corneal perforation. More commonly, however, tear production decreases over a more gradual period of time. Initially, the eyes become red with mucoid or mucopurulent discharge. These clinical signs are frequently interpreted as allergic disease or bacterial conjunctivitis. With progression, the ocular surface becomes inflamed resulting in conjunctival hyperemia, squinting, sticky, thick discharge, corneal vascularization, fibrosis, and
pigmentation. Corneal opacification may become severe enough to affect vision. Corneal ulceration is less likely, but still very possible, in chronic KCS. Neurogenic KCS is most often unilateral and ipsilateral nasal crusting is a common supportive clinical finding.

Qualitative tear deficiencies resulting from eyelid inflammation will have evidence of abnormal meibomian glands or eyelid margins. The glands may appear prominent with thick, white secretions. The glands may become impacted and form chelazia, lipid granulomas, or small eyelid abscesses and can cause frictional irritation to the ocular surface. The cornea becomes inflamed leading to vascularization and roughened areas of epithelium. Inadequate goblet cell function will also lead to clinical signs of inflammation, conjunctivitis, keratitis, and corneal ulceration. The conjunctiva will often appear thickened and hyperemic.

**Diagnosis of Dry Eye**

A strong suspicion of KCS should exist when presented with the typical clinical appearance, especially in a predisposed breed. The Schirmer Tear Test (STT) will quantify the aqueous tear production and should be measured in any dog with ocular surface inflammation, discharge, or corneal opacification. The value obtained is the result of both basal tear secretion as well as reflex tear production. The STT is performed by placing the tear strip in the ventral conjunctival fornix, approximately midway between the medial and lateral canthi. Care should be taken not to handle the tear strip excessively as the oils present on fingers may affect the dynamics of absorption. The strip is left in place for 1 minute, and the measurement should be interpreted immediately following removal. The normal STT value for dogs is >15 mm of wetting per minute. Values between 10 – 14 mm/min are considered early KCS, values between 5 – 10 mm/min result in moderate KCS, and values <5 mm/min will be associated with severe KCS. Certain factors may affect the STT measurement, including sympathetic tone and topical atropine therapy. In very nervous patients or those recently treated with atropine, a repeat STT should be considered. Diurnal variation in tear production does occur in the dog, however the fluctuations are not clinically significant. Dogs with low STT values in the absence of clinical signs should have serial exams and STT measurements to monitor for the development ocular surface disease. Once KCS is confirmed with the STT, a thorough evaluation of the patient’s ocular and systemic health should be performed to rule out underlying conditions such as hypothyroidism. Close attention should be paid to the eyelids and their function during the ocular exam.

**Treatment of KCS**

The majority of dogs with KCS are managed medically with a combination of tear stimulants, tear substitutes, antibiotics, and anti-inflammatories. Treatment regimens require adjustments based upon serial eye exams and STT measurements. Surgical therapy for KCS is reserved for dogs that do not respond to aggressive medical therapy and are persistently painful.

**Tear Stimulants**

There are two main categories of tear stimulants: cholinergic agents stimulate lacrimal secretion via parasympathetic fibers, and immunomodulators increase tear production by controlling glandular inflammation and dysfunction.
Cholinergic agents are only used in rare cases of KCS when a neurologic component is suspected. Pilocarpine is administered topically as a 0.125% or 0.25% drop, or orally on the food using the commercially available 1% or 2% ophthalmic solution. Topical administration is often quite irritating, resulting in squinting, conjunctival hyperemia, and a miotic pupil. Oral administration can induce systemic side effects including salivation, vomiting, diarrhea, and cardiac arrhythmias and the margin of safety is exceedingly narrow. The dose should be adjusted slowly and owners should be counseled strongly regarding monitoring.

Immunomodulating agents such as Cyclosporine (CsA) and Tacrolimus are the most commonly utilized medications for the treatment of KCS. These drugs exert their action by inhibiting T-cell activation, which results in a decreased lymphocyte function, reduced glandular inflammation, and an improved secretory potential. Both CsA and Tacrolimus have been shown to increased tear production significantly over time. CsA is available commercially in a 0.02% ointment (Optimmune®, Merck & Co.) or may be compounded into 1%-2% oil-based solutions. The oil vehicle allows for an increased contact time with the ocular surface and improved bioavailability of the drug. These medications are used every 8-12 hours and 30-45 days are required for full response. Dogs which respond well to the initial therapy and achieve STT values > 20 mm/min may be reduced to once or twice daily for long term maintenance. Dogs with severe KCS (STT < 5 mm/min) have a 50-80% chance of responding to CsA. Clinically, dogs should have reduced squinting, a resolution of the redness and ocular discharge, and an improvement in the corneal vascularization and / or pigmentation.

**Tear Substitutes**
A large number of commercially available products exist that provide replacement therapy for tear deficiencies and the choice is often based upon clinician preference, availability, and cost, as well as the specific need of the patient. These medications play a crucial role in the management of KCS and should be used in combination with tear stimulant therapy. Ointments, gels, and viscous drops are available and some are preservative-free. Frequency of use is dictated with the severity of KCS, however products containing preservatives should be limited to 6 times daily to avoid epithelial toxicity to the cornea.

**Antibacterials**
Secondary bacterial conjunctivitis is common in dogs with KCS due to reduced debris removal, accumulation of debris, and a lack of the natural antimicrobial tear properties (lysozyme, IgA). Broad-spectrum topical antibiotics should be administered in the early stages of treatment, usually at a frequency of 3-4 times daily. As the tear levels improve and ocular surface inflammation subsides, these antibiotics can be reduced and eventually stopped. Bacterial culture and sensitivity is reserved for chronic, non-responsive mucopurulent discharge despite an improvement in tear levels.

**Anti-Inflammatories**
Topical anti-inflammatories or anti-inflammatory and antibiotic combinations are useful in reducing ocular surface inflammation, improving comfort, and diminishing corneal opacities and vascularization. Due to the propensity for corneal ulceration, caution should be used when prescribing topical steroid medications to patients with KCS. Fluorescein staining should be performed and owners should be counseled on the clinical signs and appearance of ulcerative disease.
Surgical Therapies

Surgery for qualitative tear deficiencies is reserved for patients who have failed medical tear stimulant therapy and whose comfort level cannot be maintained with tear replacement therapy. A parotid duct transposition (PDT) is a surgical procedure in which the flow of saliva from the parotid duct is re-routed into the conjunctival fornix. Tear and saliva are physiologically similar in their pH and osmolarity, allowing salivary secretions to be a suitable substitute for tears. The mineral content of saliva is greater than tears however, thus post-operative complications with mineral deposition in the cornea and on the eyelids is fairly common. Other complications include excessive salivary flow with resultant moist dermatitis, inadequate salivary flow due to duct occlusion or fibrosis of the conjunctival opening, and corneal ulceration.

Distributional tear deficiencies resulting from lagophthalmos or facial nerve dysfunction may benefit from temporary or permanent tarsorrhaphies. Brachycephalic patients with concurrent KCS also benefit from palpebral fissure reduction, which improves to corneal coverage and conserves the existing tear film.

References