INTRODUCTION

For the past 12 years, we've studied keratoconjunctivitis sicca (KCS) in dogs to develop a therapeutic intervention to benefit both veterinary and human KCS patients. The spectrum of ocular surface pathology in canine KCS can support a battery of assessment criteria for therapeutic evaluation. Although there are multiple causes of canine KCS, the vast majority appear to be immune mediated.

Topical application of cyclosporine (CsA) leads to a gradual recovery of lacrimation in 80% of affected dogs. Conjunctivitis and keratitis are reduced with long term application. The resolution of surface pathology is largely attributed to cyclosporine's anti-inflammatory activity because improvement occurs with or without increased lacrimation. Current hypotheses on the mechanism of action of cyclosporine on lacrimation include 1) modulation of lymphocyte cytokine production in the lacrimal gland, 2) decreased recruitment of autoreactive lymphocytes from the conjunctiva to the lacrimal gland, and 3) a direct neurohormonal effect of cyclosporine mediated through prolactin receptors identified on lacrimal acinar epithelium.

CHARACTERIZATION OF KCS IN DOGS

Clinical Signs

The ocular lesions seen in dogs are much more severe than those seen in people. The increased severity may be attributed to delayed diagnosis in dogs related to the patient's
inability to report discomfort as an early sign, and to their inability to self medicate at a frequency compatible with comfort. Lagophthalmos and exophthalmos, common in many breeds, further exacerbate the effects of an insufficient tear film.\(^1\)

**Conjunctivitis.** Clinical signs of conjunctivitis of the globe, lids and third eyelid include; mucoid to mucopurulent discharge, hyperemia, chemosis, and hypertrophy. Opportunistic bacteria can be cultured from the ocular discharge, but their abundance is secondary to the effects of aqueous deficiency. Conjunctivitis is the consistent component of KCS, whereas keratitis occurs only in more advanced cases and in exophthalmic or lagophthalmic breeds. Conjunctivitis is irritative, but, typically, not painful.

**Pain.** Discomfort in dogs with KCS is highly variable; often the apparent discomfort is inconsistent with the apparent clinical signs. Dogs respond to conjunctivitis by pawing or rubbing the eyes against rugs and furniture, but blepharospasm is unusual unless corneal ulcers have also occurred. Corneal sensation was evaluated by anesthesiometer and found to vary with head conformation (brachiocephalics have less sensitivity than doliophealics),\(^2\) consistent with differences in the density of corneal nerves. Corneal sensation is much less sensitive in dogs than persons, and is often further diminished in chronic KCS, therefore, even ulcers may not be associated with signs of discomfort.

**Keratitis.** In severe cases of KCS, the corneal epithelium becomes keratinized, vascularized, and hypertrophic, as much as 30 cells thick.\(^3\) Corneal hypertrophy can become so extreme as to preclude lid closure, and lagophthalmos compounds the effects of tear deficiency. An undulated corneal surface can occur from extreme hypertrophy with inflammation induced subepithelial stromal edema. Concurrent with epithelial and subepithelial vascularization, dystrophic superficial or subepithelial precipitates can include lipids, calcium, and/or pigment.

**Pigmentary Keratitis.** In exophthalmic breeds, and in breeds with periocular pigmentation such as the Chinese pug, miniature schnauzer, and dachshund, pigmentary keratitis can be a devastating consequence of KCS. Free pigment granules, melanin in macrophages, and melanocytes can be deposited beneath the corneal epithelium.

**Blindness.** Is frequently the presenting complaint in dogs with KCS. Advanced pigmentation and corneal scarring cause sight loss. Superficial hypertrophy and, to a lesser degree, subepithelial fibroplasia are reversible with antiinflammatory treatment (corticosteroids and/or cyclosporine), but pigmentary keratitis is relatively recalcitrant.

**Corneal Ulcers.** Ulcers caused by dessication generally occur in the central cornea, the area exposed within the lid fissure. Large deep melting ulcers also occur occasionally; rapid resolution has been seen with cyclosporine ophthalmic (unreported clinical observation).