Many anatomic and physiologic factors are required for corneal transparency, including a healthy epithelium and tear film, an orderly lamellar arrangement of stromal collagen and glycosaminoglycans, the absence of blood vessels and pigment, and the relative dehydration of the stroma courtesy of intact epithelium and functional endothelium.

Nonulcerative corneal opacification can be categorized according to the host’s age at onset (congenital or acquired), the lesion’s extent (localized or generalized, superficial or deep), and its color (white, blue, red, or brown/black). Congenital opacities are usually static, while acquired lesions are often progressive owing to imbalances in the equilibrium of corneal protection and nutrition, as might occur with exposure or inadequate tear production.

### Congenital Disorders

#### Superficial, Localized

Superficial faint opacities are often observed extending across the central cornea of 6- to 8-week-old puppies. When observed against the tapetal reflection, lesion margins are usually distinct but irregular in outline, giving a “map-like” appearance to the lesion. This form of epithelial dystrophy is self-limiting, with negligible impact on vision.

Dermoids are congenital masses of tissue containing skin, hair follicles, sebaceous glands, and fat. They are most frequently encountered in the temporal perilimbal conjunctiva and cornea. Hairs arising from the dermoid produce ocular irritation and epiphora. Treatment involves careful dissection of the dermoid via superficial keratectomy and conjunctival resection.

#### Deep, Localized

Persistent pupillary membranes are remnants of embryonic vasculature that supplied blood to the developing lens and anterior segment. Strands of pigmented tissue originate from the mid-iris face. Deep corneal opacities are created by focal attachments of these vascular remnants to the corneal endothelial surface. Heritability has been implicated in the Basenji, Chow, and Welsh corgi. The opacities are usually focal and nonprogressive, although corneal edema may occur in rare cases.

### Acquired Disorders

#### Superficial, Localized

Corneal lipidosis is characterized by the deposition of cholesterol and other fats within the corneal stroma. Familial lipid dystrophies are recognized in a number of breeds, including Siberian huskies, cocker spaniels, poodles, beagles, Cavalier King Charles spaniels, and collies. Clinical signs include central, bilaterally symmetrical white refractile corneal opacities. The overlying epithelium is intact and the surrounding cornea is typically normal. Lesions progress to a certain density but rarely compromise vision. Lipid degeneration develops in association with hyperlipidemia of various causes, including systemic metabolic disturbances such as hypothyroidism. A diet with more than 14% fat may contribute to lesions in susceptible individuals. Lipid may accumulate as a consequence of focal disturbances in corneal metabolism, as in the perilimbal arcus accompanying episcleritis. Topical corticosteroids may promote additional deposition when used in patients with preexisting lipidosis.

Superficial punctate keratitis is a condition of unknown etiology seen most commonly in Shetland sheepdogs and dachshunds. The disorder may represent a corneal dystrophy, although symptomatic dogs often demonstrate tear film abnormalities, particularly decreased tear film breakup times. Multiple 1- to 3-mm grayish-white round or irregular ring-like opacities are scattered across the corneal surface. Focal epithelial erosions may develop at these sites over time, with concurrent discomfort. Vascularization is seen with chronicity. Topical cyclosporine is usually effective in stabilizing the tear film and controlling clinical signs.

Calcific degeneration is not as common as corneal lipidosis in the dog. Distinguishing the two disorders may be difficult in the early stages when only a faint crystalline opacity exists. Calcium deposits usually appear duller and chalky white, ultimately coalescing into raised plaques and often accompanied by signs of discomfort. Vascularization is more likely to accompany calcific degeneration than lipidosis. Refractory or rapidly progressive ulcers can occur as these plaques slough. The problem is more often seen in geriatric patients, perhaps as a consequence of lifelong surface insult due to exposure/drying or other chronic corneal disorders.
Hyperadrenocorticism has been reliably linked to calcific degeneration in some dogs. Palliative therapy with 2% EDTA ointment is indicated 2 to 4 times daily to chelate the mineral and discourage ulcer formation. Noticeable response may take weeks. Patients with deep ulcers respond better to corneal-conjunctival transposition than conjunctival grafting alone.

Nodular episcleritis appears as a proliferative pink mass, most often at the temporal limbus. The lesion is thought to be an immune-mediated disease based on the presence of lymphocytes, plasma cells, and histiocytes and its response to anti-inflammatory therapy. Topical, intralesional, and/or systemic steroid therapy is commonly used for control. Alternatives include oral tetracycline/niacinamide (500 mg q 8 hrs, tapering to q 12–24 hrs), oral azathioprine, cryotherapy, or surgical excision.

Superficial, Generalized
Tear film abnormalities may be either quantitative or qualitative in nature. Keratoconjunctivitis sicca (KCS) is a common syndrome of progressive inflammation and degeneration of the cornea and conjunctiva caused by inadequate tear production. Commonly affected dogs include the English bulldog, Lhasa apso, West Highland white terrier, pug, cocker spaniel, Yorkshire terrier, and Boston terrier.

Documenting the specific cause in individual cases is often difficult. Congenital anomalies, infectious agents, and toxic, neurologic, inflammatory, immune-mediated, and iatrogenic factors are all possibilities. Congenital sicca is usually unilateral and occurs in small-breed dogs. Neurogenic sicca resulting from lesions of parasympathetic innervation create ipsilateral nasal dryness/crusting, along with the dry eye. The majority of dogs with KCS are thought to have an autoimmune adenitis, suggested by elevated gamma globulin in 90% and elevations of antinuclear antibodies and rheumatoid factors in 42% and 50% of KCS cases, respectively. Of the iatrogenic causes, several drugs have been incriminated, including etodolac, various sulfa drugs, and atropine. Topical atropine applied to one eye decreased Schirmer tear test (STT) values in both eyes for up to 5 weeks in normal dogs. In certain breeds at risk for KCS (e.g., cockers, bulldogs), surgical excision of the nictitans gland in the treatment of “cherry eye” may promote or accelerate KCS. Megavoltage therapy of nasal and paranasal tumors resulted in ocular complications in 75% of patients, of which 25% developed KCS.

The severity of clinical signs is proportional to the degree of dryness and its duration. The hallmark of KCS is the presence of a mucoid or mucopurulent discharge. In the early stages, the cornea may appear dull and the conjunctiva hyperemic. If KCS persists, superficial corneal vascularization and pigmentation may ultimately opacify the cornea to such a degree that blindness results. Secondary ulceration is always a threat.

Confirmation of KCS is made utilizing the Schirmer tear test. Normal values in the dog are 20 mm wetting/minute (+/- 5mmSD). Values less than 10 mm/min are indicative of KCS. In brachycephalic canine breeds, STT values less than or equal to 15 mm/min are considered significant.

With the advent of topical cyclosporine (CsA), treatment of KCS has been greatly simplified. The drug is theorized to suppress autoimmune injury to the lacrimal gland by an interleukin blocking effect, combined with a direct effect on tear production via action as a prolactin analog that binds with lacrimal prolactin receptors. Even in the absence of improved tear volume, CsA improves surface health by reducing conjunctival cell apoptosis and restoring goblet cell mucin production. For best results, CsA should be initiated early in the course of the disease before significant damage to the lacrimal gland occurs. Commercially available 0.2% ointment (Optimmune, Schering-Plough) or compounded 1% to 2% solution is applied twice daily. Less consistent response is seen in dogs with STT values below 2 mm/wetting/min. Response to CsA is not immediate, so topical lubricants, antibiotics, mucolytics, and/or steroids are generally indicated in the initial management. Reevaluation is recommended 2 to 3 weeks after beginning cyclosporine and should be performed 3 to 6 hours after cyclosporine application when the STT values are greatest.

If response to cyclosporine is limited, topical tacrolimus may be substituted or added to the regimen in conjunction with cyclosporine. Tacrolimus is reportedly 10 to 100 times more potent in vitro than cyclosporine and utilizes different cell receptors, potentially providing a synergistic effect. Twice daily application of 0.02% to 0.03% tacrolimus in aqueous or oil-based formulations has been beneficial in KCS-affected dogs.

Supportive therapy using a combination of topical agents, including artificial tears, mucolytics such as 5% acetylcysteine, corticosteroids (in the fluorescein-negative patient), and antibiotics may be indicated in severe or
chronic KCS. The frequency of this therapy is dictated by the severity of the dryness and clinical signs. Oral 2% pilocarpine (2–4 drops in food b.i.d. in medium-sized dogs) may directly stimulate tear production and is especially indicated in patients with dry nares indicative of a neurogenic etiology. If clinical signs are not controlled with topical therapy in 4 to 6 months, surgical treatment for KCS includes parotid duct transposition (PDT), combined with shortening of the palpebral fissure to reduce exposure. While PDT is reportedly successful in 63% to 90% of patients, common sequelae include epiphora and corneal mineralization.

Qualitative tear film disorders characterized by deficiencies of lipid and/or mucin may also cause clinical signs suggestive of KCS, despite a normal STT. Disturbances of the meibomian glands from inflammation, infection, or chronic skin disorders such as seborrhea may result in abnormal secretions and disruption of the superficial lipid layer of the tear film, resulting in tear evaporation. Insufficient production of preocular mucin by conjunctival goblet cells results in diminished tear film stability, with premature breakup of the tear film and corneal desiccation. Chronic infectious or immune-mediated conjunctivitis may reduce goblet cell numbers. Diagnosis of qualitative deficiencies requires careful assessment of the meibomian glands, assessment of tear film breakup time, and quantification of conjunctival goblet cells with biopsy. Applying a drop of fluorescein dye to the corneal surface, observing with a cobalt blue filter, and recording the time necessary for a dark spot to appear in the fluorescent film following the last blink establishes tear film breakup time (BUT). Normal canine BUT is 20 seconds; mucin deficient tears will disperse in less than 5 seconds.

Chronic superficial keratitis or pannus is believed to be a T-lymphocyte-mediated disease. The exact etiology is unknown, but cell-mediated immunity to corneal and uveal antigens may have been demonstrated in affected eyes. Ultraviolet radiation or other unknown factors may alter the antigenicity of the tissue in susceptible corneas, initiating the cell-mediated response. In the early stages, the superficial corneal stroma is infiltrated by plasma cells and lymphocytes, followed by superficial corneal vascularization and pigmentation. The opacity begins in the lower lateral aspect of both eyes, then sequentially affects the medial, ventral, and dorsal quadrants until the entire cornea is affected.

The problem is especially prevalent in the German shepherd but also occurs in the greyhound, Belgian tervuren, border collie, dachshund, and mixed-breed dogs originating from these breeds. The age of onset is usually 3 to 6 years of age, but it can occur as a rapidly progressive disease in younger animals. Diagnosis is based on clinical appearance and breed predisposition after other causes of superficial keratitis such as KCS and adnexal abnormalities have been ruled out.

Corticosteroids have traditionally been used to control this incurable disease, but topical cyclosporine has been advocated in recent years. Topical 1% prednisolone acetate or 0.1% dexamethasone are applied 4 times daily for 2 weeks, then reduced at 2-week intervals to a maintenance level of 1 to 2 times daily. Topical cyclosporine applied twice daily may work synergistically, decreasing the steroid requirement. In poorly responsive cases or when client compliance is a problem, a subconjunctival repositol corticosteroid may be injected. Animals living at higher altitudes (> 4,000 feet above sea level) respond less favorably to therapy. Beta-radiation has been used in refractory cases to reduce vascularization, but access to these handheld units is restricted. Superficial keratectomy should be reserved for patients that are blind due to chronic pigmentation. Also, active inflammation must be well controlled prior to surgery or vascularization and opacification of the cornea will recur rapidly.

Pigmentary keratitis is characterized by superficial corneal pigmentation. The discoloration results from migration of limbal melanocytes along blood vessels or activation of latent melanocytes by limbal stem cells. The disorder is especially common in brachycephalic breeds, including the Pekingese, pug, Boston terrier, Shih Tzu, Lhasa apso, and English bulldog. Focal pigmentation is more likely a consequence of adnexal abnormalities such as medial entropion or facial fold irritation and appears as a limbal-based triangle of pigment in the medial cornea, with its point directed centrally. Central and/or generalized pigmentation accompanies KCS, exophthalmos, lagophthalmos, or immune-mediated keratitis such as pannus. Blindness occurs when the condition is bilateral and diffuse. If the cause is eliminated, epithelial pigmentation may decrease spontaneously due to natural epithelial turnover. Stromal pigmentation remains indefinitely. Prevention is therefore the best “therapeutic” option. Topical corticosteroids may control concurrent vascularization and slow secondary pigmentation while artificial tear preparations will counteract surface drying. Topical cyclosporine is credited with reducing corneal pigmentation when used long term, but it is unknown whether this is a direct effect of the drug or a secondary response to the improved surface environment. Surgical procedures that may be of benefit in addressing the adnexal and globe-orbit abnormalities include permanent partial tarsorrhaphy, medial entropion correction, and facial fold reduction.
Deep, Generalized

Boston terriers, Chihuahuas, and dachshunds are afflicted with an inherited *endothelial dystrophy* that causes progressive bilateral corneal edema. A deepening blue color develops first temporally, gradually affecting the entire cornea and significantly impacting vision. Older patients of any breed may also develop corneal edema as endothelial cell numbers decline. Initially painless, the condition can cause recurrent corneal erosions when stromal and epithelial edema becomes excessive. The disorder must be differentiated from endothelial degeneration secondary to intraocular inflammation, glaucoma, and anterior lens luxation. Use of a thin Gunderson-type conjunctival flap in the early stages of the disorder may slow progression of the edema. When stromal and epithelial edema becomes advanced, topical 5% sodium chloride ointment may discourage the development of subepithelial bullae and corneal erosions. If erosions do occur, debride any nonadherent epithelium and administer topical broad-spectrum antibiotics. Surgical options to control recurrent ulceration in the late stages of the disease include keratectomy, thermokeratoplasty, a 360-degree conjunctival graft, or a penetrating corneal graft.

References available upon request.