KNOW THE BREED TO DIAGNOSE CORNEAL AND SCLERAL DISEASES IN DOGS

Kerry Ketring, DVM, DACVO
All Animal Eye Clinic
Whitehall, MI 49461

After more than thirty years in private practice, I realize the majority of canine ocular diseases have a breed predisposition. This talk will reflect the most common inherited corneal and scleral diseases in the breeds seen in my practice. It is pertinent to keep in mind, the breed incidence may reflect just the popularity of the breed. Also just as certain lines in a breed may have different conformation and behavior traits, they may also have a different incidence of ocular diseases. The awareness of breed-specific diseases is a head start in making the correct diagnosis. Canine Eye Registration Foundation (CERF) at www.vmdb.org/cerf.html has lists of breed inherited diseases available to their membership. The American College of Veterinary Ophthalmologists also has a CD on breed incidence of ocular diseases which can be ordered direct. Additionally, many veterinary ophthalmology textbooks have lists of inherited eye diseases.

My personal preferences for the treatment of each disease are included in the discussion. However, once the diagnosis is made, there are many literature sources that will give you additional treatment options.

DERMOID
These are congenital, skin-like lesions found especially at the temporal limbus. Dermoids may also involve the nictitans or lids margins and may be unilateral or bilateral. They can be found in any breed but have a higher incidence in the Dachshund, Dalmatian, German Shepherd, Rottweiler and Shih Tzu.

Stromal keratectomy and a superficial sclerectomy are indicated. Seldom do dermoids in the dog extend deep into the stroma, therefore a conjunctival flap or additional support is not indicated. Post-op antibiotics, atropine ointment and possibly oral NSAIDs are also indicated. Once re-epithelialization is complete, topical steroids are applied to clear the pannus.

PERSISTENT PUPILLARY MEMBRANE (P.P.M.)
This is a congenital disease resulting from the pigmented remnant of the vascular supply in the anterior segment. The pigmented strands originate from the large vessel in the mid-iris and insert on the lens, cornea or iris. The resulting insertion results in focal or diffuse corneal pigmentation and/or edema. The term Peter’s anomaly is used in cases of extensive strands resulting in corneal edema. Anterior capsule lens opacities are also possible. The condition is usually non-progressive and not blinding.
P.P.M. may be found in any breed. It may also be associated with microphthalmia and multiple ocular defects. The incidence is greatest in the Basenji, Chow Chow, English Mastiff and Pembroke Welsh Corgi.

Seldom does a P.P.M. require any treatment. Severe corneal involvement, referred to as Peter’s anomaly, can result in significant edema, bullae and ulcer. The worse cases I have seen have been controlled with topical hyperosmotics, i.e. sodium chloride ointment.

CORNEAL DYSTROPHY
Corneal dystrophy is a developmental disease that is bilateral and usually axial. The white deposits may be in any layer of the cornea and consist primarily of lipid. Dystrophies are not associated with vascularization or systemic diseases. These facts separate the dystrophies from corneal degeneration. Superficial dystrophy usually causes no vision loss or ocular pain, but there are a few exceptions. For example, the Shetland Sheepdog has a wide range of clinical presentation, some of which result in corneal erosions and ocular pain.

Any breed may develop a corneal dystrophy but the occurrence is high in the Afghan Hound, Akita, Boxer, Cavalier King Charles Spaniel, Cocker Spaniel, Collie, Dalmatian, Golden Retriever, Labrador Retriever, Löwchen, Miniature Pinscher, Shetland Sheepdog, Siberian Husky, and Weimaraner.

In 90% of the cases of corneal dystrophy, treatment is neither indicated nor beneficial. Reduction of opacities has been reported with topical cyclosporine and tacrolimus (D. Hacker, DACVO, personal communication). In my practice, this treatment regime has not proven to be beneficial.

Shetland sheepdogs have been presented with small areas of superficial epithelial erosion over the dystrophic cornea. These cases are presented with a history of episodes of hyperemia and blepharospasms. Many of the cases have borderline Schirmer tear test (STT) values. Topical corticosteroids, cyclosporine and tear replacements together and individually have been used to control these cases.

Topical corticosteroids at high frequency and prolonged use can result in an axial mineral deposit that can reduce when the drug is discontinued. Any puppy 4-10 weeks of age may have a corneal opacity similar to a dystrophy that is transient.

CORNEAL LIPIDOSIS/DEGENERATION
Comprised of lipid deposits, this disease is normally limbal and associated with corneal vascularization. It may be unilateral or bilateral and can be slowly progressive. Unlike corneal dystrophies, this disease is frequently associated with a systemic disease which also causes abnormal serum lipid levels. The most common disease is hypothyroidism. The most common breeds are Cocker Spaniels, Golden Retrievers, Shetland Sheepdogs and German Shepherds. Corneal lipidosis may also be seen in association
with scleral shelf melanoma, nodular granulomatous episclerokeratitis (NGE), proliferative keratoconjunctivitis and chronic superficial keratitis.

Seldom is a stromal keratectomy indicated to remove the area of dense lipidosis. Prior to any surgery, it is imperative to identify the cause of elevated systemic lipids and treat accordingly. I have seen cases where the lipid deposits thin or at least stop progressing once the etiology is corrected. I have also placed idiopathic cases on low fat diets with subjective improvement. Topical corticosteroids and/or cyclosporine or tacrolimus, may be used to control associated corneal vascularization and conjunctivitis.

ENDOTHELIAL CORNEAL DYSTROPHY
This disease is found in geriatric dogs in any breed but the highest prevalence is in the Basset Hound, Boston Terrier, Chihuahua, Cocker Spaniel, Dachshund, English Springer Spaniel, Shih Tzu, West Highland White Terrier and Wire Fox Terrier.

This condition is due to degeneration of the endothelium and the resulting imbibition of fluid into the stroma and epithelium. The edema usually starts temporal and progresses axial. The result may be complete bilateral edema. Bullae, ulcers and corneal vascularization may develop. Vision can be impaired in advanced cases.

The treatment will vary considerably depending on the stage of involvement. Topical hyperosmotics (sodium chloride ointment) are used to control the edema in the epithelial layer and may reduce bullae preventing superficial ulceration. Topical corticosteroids are used to control vascularization of the cornea which further compromises the clarity of the cornea. Deep stromal ulcers require aggressive treatment similar to cases of keratomalacia. In advanced cases, conjunctival flaps, corneal grafts, and / or synthetic corneal implants may be indicated to maintain the integrity of the cornea. Sling conjunctival flaps have been used to ‘control’ edema. Topical carbonic anhydrase inhibitors (Trusopt®, Azopt®) have been reported to reduce corneal edema (D. Ramsey, DACVO, personal communication). Low heat cautery has been recommended by some ophthalmologists. The theory is by scarring the epithelium, superficial fluid cannot increase resulting in bullae, ulcers and pain.

No treatment ‘cures’ this disease. The owner must continue to treat aggressively and watch for complications.

INDOLENT ULCERS
An indolent ulcer is a geriatric disease which results in spontaneous separation of the corneal epithelium from the stroma. The disease has also been referred to as a basement membrane dystrophy, boxer ulcer, refractory ulcer, superficial corneal erosion, canine dendritic ulcer, canine persistent superficial corneal ulcer and recurrent erosions. The most recent name given this disease is spontaneous chronic corneal epithelial defect (SCCED). Any older dog may develop the condition but the Boxer, Golden Retriever, Labrador Retriever, Pembroke Welsh Corgi, Poodle and West Highland White Terrier have a high incidence.
This is a superficial ulcer involving only the epithelium. When stained with fluorescein dye, the stain will extend under the loose epithelium at the margin, resulting in a lighter green border. Corneal edema is always present and superficial vascularization is common if the ulcer becomes chronic. The resulting superficial ulcer proves difficult to resolve. Both eyes would be predisposed but blindness is never the outcome.

There is a great deal of disagreement on how to handle these cases among ophthalmologists. All agree the loose epithelium must be removed and a punctate or striate keratotomy over the debrided stroma is indicated. A 22 gauge to 30 gauge needle (bevel up) is used to grid the superficial stroma after the loose epithelium is removed with a cotton swab and the cornea irrigated with an eyewash. Grid lines are approximately 2-3mm apart and extend 1-2mm onto the surrounding epithelial layer. The grid lines only involve the superficial one third of the stroma. From this point on, the treatment varies. I use topical tobramycin t.i.d. (prophylactic), atropine ointment s.i.d. (cycloplegic and mydriatic), and hyperosmotics q.i.d. (sodium chloride ointment) to dehydrate the superficial stroma. Systemic NSAIDs (low-grade anterior uveitis) are used in most cases. I also have the patient wear an E-collar or other device to prevent rubbing. I recheck in 7-10 days and expect improvement. If re-epithelialization is complete, I may start topical corticosteroids if pannus formation is significant.

If ulceration is still present, what I advise is based on the age and comfort level of the patient, their general health and the owners' patience. The initial procedure may be repeated. Topical and/or oral tetracycline (Terramycin®, oxytetracycline, doxycycline) may be dispensed. They are reported to improve the adhesion of the epithelium to the stroma.

In non-responsive cases, a keratotomy and temporary tarsorrhaphy is done under general anesthesia. If general anesthesia is used, the entire epithelium is removed to the limbus and a #64 Beaver blade is used to remove (scrape) the epithelium and superficial stroma. The area is then gridded as previous and a temporary tarsorrhaphy or 3° eyelid flap is applied. Medication is as previously described and the lids are closed for 7-14 days.

Client communication is important. The owners need to know this is a spontaneous disease; can recur in either eye; but never do these animals go blind or require enucleation.

Other treatment regimes used by veterinary ophthalmologists include therapeutic soft contact lenses (B & L PureVision, 14mm, 1-800-828-9030; Acrivet Inc., size D2 and C1, 1-801-256-9800) cyanoacrylate adhesives, epithelial growth factors and polysulfated glycosaminoglycan (Adequan®). In my opinion, conjunctival flaps and stromal keratectomies are never indicated. Recently diamond burr debridement has been popular with ophthalmologists. There are no proven effective means of preventing recurrence. Continual b.i.d. treatment with NaCL has reduced the incidence of recurrence. The use of estrogen, testosterone and thyroid replacements has not been found to be effective in preventing recurrence.
**PUNCTATE KERATITIS**
This bilateral disease is found primarily in young adult dogs. They present with a history of acute blepharospasms and conjunctival hyperemia. Multiple pinheads to pinpoint opacities may be present in the corneal epithelium. In some cases, there are small divots or craters. Some opacities may be fluorescein positive. If the disease becomes chronic, superficial corneal vascularization is present. Punctate keratitis is found in the Cocker Spaniel, Dachshund, German Shepherd, Italian Greyhound, Parson Russell Terrier, Poodle and Shetland Sheepdog.

This disease is one of the few ulcerative diseases where corticosteroids are indicated. I prefer prednisolone acetate or dexamethasone q.i.d. initially. Topical cyclosporine or tacrolimus have also been used in conjunction with the corticosteroids. Results are rapid with significant improvement in 72 hours. Treatment can be reduced to b.i.d. or q.d. with one or both drugs for control. The disease is seldom cured.

**PROGRESSIVE NECROTIZING KERATITIS**
A rapidly progressing disease, this keratitis manifests as large, limbal stromal ulcers and corneal vascularization. The disease can lead to corneal rupture and is seen most frequently in young long haired Dachshunds.

This disease may be a variant of the previous one. The deep ulcers seen in this disease are of even more concern when you treat with topical corticosteroids and / or cyclosporine and tacrolimus. Response is rapid and impressive. Control is always possible.

**CHRONIC SUPERFICIAL KERATITIS**
Also known as degenerative pannus, German Shepherd pannus and Überreiter’s syndrome, this bilateral disease causes corneal vascularization, pigmentation and edema. Corneal lipidosis may also be present. Starting temporally, the disease progresses axially and can involve the entire cornea. In many cases, the third eyelid becomes severely hyperemic, thickened and depigmented. This involvement has been referred to as a plasmoma. Untreated, chronic superficial keratitis can result in blindness. The disease has been diagnosed in the Belgian Tervuren, Borzoi, Dachshund, German Shepherd Dog and the Greyhound.

Topical corticosteroids such as prednisolone acetate or dexamethasone are used initially q4-6h. I also start cyclosporine or tacrolimus b.i.d. initially. I treat aggressively for 2-4 weeks depending on the severity. In most cases, treatment is slowly reduced to b.i.d. with the cyclosporine / tacrolimus and q.d. or q2d with the topical steroids. The goal is to eliminate the corneal vascularization. Corneal pigment is slow to decrease and the associated lipidosis remains. Associated involvement of the nictitans (i.e. plasmoma) does not respond as rapidly.
This disease must not be confused with pannus. Pannus is a subepithelial vascularization, pigmentation and fibrosis resulting from previous corneal ulceration or irritation. The primary disease such as sicca or entropion must be corrected and/or treated to prevent recurrence.

**EXPOSURE KERATOPATHY/KERATITIS SYNDROME**
This disease occurs because of a functional lagophthalmos seen in the exophthalmic brachycephalic breeds. The syndrome can present as axial corneal ulcers and/or corneal pigmentation. The term ‘pigmentary keratitis’ should not be used to refer to a specific disease entity. The pigment can result from any chronic irritation which must be identified and corrected.

These cases should also be evaluated for tear production. A STT of 15-20mm/min may not be adequate for a dog that does not cover the cornea with each blink. In some cases, the owner will report that the dog sleeps with the eyes open. Topical lacrimomimetics (cyclosporine, tacrolimus) and tear replacements are indicated. Topical antibiotics and/or corticosteroids and more aggressive treatment may be indicated depending on the severity and type of corneal disease. In some severe cases, a permanent medial and/or lateral tarsorrhaphy may be indicated to aid in preventing recurring ulcers.

**SCLERAL ECTASIA/STAPHYLOMA**
This congenital disease is seen primarily in the Australian Shepherd Dog. This outpouching of the sclera may involve the anterior sclera and appear as an elevated blue area or the posterior sclera, resulting in retinal detachments.

There is no medical or surgical treatment for this disease. Affected dogs should not be used in a breeding program.

**PROLIFERATIVE KERATOCONJUNCTIVITIS**
Previously termed fibrous histiocytoma, this bilateral disease is seen primarily in the Collie. Histologically, this is similar to nodular granulomatous episclerokeratitis (NGE) seen as isolated lesions in other breeds. In the Collie, this proliferative pink mass involves the limbus, lids margins, and nictitans. Rare cases have been found with intraocular involvement. Corneal lipidosis is frequently present at the leading edge of the proliferative mass.

Depending on the severity of the condition, topical corticosteroids and tacrolimus may be adequate to reduce the infiltrate and control the disease. Severe corneal and scleral cases and cases with associated adnexa involvement will require oral medication in the form of corticosteroids, cyclosporine (Atopica®) or azathioprine. Several collies did not tolerate azathioprine and were reported to have developed neutropenia. Treatment frequency is reduced based on response. All cases will require life-long treatment. Cryosurgery has been used to reduce initial involvement but medical management is still needed for control.
SCLERITIS, EPISCLERITIS, NODULAR GRANULOMATOUS EPISCLEROKERATITIS (NGE)

Isolated hyperemic nodules involving the sclera and extending into the cornea are seen unilateral or bilateral. Diffuse thickening and hyperemia of the sclera and associated conjunctiva may also be seen. In these cases, limbal edema and vascularization may also be present. In both forms, the posterior segment may be involved, causing chorioretinitis, retinal detachment, and optic neuritis. In the diffuse form of the disease, anterior uveitis may also be present. The disease in both forms may be seen in the Airedale Terrier, Cocker Spaniel, Golden Retriever, Poodle, and Rottweiler.

In early cases, topical corticosteroids q4-6h and tacrolimus b.i.d. are instituted. In severe cases or cases with posterior segment involvement, I use topicals plus prednisolone 1mg/# divided b.i.d. and azathioprine 2mg/kg q.d. for 1 week and then every second day. As the clinical signs improve, the frequency and dose are reduced. I try to reduce the prednisolone first due to the associated side effect. Prior to starting oral medication, I submit a baseline CBC and chemistry profile. Liver enzymes, especially alkaline phosphatase will be elevated at a two week recheck. As long as there are no clinical signs of liver disease and other liver enzymes are not significantly elevated, I continue azathioprine but will possibly reduce it to q3d. Most cases can be controlled with topicals q.d. to b.i.d., oral prednisolone (.25mg/# q2d-q3d) and azathioprine (q3h).

I have only had complications from the azathioprine for long-term management in one Shetland sheepdog and sibling collies. These cases improved completely when the drug was discontinued. I have not used oral cyclosporine (Atopica®) but it has been used by other ophthalmologists.

NECROTIZING SCLERITIS

Rapid necrosis of the sclera causing an iris prolapse is a rare disease in Shetland Sheepdogs. These are cases with no associated infection.

This is a rare disease that a routine treatment protocol has not been established. Oral anti-inflammatories (prednisolone, azathioprine, cyclosporine) are indicated. Antibiotics both topical and oral are also reasonable. If I were presented with a case today, I would also use Duralactin® to inhibit neutrophil infiltration.

SQUAMOUS CELL CARCINOMA

A pink elevated and cauliflower-like mass is seen in the axial cornea in exophthalmic breeds with a history of chronic corneal disease. The corneal disease is usually associated with KCS or exposure keratitis.

This isolated mass is most commonly seen in older Cavalier King Charles Spaniels, Pugs, and Shih Tzus.

These tumors can be removed with care by a stromal keratectomy. Laser therapy, B-radiation, and cryotherapy have been recommended following the keratectomy. I feel
these last three procedures are either not practical or very risky to the integrity of the cornea. Following a keratectomy, the cornea should be protected with either a 3rd eyelid flap or temporary tarsorrhaphy and treated aggressively for the ulcer. Even with clean margins as reported by a pathologist, I have had recurrence. Since these are slow growing and do not tend to penetrate, benign neglect with treatment for primary disease may be adequate in some older dogs with this condition.

SCLERAL SHELF MELANOMA/ LIMBAL MELANOCYTOMA
This slow growing tumor originates from pigment within the scleral shelf near the limbus and extends in all directions including the cornea. The incidence of metastasis is extremely low but in advanced cases, the globe could become painful and blind.

The incidence is higher in the German Shepherd Dog, Labrador Retriever, Golden Retriever and Giant Schnauzer. This disease has been seen in dogs as young as 2 years old. Choice of treatment would depend on the dog’s age and current size of this benign tumor. Geriatric dogs with minimal involvement probably do not need treatment since this is a slow growing tumor. Tumors which have extended into the iridocorneal angle as viewed by gonioscopy have a poor prognosis for any surgical management. Large extensive tumors with significant corneal and posterior extension in the sclera are best dealt with enucleation if the patient is uncomfortable.

Small to medium size tumor in young dogs can be treated surgically by an ophthalmologist. A deep keratectomy and sclerectomy can be performed to remove the mass followed by cryosurgery, laser surgery, corneal grafting and/or synthetic implants. Cryosurgery and laser ablation have met with poor success as has chemotherapy. The canine melanoma vaccine is not effective in ocular melanomas. Enucleation may be indicated in advanced cases if the large tumor is causing ocular pain.

OCULAR MELANOSIS
Seen primarily in the Cairn Terrier but also in the Maltese and Scottish Terrier, this disease is bilateral and slowly progressive. It is first seen as multiple flat, black pigmented areas of the sclera. The disease will progress to severe pigmentation of the sclera. Anterior uveitis and glaucoma are also possible. The iris will be heavily pigmented. Secondary cornea involvement with exposure keratitis is also present. Treatment protocol depends totally on the stage of the disease. No treatment has been found to arrest or reverse the progressive pigmentation of the sclera and uvea. In cases of uveitis, I treat with prednisolone acetate and topical NSAIDs i.e. flurbiprofen. I use atropine sparingly. In cases of glaucoma oral or topical carbonic anhydrase inhibitors are also indicated. Miotics such as the topical prostaglandins (Xalatan®) and parasympathomimetics (demecarium bromide) may lower IOP but cause severe miosis and possible complications. In cases of buphthalmia, the cornea should be protected with lubricants. Irreversibly blind eyes with glaucoma should be enucleated.