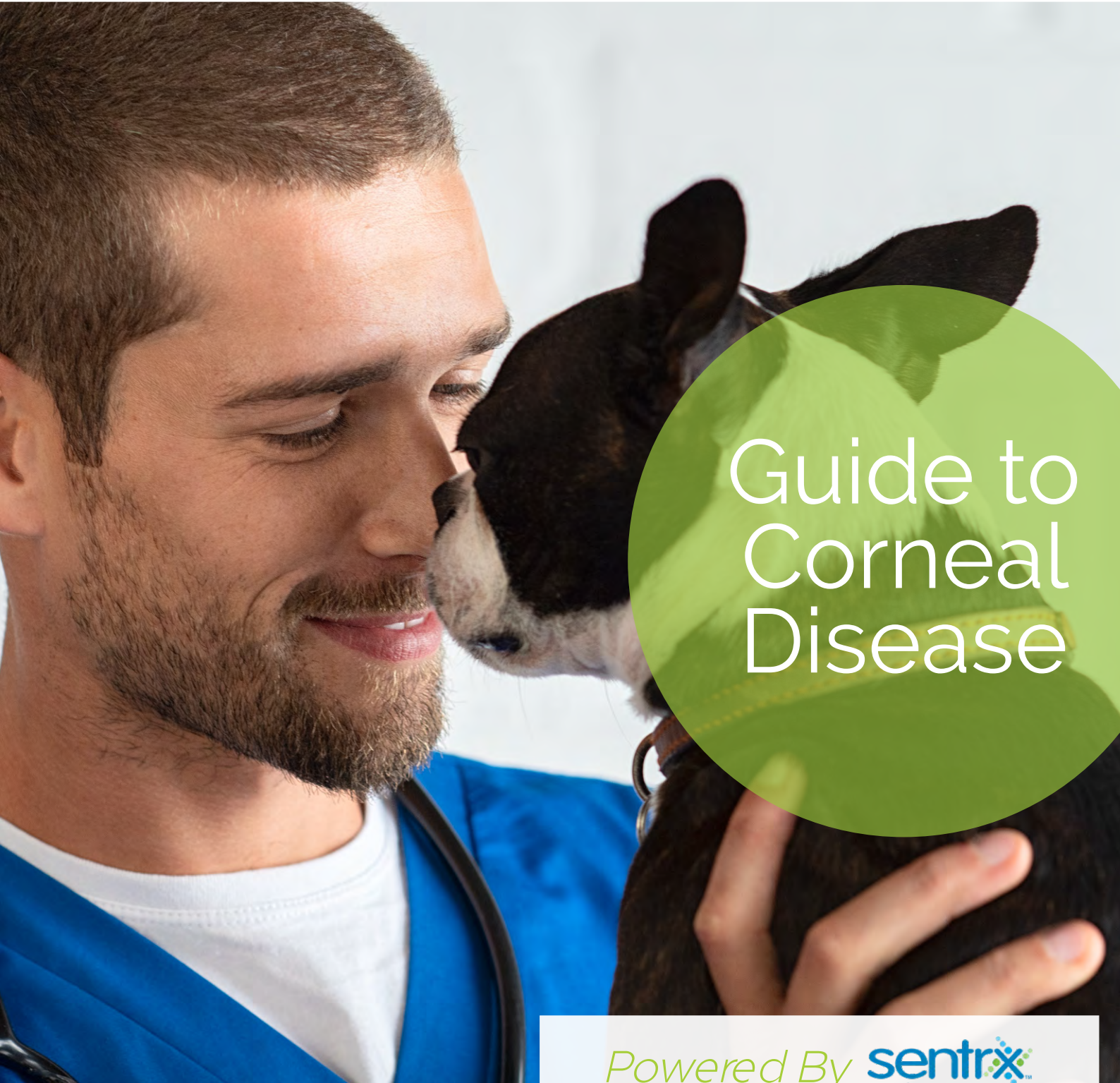


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Guide to
Corneal
Disease

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Anatomy and Physiology of the Cornea

Taylor Wickware, BS, DVM
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The cornea is composed of four layers; the outer epithelium, stroma, Descemet's membrane, and endothelium. The healthy cornea should be clear in order to refract sufficient quantity and quality of light into the eye. This light is then focused to form an image on the retina. Clarity is maintained by specific characteristics of each of the four layers.

Epithelium

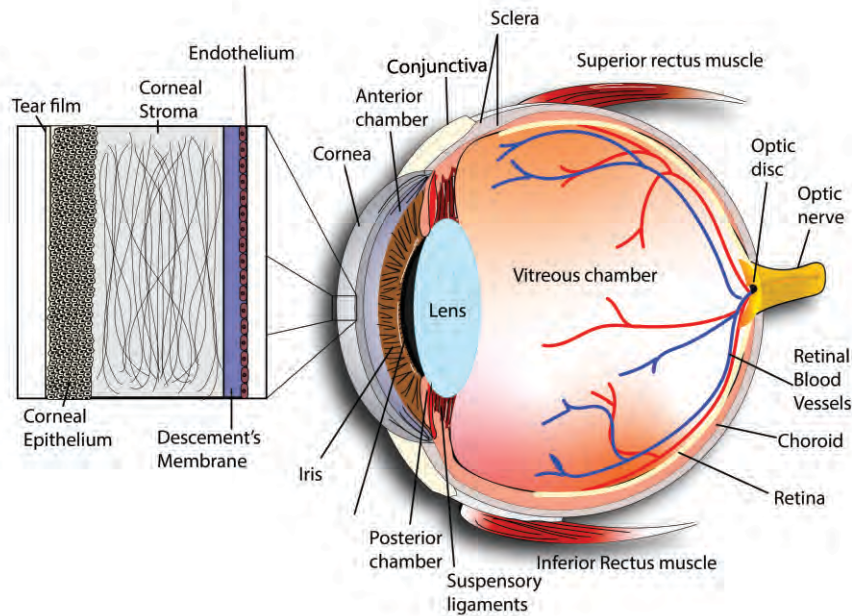
The corneal epithelium is composed of non-keratinized stratified squamous cells. The epithelium is lipophilic, working as a barrier to the underlying stroma to maintain clarity. Absence of pigment, and vessels are also important for maintaining clarity and vision in the cornea. The entire epithelium has a turnover rate of approximately seven days and undergoes a constant cycle of proliferation and shedding in a healthy state. Healing of the entire corneal epithelium can occur within 72 hours in some species when damaged. Damage to this layer can result in focal or diffuse corneal edema from a decreased barrier to fluid. Chronic inflammation may result in vascularization or pigmentation of the cornea, thus impacting vision.

Stroma

The corneal stroma makes up approximately 90% of corneal thickness. This layer is hydrophilic and will swell with water uptake, reducing clarity. Blood vessels should not be present, though there is sensory innervation to the outer third of the cornea. This innervation is the cause of extreme pain for corneal ulceration. This layer is made of collagen fibrils arranged in a parallel fashion. Stromal replacement occurs after the epithelium works to cover defects. Over time, proliferation of collagen occurs to restore the corneal curvature. Disorganized arrangement upon healing may result in scarring and decreased vision and inflammation leading to vascularization of this layer may also impact vision.

Descemet's Membrane

Descemet's membrane is the basal lamina of the endothelial layer. This layer has mild elastic properties and does not retain fluorescein dye. In health, this layer becomes thicker throughout an animal's life and during corneal healing, endothelial cells are able to produce new Descemet's membrane after several weeks of healing for full thickness injuries.



Endothelium

The endothelium is the last layer consisting of a monolayer of hexagonal cells that do not undergo mitosis. Similarly to the epithelium, this layer is a barrier to the stroma to maintain corneal clarity which is aided by tight cellular junctions. Healing of this layer is accomplished via cell enlargement and migration or sliding. This results in decreased cell density of the endothelium after healing and with age. The endothelium contains Na^+, K^+ -ATPase ion pumps which work to remove fluid from the stroma to regulate its hydration. Thinning or damage of the endothelium can affect clarity as the hydration status of the stroma increases, resulting in corneal edema. Corneal endothelial dystrophy is an inherited condition leading to corneal stromal and epithelial edema. This can cause bullae, painful ulceration, and pigmentation in addition to the edema that reduces clarity and vision. Similar sequelae can be observed in older dogs that develop corneal epithelial degeneration as this corneal layer thins with age.

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Conditions Commonly Related to a Reduction in Canine Corneal Health

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Corneal health starts at the adnexa of the eye. Every eye exam should begin with a thorough gross examination of the patient at rest, along with appropriate preliminary diagnostics. Good eyelid conformation, as well as appropriate tear production and quality, are crucial for the lasting health of the cornea. There are many breed related conditions, especially in the dog, that should be addressed by a veterinary ophthalmologist early on for treatment to prevent the development of corneal damage and promote the lasting health of the cornea. The following are some examples of such conditions:

Keratoconjunctivitis Sicca (KCS) is a quantitative tear film deficiency disorder that is most commonly seen in dogs as an immune mediated condition. KCS can also be neurogenic, drug-induced, or secondary to systemic disease, such as distemper or other metabolic diseases, such as hypothyroidism, diabetes mellitus, or Cushing's disease. This is a common disorder diagnosed in dogs, which is why it is crucial to perform a Schirmer Tear Test (STT) on every patient presenting with an ocular complaint. In a normal dog, a STT should exceed 15mm in 60 sec. Diagnosis of KCS is based on a STT of <10mm/min; however, a STT of 11-14 mm/min is suspicious of the disorder. Clinical manifestations of KCS include conjunctival hyperemia, mucoid to muco-purulent discharge, keratitis, blepharitis, and even corneal ulceration. Patients with underlying systemic disease, such as diabetes mellitus, are at an even higher risk of developing severe corneal ulceration due to presence of decreased corneal sensitivity in addition to KCS. Therapy for KCS includes lacrimostimulants (i.e., Cyclosporine A or Tacrolimus), lacrimomimetics (i.e., HA containing ophthalmic ointments), prophylactic antimicrobials, mucinolytic agents (i.e., Acetylcysteine), and anti-inflammatories (i.e., topical steroids, if no concurrent ulceration is present). The use of tear replacement ointments

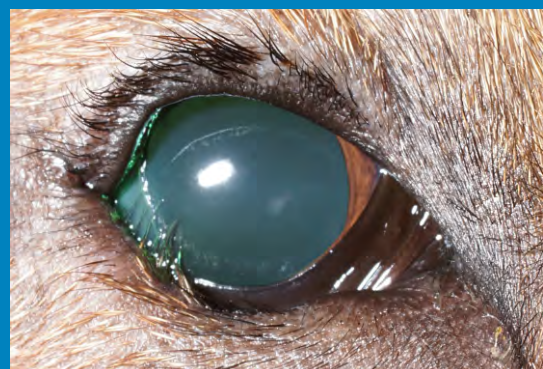
containing HA or cross-linked HA can be helpful in the prevention of severe corneal ulcerations in these cases, especially during the initial four weeks of treatment due to the delayed onset of action of the lacrimostimulants. Severe cases, such as neurogenic KCS or cases which are refractory to medical management, may ultimately require a Parotid Duct Transposition in order to maintain appropriate lubrication of the cornea to prevent the development of severe corneal ulcers secondary to KCS.

Euryblepharon (aka Macropalpebral Fissure) is a congenital condition where the eyelid fissure is larger than normal and causes increased scleral exposure. This condition is commonly seen in both large breed dogs and small brachycephalic dogs. Euryblepharon is commonly associated with lagophthalmos, pigmentary keratitis (brachycephalic dogs), and entropion/ectropion (large breed dogs). In canines, the length of the eyelid fissure when stretched should measure approximately 33 mm. For the diagnosis of euryblepharon, the fissure will measure 5 to 15 mm longer. Referral to a veterinary ophthalmologist is recommended for evaluation and surgical correction, which might involve a medial and/or lateral canthoplasty, keeping in mind that other more extensive blepharoplasty procedures might be indicated depending on the severity of the condition. Eye lubrication with HA-containing ophthalmic ointments can be helpful in the management of severe cases, or cases where lagophthalmos is present, until the condition is able to be surgically corrected.

Ectropion is a developmental condition where the eyelid margin is everted. This condition is most commonly seen along the inferior lid and is often diagnosed in large and medium breed dogs with accompanying secondary euryblepharon or canthal ligament laxity. Ectropion can also be an

acquired condition often caused by other disease processes such as facial nerve paralysis, scar tissue formation secondary to previous trauma, or overcorrection from a previous entropion surgery. Ectropion predisposes the cornea to exposure keratitis, which can ultimately lead to corneal ulceration. Referral to a veterinary ophthalmologist for evaluation and appropriate surgical correction is recommended.

Entropion is most commonly a developmental condition where the eyelid margin is inverted, potentially leading to secondary trichiasis, blepharospasm, epiphora, enophthalmos, secondary conjunctivitis, and ulcerative keratitis. Entropion is frequently seen in young, large breed dogs secondary to their eyelid conformation; however, it can also be an acquired condition secondary to marked blepharospasm. Entropion arises due to excessive eyelid length (i.e. euryblepharon), lack of support of the eyelids by the globe (i.e. enophthalmos, microphthalmos, phthisis bulbi), excessive skin on the forehead and subsequent upper lid ptosis, and increased tone of the orbicularis oculi muscle (i.e. spastic entropion). Referral to a veterinary ophthalmologist is recommended for evaluation and surgical correction via the Hotz-Celsus surgical technique, and/or more extensive blepharoplasty procedures depending on the extent of the condition.



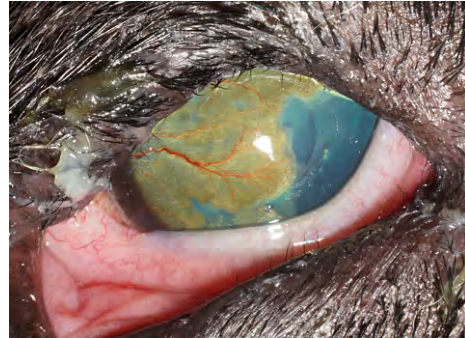
Puppies can also develop a transient entropion during growth. The use of temporary tacking sutures can be utilized to save the cornea while they are growing. Permanent procedures are recommended if the entropion persists once they are full grown.

Trichiasis is a developmental condition where the eyelid hairs, or facial hairs, are abnormally positioned towards the cornea. This is especially common in brachycephalic breeds. Clinical manifestations include epiphora, pigmentary keratitis, chronic conjunctival hyperemia, and occasionally corneal ulceration. For severe cases, referral to a veterinary ophthalmologist is recommended for evaluation and appropriate surgical correction depending on the type of trichiasis that is present. Some less severe cases may be able to be managed successfully with the long-term use of eye lubrication using HA-containing ointments and proper grooming.



Distichiasis is a condition where there is abnormal growth of cilia through the meibomian gland openings of the eyelid margin. It is one of the most common inherited eyelid diseases in the dog and can involve both the upper and lower eyelid, and can be a unilateral or bilateral disease. Distichiasis can be difficult to appreciate without

the use of biomicroscopic examination. Some of these cases can be subclinical; however, if there is resulting keratitis, then referral to a veterinary ophthalmologist for evaluation and potential cryoepilation or electroepilation of the abnormal cilia is recommended.



Ectopic Cilia is a condition where there is abnormal growth of cilia through the palpebral conjunctiva. Ectopic cilia can appear on the superior or inferior eyelid and can involve one or both eyes. Clinical manifestations include blepharospasm, increased blink rate, epiphora, and are commonly associated corneal ulceration. Diagnosis of this condition can be challenging and requires the use of biomicroscopic examination. Treatment includes referral to a veterinary ophthalmologist for en-bloc resection +/- cryotherapy of the abnormal cilia due to the high likelihood of corneal ulceration and ocular pain that they can cause.



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Hyaluronic Acid: Can We Use This To Better Canine and Feline Corneal Health?

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What is it:

Hyaluronic Acid (HA) is found in many commercial topical tear film replacement therapies. It is a high molecular weight glycosaminoglycan that is naturally occurring in the body that helps support the wound healing process. HA has been found to have ameliorative effects in cases of keratoconjunctivitis sicca (KCS)¹. HA-containing artificial tear products can recreate the viscous nature of natural tears due to its mucus-adhesive properties, while at the same time containing properties that facilitate the natural blinking process¹. Ultimately, HA helps stabilize pre-corneal tear film and improves corneal hydration and lubrication. HA has also been shown to stimulate corneal epithelial cell migration and adhesion²⁻⁴.

Why cross-linked HA: The main limitation of non-cross-linked HA containing tear replacement therapies is the frequency at which owners need to apply the medication (4 to 6 times daily) in order to achieve an appropriate response to treatment. It has been found that cross-linked HA formulations have increased the amount of time HA exists on the cornea, thus leading to the same benefits that regular HA solutions provide, with the added benefit of decreased dosing frequencies^{5,6}. Cross-linked HA has also been found to aid in the faster healing of some corneal ulcers when compared to non-cross-linked HA⁷⁻⁹. This added benefit of cross-linked HA makes these types of tear film replacements superior when choosing between a product to use for patients with existing corneal damage.

How does it work:

Cross-linking is a chemical strategy that links HA molecules to one another, creating a polymer network. This process extends the retention properties of HA and decreases its susceptibility to enzymatic degradation, which ultimately reduces the number of times it needs to be re-applied to the cornea during the day^{5,6}. The increased tissue scaffolding matrix that is formed secondary to cross-linking is also conducive for re-epithelialization over corneal defects⁷⁻⁹. There have been multiple studies performed evaluating the safety and efficacy of the use of cross-linked HA in both KCS treatment and corneal wound treatment. In one study, evaluating exaggerated dosing in rabbits for 28 days, it was concluded that cross-linked HA is very safe. The same study also evaluated the use of cross-linked HA for treatment of acute ulcer healing in dogs and cats. It was found that acute ulcers treated with cross-linked HA healed significantly faster when compared to those treated with non-cross-linked HA⁹. These findings provide insight that, when used appropriately, cross-linked HA can aid in the healing of certain corneal ulcers due to its properties on epithelial cell migration and adhesion.

Clinical Application:

Lacrimomimetics, such as HA containing ophthalmic ointments, are crucial when it comes to treating patients with KCS, as well as in patients where lagophthalmos, amongst other eyelid disorders, is present. These conditions predispose the cornea to significant ulceration, which sometimes require emergency conjunctival grafting procedures by a veterinary ophthalmologist to save the eye. Applying a tear replacement ointment to the eye throughout the day can help sustain the health of the cornea and help prevent ulcers from occurring. However, owner compliance is important for the efficacy of these medications. Cross-linked HA has shown benefits in both the healing of corneal ulcers, as well as increased owner compliance due to the decreased frequency of application. This type of tear replacement therapy may be a good choice for patients suffering from tear film deficiency disorders, as well as other disorders that predispose the cornea to ulceration.

To learn more about cross-linked HA visit sentrxanimalcare.com



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Understanding Corneal Ulceration

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Corneal ulcers are an erosion or wound on the surface of the cornea resulting in loss of the corneal epithelium. Corneal ulcers can be considered simple or complicated. Simple ulcers involve the corneal epithelium and typically heal within one week's time. Complicated ulcers are defined by an ulcer that involves the stroma, persists for over one week, or becomes infected.

Diagnosing a corneal ulcer

Determining the etiology for corneal ulcerations is important for guiding the treatment plan. A full ophthalmic examination should be performed including Schirmer tear testing, fluorescein staining, and close assessment for adnexal abnormalities, palpebral fissure size, globe movement and position, trauma, or foreign material.

Cranial nerves (CN) should also be tested to evaluate blink response (CN V and VII) and if the affected eye is visual and light responsive with menace and pupillary light reflex (PLR) testing (CN II and III). If a primary cause is noted for the ulcer, it will likely increase the risk of the ulcer becoming complicated or indicate the need for referral for additional therapeutic procedures in the future (i.e. adnexal surgery, diamond burr

debridement, dry eye management, conjunctival grafting).

Careful attention to fluorescein stain uptake patterns will also indicate if referral is necessary. Superficial ulcers have distinct borders and show positive stain uptake on the “floor” of the ulcer. As ulcers become deeper, the walls will have positive stain uptake with occasional diffusion into the nearby stroma, creating less distinct margins. Continuing to progress, descemetocelae will not stain at the center of the ulcer, though the stroma surrounding the defect will show positive stain uptake.

An ulcer at any depth should be examined for possible infection. Signs of infection can be as mild as a subtle yellowish green discoloration surrounding the defect to loss of rigidity of the corneal surface resulting in a dissolution of the stroma ventrally (melting corneal ulcer).

Simple ulcers

If no persistent inciting cause is found, or is removed (i.e. superficial foreign material), treatment may be initiated for simple, superficial corneal ulcers. Broad spectrum topical antibiotics every 6 hours (neomycin, polymyxin

B, bacitracin), pain relief via topical atropine once daily, oral pain medications (NSAIDs or gabapentin), tear stimulants if warranted, hyaluronic acid tear supplements, and an E-collar to prevent self-trauma.

Re-evaluation is recommended within 5-7 days for superficial ulcers or sooner if the owner notes worsening signs at home. If the ulcer is not healed, refer for further evaluation for anatomical abnormalities (ectopic cilia, palpebral fissure size, globe and eyelid conformation), more aggressive medical management, debridement of indolent ulcer, or possible surgery if the ulcer has progressed.

Complicated ulcers

Referral to a board-certified ophthalmologist is recommended for deep stromal ulcers, descemetocelles, and melting corneal ulcers. Referral will allow for closer monitoring and aggressive care including collecting samples for culture and sensitivity to adjust medical management as the ulcer is monitored if surgical intervention is not initially warranted. Surgical intervention is beneficial for stabilizing stromal ulcers affecting greater than half of the corneal thickness, descemetocelles, melting corneal ulcers, or already perforated globes. Perforation can be identified by visualizing synechia in the anterior chamber involving the defect or bulging of the iris (iris prolapse) as it aids to plug the corneal defect. These lesions are intricately repaired with various corneal grafts using surgical microscopes.

Owners should be counseled on the risks for rapid progression if treating complicated ulcers medically. Follow up should be scheduled within 24-48 hours of initiating aggressive treatment to monitor for corneal perforation. Antibiotics with additional gram negative and bactericidal coverage (fluoroquinolones, cephalosporins, aminoglycosides) should be used in complicated ulcers.


Application every 2-4 hours for very deep ulcers in the initial 24-48 hours is recommended along with avoiding ointments due to the risk of uveitis if corneal perforation occurs. Anticollagenase products should also be added to this protocol. Topical serum every 2-4 hours acts locally to prevent the proteolytic properties of bacteria while oral doxycycline (10mg/kg/day) acts systemically for its antibiotic, anti-inflammatory, and anti-collagenase properties. Both will act to prevent worsening infection and a melting corneal ulcer. Hyaluronic acid containing tear supplements can also be used to improve healing.

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Bacterial Culture Results From Bacterial Ulcerative Keratitis

Researchers designed a study to compare aerobic bacterial culture results between samples obtained from the corneal ulcer versus lower conjunctival fornix in eyes with presumed bacterial ulcerative keratitis. The study evaluated 55 client owned animals with ulcerative keratitis diagnosis. Microbial swabs were collected by direct sampling of the infected corneal ulcer as well as the lower conjunctival fornix, of the same eye, using a sterile rayon-tipped swab. Samples were submitted to an outside reference laboratory for aerobic bacterial culture and sensitivity.

Results:

One hundred twelve samples were obtained.

Sixty-eight samples yielded bacterial growth.

Positive growth from both sites was obtained in 31 eyes (55%).

Six eyes yielded bacterial growth from the conjunctival fornix but not from the cornea.

No bacterial growth was obtained from either sampling site in 19 eyes.

Fifty-five percent of corneal samples were positive while 66% conjunctival fornix samples were positive.

Twenty different bacterial isolates were obtained from 68 positive samples with Gram-positive (71%) organisms were more common than Gram-negative (29%).

The most commonly isolated organisms were *Staphylococcus pseudintermedius* (25%), *beta-hemolytic Streptococcus* spp. (23%), and *Pseudomonas aeruginosa* (12%). Methicillin-resistant organisms were isolated in 9% of samples.

Read more by clicking on the link below:

[Comparison of bacterial culture results collected via direct corneal ulcer vs conjunctival fornix sampling in canine eyes with presumed bacterial ulcerative keratitis.](#)

Exophthalmos is the term used for a forward deviation of the eye out of the bony orbit. The most common causes of exophthalmos will affect one rather than both eyes, although there are a few conditions which can affect both eyes. There are many structures near the eye and orbit including muscles, salivary glands, tooth roots, bone and nerves, and abnormalities or inflammation of these tissues can affect the positioning of an otherwise normal appearing eye.

Small animals with exophthalmos will present with a forward deviation of the eye. This condition can commonly be confused with proptosis, or a sudden forward displacement of the globe with an entrapment of the eyelids behind the eye. Pets with exophthalmos most often have a slow progression of clinical signs and change in the appearance of the eye and affected side of the face. Small animals with exophthalmos may or may not be painful around their face and mouth depending on the underlying cause. There may be inflammation of the conjunctiva and other tissues surrounding the eye and orbit and the third eyelid may be raised. If the condition is progressed, a pet may not be able to fully blink their eyelids leading to corneal ulceration and irritation. Depending on the cause of exophthalmos, animals may demonstrate systemic signs of illness such as decreased appetite, fever and lethargy.

Possible causes for exophthalmos in dogs and cats include infection or inflammation behind the eye, inflammation of the salivary glands or muscles, and tumors of the orbit. Small animals can develop abscesses behind the eye due to foreign material, trauma or bite wounds which introduce bacteria under the skin, or advanced dental disease. Certain infections can also travel to this area through the blood stream, causing inflammation behind the eye. Inflammation of the muscles surrounding the eye (myositis) can occur with certain infectious

Exophthalmos In Pets

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diseases and can also be due to an inherited condition (extraocular muscle myositis or masticatory muscle myositis). Many of these conditions will cause discomfort to a pet when trying to eat or when the affected side of their face is touched. Cancer of the tissues surrounding the eye, nasal sinuses and mouth can also lead to an abnormal position of the eye.

Based on an animal's history of progression, clinical symptoms, any known traumatic event and other history, a number of tests may be recommended. It can be important to identify the underlying cause of exophthalmos to provide the best medical care and to assess prognosis for the pet. Systemic blood work and blood or urine fungal testing may be recommended. Abdominal ultrasound and chest x-rays are useful if a cancerous cause or fungal disease is suspected. Advanced diagnostic imaging such as a CT scan is oftentimes advised to better understand the cause of exophthalmos, but also to evaluate the extent or size of abnormal tissue.

Oral antibiotics and anti-inflammatory medications are commonly used for treating orbital abscesses and inflammatory conditions. If salivary gland swelling or an abscess is considered likely, surgical drainage and sampling of fluid for analysis can help in diagnosis and guide the doctor in forming the appropriate treatment plan. If diagnosed, fungal diseases require oral antifungal therapy and close monitoring for response to therapy. Topical lubricants are used to protect the eye from drying due to decreased blinking. Additional treatment for a corneal ulcer may also be needed. If a tumor is suspected, consultation with an oncologist is most often recommended to discuss different treatment options or pain management after diagnosis. Feeding soft foods is recommended if a patient shows discomfort

when eating and warm compresses can provide additional comfort.

Pets with many inflammatory conditions can regain normal comfort and position of the eye long term. It is important that any animal with exophthalmos receive an eye exam to determine the most likely cause and best course of action.



About the author



Dr. DJ Haeussler received his DVM from the Ohio State University. He then went to New Jersey where he finished two internships at Garden State Veterinary Specialists and then returned to his alma mater, The Ohio State University to complete his residency.

While at Ohio State University for his residency, he completed a Master of Science degree and earned the top award for professional student research at Ohio State as well as the top resident award for professional research at the annual American College of Veterinary Ophthalmologists (ACVO) in 2010.

Dr. Haeussler is a board certified diplomate of the American College of Veterinary Ophthalmologists (ACVO). Dr. Haeussler also serves on the ACVO Public Relations committee as the committee chair and is a member of the Cincinnati Veterinary Medical Association Board of Trustees.

He currently owns and operates The Animal Eye Institute in Ohio and Kentucky.