

Corneal Ulcers

Ulcers represent the most common ophthalmic disease in dogs and cats as well as most species. Treatment of an ulcer depends on the underlying causes, presence or absence of bacterial, viral, or fungal infections, presence or absence of eyelid and tear film abnormalities, risk to the structural integrity of the globe, and temperament of the patient.

The signalment and history of the patient can often point you in the direction to the cause of the ulcer. While trauma is a common cause, the vast majority of ulcers referred to a ophthalmologists are not the direct result of trauma, but due to the presence of other eye abnormalities that led to the development of an ulcer.

Signalment. The age, breed, and to some degree sex of an animal can help ascertain the underlying cause of an ulcer and alert the clinician to look for problems associated with specific breeds. When you pick up an animal's record before entering the room, keep these points in mind:

Age

a. Neonates - think infectious disease, especially in cats as herpes virus infection and Chlamydia infections are often more severe and more likely to cause corneal ulceration in a younger animal.

b. Juveniles. Juvenile animals are more likely to make a bad decision and traumatize their eye. The 2 to 4 month old puppy with an acute ulcer may have just meet the cat. In-coordination of youth can lead to running into the holly bush or other unintentional traumatic diseases of the cornea. This is especially true in horse.

c. Young adult. Ulcers in 6 month to 18 month old animals are often associated with eyelid abnormalities. Distichia, ectopic cilia, and entropion often present as corneal disease in this age group. Juveniles can also experience problems with these inherited disorders. With the exception of macropalpebral fissure syndrome, most eyelid abnormalities manifest clinical problems during the first few years of life.

d. Middle aged. Traumatic ulcers are less common as animals mature. They are wiser and more coordinated and make fewer bad mistakes. However, corneal exposure in brachycephalic dogs, dry eye, and metabolic diseases such as corneal lipid dystrophy's are more common in middle aged animals.

e. Geriatric animals. After juvenile animals, geriatric dogs have the highest prevalence of corneal ulcers. Spontaneous indolent or refractory ulcers are common and rarely occur in animals less than 8 years of age. Ulcers secondary to corneal degenerations occur commonly in dogs older than 14 years.

Breed

a. Brachycephalic breeds - Corneal ulcers secondary to exposure, poor blinking, relative dry eye, and trichiasis are common in brachycephalic dogs and cats. Ulcers in these breeds often are slower to resolve as well and we need to keep their poor ability to protect their eye in mind when determining the appropriate therapy.

b. Indolent or Refractory ulcers. This type of ulcer can occur in any breed, but boxers and retrievers are over represented and predisposed.

c. Certain breeds are prone to other ocular diseases that lead to ulcers such as entropion (Shar Peis, chows, Rottweilers, retrievers, std poodles, etc) distichia (Retrievers, boxers, weimaraners, cocker spaniels, Jack Russell terriers, Old English bull dogs etc) ectopic cilia (Retrievers, boxers, weimaraners, cocker spaniels, Jack Russell terriers, Old English bull dogs, poodles) or dry eye (all brachycephalic dogs, cocker spaniels, westies and cairn terriers, Old English Bull dogs, etc).

History. The etiology of many ulcers can be ascertained simply by knowing the signalment and an obtaining accurate history. Many owners assume the ulcer was the result of a traumatic episode. While clearly eye trauma is a common cause of ulceration, it likely the underlying etiology in only 50% of patients. Critical aspects of the history include:

a. Duration of signs. Is this an acute change as expected with a traumatic lesion, or have the clinical signs waxed and waned and resolved only to recur suggesting an eyelid abnormality or tear film deficiency.

b. Did the young dog yelp and suddenly run into the house, and the cat had a sheepish look on its face. Most sharp traumas result in immediate severe discomfort that improves. Most minor traumas or exposure and tear problems result in subtle discomfort that progressively becomes worse over days as bacteria grow at the ulcer site.

c. Has the patient had similar problems in the past. He had the same problem last year at this time - refractory ulcers in older patients are often seasonal as can be intermittent dry eye. Herpes virus recrudescence is also seasonal in some cats. A history of recurrent problems for several months in a younger dog suggests an ectopic cilia or other eyelid problem.

d. Recent trip top the groomers - chemical irritants to the cornea often result in slow to heal refractory ulcers and clinical sign often develop within hours of being groomed. Owners are quite sensitive to squinting post coming home form the groomer.

e. Other systemic disease problems.

Dry eye occurs with a higher prevalence in dogs with atopy. Often, acute dry eye associated with a change in environment (such as boarding) is due to an acute allergic reaction to something in the new environment leading to inflammation in both dermal sweat glands and also lacrimal glands - the result is sudden severe ulcers, often in both eyes.

Hypothyroidism - both corneal lipid deposits with secondary erosions and dry eye are more common in dogs with hypothyroidism

Diabetes mellitus - cats with diabetes mellitus can develop very slow to heal non-infected epithelial ulcers.

Recent upper respiratory problems - in cats this is a strong sign that the cat may have recrudescence herpes virus, or herpes virus, or then again herpes virus. Over 90% of all cats have this virus.

Renal insufficiency - transient severe dry eye due to dehydration in older animals with renal disease is common, especially in cats.

Otitis externa - facial nerve paralysis secondary to severe otitis or spontaneous Bell's palsy can lead to corneal ulcers.

Recent anesthesia - atropine associated dry eye or post anesthesia exposure from not blinking (ketamine) can result in ulcers.

Osteoarthritis - dry eye related to etogesic use in older dogs does occur and usually presents as corneal ulcers.

Exam Findings. When entering the room to examine the patient, it is important to develop a constant systematic approach to examining the eye. This helps prevent overlooking problems contributing to the formation of the ulcer.

a. Overall Attitude of the dog. Take to to simply observe the dog before jumping right into your eye exam. Note if the dog squinting in the room or holding the eye open. What is the level of discharge from the eye and is it mucoid or serous. Is there an obvious defect in the surface of the cornea that you can see from across the room and is the eye cloudy.

b. Directly visualization of the eye and cornea with a strong light source in a dimly lighted room. Decreased light levels will make the patient more comfortable and allow you to visualize the eye better. Note the following:

Is there an obvious stromal defect in the cornea or foreign material (brown iris, brown sequestrum, blood or fibrin) on the surface of the eye.

Is there is clotted blood, protruding fibrin, or tissue raised form the surface of the cornea - if so proceed with CAUTION as you likely have a perforated globe.

What is the size of the pupil, miotic or dilated?

Did the pupil become smaller when exposed to your strong light source

Did the patient exhibit a dazzle reflex with the light.

Is the patient squinting? If not, make sure he can blink - no facial nerve paralysis.

Remember, a standard ulcer should have a normal to smaller pupil and still have a normal to exaggerated dazzle reflex.

Is there blood or fibrin inside the eye - these are signs that the globe received either a penetrating wound, severe blunt trauma, or has ruptured.

Is there a mountain of white creamy cells (hypopyon) at the ventral aspect of the eye - this indicates a severe, often gram positive corneal infection, but not necessarily an intraocular infection.

How much corneal edema is present - aggressive bacterial infections often cause rapid and wide spread edema.

c. Schirmer Tear test. Dry is still a leading cause of ulcers in dogs. Unfortunately, ulcers are a strong stimulus to produce tears and therefore, tear levels may be normal by the time the patient present to you. If there is mucoid discharge, or evidence of corneal vascularization or pigment in an acutely ulcerated eye, perform a Schirmer tear test. DO NOT perform a Schirmer tear test in a perforated eye or in an eye with marked clear ocular discharge.

d. Give the patient topical proparacaine. Now make your patient more comfortable before going on. Once you have either performed a Schirmer tear test or decided that one is not needed, give the patient some pain relief. Repeat your examination as listed in b. in greater detail. This is not only great temporary pain relief for the patient but it is diagnostic. Dogs with non-perforated ulcers will have almost complete resolution of blepharospasm 2 to 5 minutes after receiving topical proparacaine. If topical anesthetic does not improve comfort, look for a possible perforation or the presence of other intraocular disease. Secondly, by improving the patients comfort, you can more easily perform a detailed diagnostic exam.

e. Administer fluorescein dye. Fluorescein is a water based dye. The hydrophobic epithelium prevent uptake of the dye by the hydrophilic corneal stroma. Loss of epithelial cells leads to dye uptake. There are several important points when interpreting corneal dye retention

Use MINIMAL dye (1 to 2 drops off the end of a paper fluorescein strip wetted with eye wash)

Rinse thoroughly. Fluorescein nonspecifically will pool in the tears or stick to mucous.

True epithelial and stromal ulcers typical stain BRIGHT green. Mild green stippling can simply indicate a rough area in the corneal epithelium from previous scar tissue or recent tonometry.

Fluorescein dye can lie!!!!!! Not all ulcers will retain fluorescein. Descemetocelles do not as Descemet's membrane is not water soluble. Melting ulcers or ulcers with marked corneal degeneration will not retain fluorescein poorly, ulcers associated with corneal sequestrums do not as the sequestrum represents dead collagen and does not retain fluorescein, and corneal erosions or punctate ulcers associated with herpes virus often are so small that without significant magnification they are not visible.

Important rule of thumb. Do not use topical corticosteroids just because the cornea was fluorescein negative. Especially if the patient was much more comfortable after topical proparacaine. The latter indicates some form of erosive corneal disease is likely present and corticosteroids could inhibit resolution of epithelial defects and clearance of infectious organisms. Leads to sequestrum formation in cats with herpes virus infections.

f. Assess the depth and diameter of the ulcer and its relative location. These parameters are critical in determining the appropriate course of action. Large diameter ulcers or deep stromal ulcers represent a severe risk to the eye whereas shallow smaller ulcers and ulcers near the limbus are less vision threatening.

g. Examine the adnexa. Search the eyelids for evidence of entropion, distichia, or ectopic cilia. The latter can be difficult to identify. Use the ulcer as a guide. Critically evaluate the upper and lower eyelid sections that pass over the ulcer when the patient blinks. This is likely the location of any offending hairs.

Treatment plan. Now that we have established the etiology of the ulcer, the depth and severity of the ulcer, and the likelihood of an infectious process, we can formulate a treatment plan. We have several goals in treating the ulcer:

- Prevent structural loss of integrity of the globe - prevent rupture or repair rupture if present.
- Resolve any underlying causes
- Resolve any contributory infectious diseases
- Improve the patient's comfort
- Minimize scar tissue development and maximize corneal clarity.

a. Structural integrity - when is surgery needed? Surgical repair of corneal ulcers is used to strengthen the cornea and prevent rupture, remove infected and/or degenerative tissue, and help eliminate bacterial or fungal infections by bringing a blood supply to the cornea.

The deeper the ulcer and the larger the diameter the more likely the cornea is to rupture. In general, ulcers greater than 1/2 depth are at risk of rupture. In addition, rapidly meting or rapidly progressing ulcers often will require surgery to prevent loss of the eye. It is important to monitor ulcers closely. Many ulcers will continue to lose corneal tissue for 48 hours after successful initiation of antibacterial therapy. Proteases released by neutrophils, macrophages, and dying bacterial lead to collagen lysis and liquefaction. Ulcers with marked cloudiness (cellular infiltrates) around the ulcer or severe edema are at risk for significant tissue loss even with appropriate antibiotic therapy.

Methods of surgical repair include various conjunctival grafts, xenogenic freeze dried collagen, frozen corneal allografts, sliding or free autografts, and fresh allografts. The type of surgery performed depends on the depth location and infected status of the ulcer. Perforated ulcers benefit from both structural grafts such as collagen grafts and frozen allografts in combination with rotational conjunctival grafts. The latter brings a blood supply to the ulcer to help both clear infectious agents as well as build new collagen and repair the ulcer.

The benefits of surgical repair include an exceptionally high success rate, rapid decrease in discomfort, prevention of globe rupture, and rapid resolution of bacterial and fungal infections. Proper magnification (5 to 10 x), the use of appropriate suture and needle sizes (8-0, 9-0, and 10-0 vicryl or dexon) on spatula needles (cutting and taper needles leave large holes in the cornea and allow fluid leakage) and proper preparation of the graft to maintain good blood flow and minimize tension are the keys to successful surgical repair.

The down side of surgical repair includes cost, the need for general anesthesia, and the potential for increased fibrosis and scarring.

Nictitans flaps have been commonly used in veterinary medicine to help protect the cornea as it heals. This technique is useful in non-infected shallow ulcers in dogs with corneal exposure or eyelid abnormalities. Be careful, nictitans grafts are NOT recommended for infected ulcers or deep ulcers as they can decrease antibiotic administration into the eye and prevent visualization of the ulcer. Nictitans grafts provide no structural support to the globe. In reality, the use of artificial tears and adequate corneal lubrication are as beneficial and safer than a nictitans flap in many cases.

b. Topical Antibiotic therapy. Antibiotic therapy is often initially chosen based on empirical findings. Bacterial culture and sensitivity testing is useful for determining proper antibiotic use. However, for the eye several drawbacks exist. Rapidly progressing ulcers can progress significantly before the results of testing are

available. The eye is not normally sterile and it is difficult to harvest sufficient bacteria from the ulcer with normal culturettes. This leads to false negative results or simply growth of normal conjunctival flora. Lastly, standard sensitivity testing is based on inhibitory concentrations obtainable in blood. With topical medication, significantly greater antibiotic levels are obtainable.

Triple antibiotic is still an excellent first choice. It has a broad spectrum of activity and is relatively safe. Beware that fatal anaphylactic shock to triple antibiotic solution has been reported in cats. Give the first drop while in the office and observe the cat for one hour. Melting ulcers caused by *Pseudomonas* and *Aeromonas* species and many species of *E. coli* are best treated with aminoglycosides such as tobramycin and gentocin. Erythromycin has excellent activity against staphylococcus and several gram positive species. Topical fluoroquinolones such as ciprofloxacin and ofloxacin have the benefit of broad activity and good penetration. However, they are topically irritating and are not as good as aminoglycosides against *Pseudomonas*. Fluoroquinolones are good secondary or tertiary choices. Chloramphenicol has good corneal penetration, but this is a minor benefit as bacteria are present predominately at the surface of the ulcer. Chloramphenicol's main drawback is that it is static and not bacteriocidal. Topical tetracycline is effective against *Chlamydia* and some mycoplasma species. However, it can cause significant irritation. Beware of tetracycline conjunctivitis in cats where their ocular disease persists simply due to continued use of tetracycline.

c. Systemic antibiotics. Normally systemic antibiotics reach the tear film and intraocular fluids in low concentration. However, in the presence of vascular leakage associated with the presence of inflammation greatly enhances their penetration into these fluids. Therefore, oral antibiotics are often useful when treating severely infected ulcers, deep ulcers, and vascularized corneal abscess. This level of therapy is not required for standard epithelial ulcers. Systemic zithromycin is highly effective against chlamydia.

d. Anti-collagenases. Loss of corneal tissue is a major complication of corneal ulcers. Blocking proteases released from leukocytes and bacteria helps prevent continued collagen loss. Serum has potent anti-proteases and can be used as an eye drop (use straight and keep in the refrigerator - throw out after 72 hours). Bacitracin topically has excellent anti-protease activity as does doxycycline systemically. Acetylcysteine has moderate anti-collagenase activity as well as 5% EDTA solution as it binds cations required by many proteases. Serum is the most convenient and one of the most potent collagenases. Anti-collagenases are predominately helpful in melting ulcers and ulcers with marked degeneration. Such therapy is not required for standard epithelial ulcers and offer little to no benefit. Similarly, descemetocelles have already lost their collagen and therefore anti-collagenase activity is of minimal help.

e. Pain management. Systemic narcotics and NSAIDs offer excellent relief from ocular pain associated with ulcers. They are far more potent than atropine or topical NSAID therapy. However, the latter are certainly also beneficial. Topical non-steroidal anti-inflammatory medications including flurbiprofen, Diclofenac Sodium 0.1%, and Ketorolac Tromethamine 0.5% are beneficial in reducing inflammation associated with an ulcer and the level of pain. However, they have several drawbacks. They can cause topical irritation due to their carriers, and decrease clearance of bacteria and fungi. While NSAIDs do not inhibit corneal epithelial growth and fibrosis to the level that corticosteroids do, NSAIDs can significantly hamper the clearance of bacteria. **THEREFORE, IT IS NOT RECOMMENDED TO USE TOPICAL NSAIDS IN THE FACE OF INFECTED ULCERS.**

Atropine is a commonly used and misused drug. It blocks ciliary muscle spasms that can contribute to the discomfort associated with an ulcer. It does not directly decrease corneal pain. There are several important points of using atropine correctly:

- Atropine is NOT beneficial if the pupil is not smaller in the affected eye. If the pupil is the same size or larger, there is unlikely to be significant ciliary body spasms.
- Atropine lasts 3 to 20 days after a single administration. Give one time in the office. DO not dispense to go home
- NEVER give atropine if you have not measured the intraocular pressure in the eye. Atropine can severely raise pressure in an eye with the potential for glaucoma and lead to rapidly blindness in dogs with acute glaucoma. Again, NEVER give atropine if you do not know the pressure in the eye.
- Hyper-salivation - particularly in cats. This combined with central nervous system side effects such as agitation and restlessness can cause more discomfort than the ulcer.
- Photosensitization from pupil dilation causes discomfort.
- Decreased tear production. Atropine can cause profound decreased tear levels for several days and further compromise healing of an ulcer.

f. Adjunct therapy. Other therapies can help resolve ulcers.

- Grid or multipunctate keratoplasty. Refractory ulcers in older dogs are associated with a layer of degenerative acellular collagen on the surface of the cornea. Cutting grooves in this degenerative layer by performing a grid keratoplasty exposes the healthier collagen below and help epithelia cells adhere to the surface.

GRID KERATOPLASTY IS ONLY BENEFICIAL IN REFRACTORY ULCERS IN OLDER DOGS.

Performing a grid procedure in ulcers associated with eyelid problems is not beneficial. Grid keratoplasties have minimal benefit in cats, and a grid procedure will cause an infected ulcer to rapidly worsen.

- Topical viscous mucin like artificial tears. Specific high quality tear replacers such as hylashield and occult can both decrease discomfort and help protect epithelial cells from the shear forces associated with blinking.

- Topical Adequate. This mucopolysacchride has been reported to speed the healing of refractory ulcers. useful???

- Contact lens and Collagen shields. These can help both improve comfort and help protect epithelial cells when treating refractory ulcers. They are also useful in ulcers associated with eyelid abnormalities. They offer minimal help for deep or infected ulcers even when saturated with antibiotics.

Follow up. Uninfected epithelial ulcers should resolve in 2 to 5 days. if they do not, then either an eyelid or tear film abnormality is present, the ulcer is refractory (older dogs only) or a resistant infection is present. the latter is actually not common and switching antibiotic therapy is helpful in resolving ulcers in only a small percentages of patients. Eyelid problems and tear film problems are much more common reasons for ulcer persistence. Recheck ulcers in 24 to 48 hours to makes sure rapid corneal degradation is not developing. Signs of improvement include less blepharospasm, decreased discharge, smoothing of the edges of an ulcer, and of

course decreased ulcer diameter. Deepening of an ulcer or increased corneal edema are negative signs and can indicate a rapidly progressing ulcer.