THE TOP TEN OPHTHALMIC MISTAKES

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INTRODUCTION

There are several 'mistakes' veterinarians make in diagnosis and evaluating clinical signs and response to therapy. These errors involve all aspects of ophthalmology from conjunctivitis, corneal, ulcers, glaucoma, cataracts, and blindness. The 'Top Ten' will be presented in the form of the typical statements I get from the owners such as "My veterinarian said…" An example of the case will be illustrated and the 'error' in thinking will be discussed. The "Top Ten" are the most critical and/or common mistakes seen.

Number Ten: "My veterinarian has used five antibiotics ointments and solutions and the ulcer in Butch's (a 9 year old boxer mix) eye isn't any better.

Error: This is usually a dog with a superficial ulcer. These indolent ulcers are caused by a degenerative change and are not bacterial! If it gets better with antibiotics, it is just luck. Surgical treatment i.e. keratotomy with additional topical hyperosmotics are indicated. The owners should be told their dog will never go blind with this disease but can recur in both eyes.

Number Nine: "My veterinarian told me Fifi (3 year old poodle) needs surgery for an undulating ulcer" (owner means indolent ulcer).

Error: Three year old dogs do not get indolent ulcer. If the ulcer is axial, it is most likely due to a decrease tear production. If it is in the superior 1/3 of the cornea, you can start looking for the ectopic cilia. This is common in the poodle, shih tzu, and in golden retriever less than a year of age.

Number Eight: "My veterinarian said Gizmo (4 year old shih tzu) has allergies causing conjunctivitis. Now she has a deep ulcer that may rupture."

Error: In my opinion, dogs do not have allergies that cause only conjunctivitis. However, many breeds have a predisposition to KCS resulting in recurring conjunctivitis that may vary based on circumstances, i.e. outside more in summer and spring. Mild affected cases (STT greater than 10mm/min) will improve with almost any topical solution or ointment that supplies moisture to the cornea. Central corneal ulcers are caused by KCS and/or lagophthalmos. In addition, all these one-eyed pugs didn't get poked in the eye. The pug is a great example of KCS with an associated lagophthalmos.

Number Seven: "My veterinarian says Blackie (10 year old DSH) has an ulcer but the routine antibiotic ointments aren't helping. He has become a part of our family since we got him from the shelter. He is healthy otherwise and doesn't want to leave my side even to go outside."

Error: Any cat from a shelter has an excellent chance of having been exposed to feline herpes virus. This virus can and often does remain dormant for years. Recrudescence is common and can be caused by stress from a number of possibilities. Feline herpes virus is the number one cause of corneal ulceration in cats. Antibiotics are of no value and can make the condition worse. There are specific antiviral drugs for both topical and oral administration.

Number Six: "My veterinarian tells me Buster (2 year old Boston Terrier) has glaucoma. He is really difficult to treat and his red eyes have only gotten worse with these drops." The owner then holds up a green lidded container of 2% Pilocarpine.

Error: Typically, the veterinarian used the Tono-Pen to measure I.O.P. With this instrument, a falsely elevated I.O.P. is a common problem, especially in an animal that is uncooperative. External pressure

on the neck or lids during restraint can easily elevate the pressure to 40mmHg. Pilocarpine frequently causes a local irritation for the first 72 hours. This is manifested by increased blepharospasms, conjunctival hyperemia, and even an anterior uveitis. Concentrations greater than 1% are more irritating and have no significant improvement in hypotensive effect. Users beware!

Number Five: "My veterinarian told me Shadow's (1 year old Siberian Husky) cloudy eye is caused by glaucoma. These really expensive drops are the same ones my mother used but I don't have insurance to pay for them like she does"

Error: Two common mistakes were made here. Phacolytic uveitis is common in the husky and several other breeds. It you measure the I.O.P. in the cloudy eye; it would most likely be below normal. The 'normal' eye also probably has a posterior cortical cataract. Even if the I.O.P. was elevated in the bad eye, it would be a secondary glaucoma and Xalatan® or any other miotic would be contraindicated. It may be time to schedule an enucleation.

Number Four: "My veterinarian said Rex (12 year old German Shepherd) needs cataract surgery. You can see his gray cataract and his eyes glow at night."

Error: The glow is the tapetal reflex. A dog cannot be totally blind due to only cataracts and still have a tapetal reflex. Additionally, a dog blind with cataracts should still have a positive pupillary light response and a positive dazzle reflex (blinks when a bright light is directed into the pupil). The gray appearance of the pupil is normal aging change of the lens termed nuclear sclerosis. They may cause reduced vision for near objects and in bright light.
Most likely, Rex has a chorioretinitis from a multitude of possible etiologies. Systemic hypertension and retinal detachments are good possibilities.

Number Three: "My veterinarian thinks I should wait until Gretchen's (7 year old miniature schnauzer) diabetes is controlled before we treat her cataracts. But now her eyes are all red."

Error: Every diabetic dog deserves a thorough ocular examination immediately or at least at the first sign of cataracts. All diabetic cataracts result in some degree of phacolytic uveitis. Untreated, this develops into a severe anterior uveitis and secondary glaucoma. The glaucoma is usually refractory to medication and requires enucleation, just to make the patient comfortable.

Number Two: "My veterinarian believes Shannon (5 year old golden retriever) has a tumor in the eye and that the eye should be removed."

Error: Golden retrievers, Labrador Retrievers, and Boston Terriers have a high incidence of iris and ciliary body cysts. These appear as free floating translucent pigmented spheres in the anterior chamber or pupil margin. These cysts may rupture and pigment may be deposited in the iris, lens, or cornea. The diagnosis is based on knowing the breed incidence and being able to transilluminate the pigmented cyst.

Number One: "My veterinarian treated Belle's right eye 6 weeks ago with antibiotics and now he is treating the left eye and she is totally blind.

Error: The list of dog breeds with primary glaucoma grows yearly. Any dog with primary glaucoma in one eye should be under the care of an ophthalmologist and on prophylactic treatment in the 'normal' eye. The ultimate 'mistake' is not in enucleating the blind, painful first eye. Dropping the globe in the kick bucket and doing nothing for the remaining eye is the sin. Blind dogs that are comfortable do great! If vision can't be returned in the second eye (poor prognosis at this time), it too should be enucleated or an intraocular prosthesis put in place. Veterinarian and clients do not relate the inactivity

in uncontrolled glaucoma dogs to the chronic pain they suffer. After over 30 years, I am still impressed with how well blind and comfortable dogs function.

KERATOMALACIA IN DOGS AND CATS

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Keratomalacia or melting of the cornea is a severe, usually acute ulcerative condition of the cornea, with an associated anterior uveitis and severe signs of ocular pain. The destruction of the corneal stroma, i.e. collagen fibers and extracellular matrix by protease and collagenase enzymes results in a gray gelatinous appearance to the cornea. The corneal surface becomes irregular and elevated, producing the melting appearance. Irritation to the axons of the trigeminal nerve initiates an axonal reflex and dilation of vessels of the iris and ciliary body and results in the anterior uveitis and aqueous flare.

Many of the bacterial organisms that are associated with keratomalacia also release leukotactic toxins. Chemical mediators, released by damaged cells also cause leukocyte migration. Both reactions may produce hypopyon.

Proteases and collagenases, released in normal corneal healing, are important in remolding of damaged cornea. Melting ulcers develop when these enzymes are produced in excess. Many tissues, including the cornea, contain naturally occurring inhibitors of protease i.e. α-2-macroglobulin and α -1-proteinase inhibitor. The source of the proteases and collagenases may be bacterial, *(Pseudomonas spp* most common), fungal, polymorphonuclear neutrophils, corneal epithelial cells, and fibroblasts.

The proteases may be divided into two groups: matrix metalloproteases (MMP2, MMP9) and serine proteases (neutrophil elastase). MMPs require calcium and zinc as a cofactor and stabilizing ion respectively to be active.

Cases of keratomalacia require aggressive therapy which included topical and sometimes oral antibiotics, anti-protease agents, and treatment for the associated anterior uveitis. Bacterial cultures, regardless of prior antibiotic therapy, are always submitted on presentation. Topical antibiotics are started q2h-q4h. The antibiotics should be effective against Gram-negative rods. Tobramycin or fluoroquinolones (Ocuflox® Allergan, Quixin™ Santen Inc.) are my drugs of choice. Tobramycin is less toxic to epithelial cells and may be the drug of choice initially. If topical treatment is difficult or if the case is severe, oral fluoroquinolones are also used (Zeniquin® Pfizer). Anti-protease agents (Table 1) are institute as well. My product of choice is serum. The serum is taken from a healthy dog not currently on corticosteroids. The importance of the lack of systemic corticosteroids is not clear. The serum should be refrigerated and replaced with fresh serum every 8 days. Fibronectin, found in serum, also reduce the pain associated with keratomalacia and has been referred to as the 'feel good factor'. It has also been suggested that whole blood is more effective but I have not used this. The serum should be applied q2h to q4h. Combining a second anti-protease such as tetracyclines orally or topically in addition to serum may be beneficial.

Duralactin® (distributed by VPL) is a purified milk protein which has been shown to inhibit neutrophil migration and therefore could reduce the release of proteases and cytokines. This drug cannot have any adverse affects.

The associated anterior uveitis is treated with topical 1% atropine once or twice daily and an oral NSAIDS. My choice is carprofen (Rimadyl® Pfizer). Tepoxalin (Zubrin® Schering Plough) has a reported Lox inhibition which may be of added benefit.

This aggressive schedule is maintained for the first 72 hours. If culture results dictate, the antibiotic may be changed. If the keratomalacia leads to an impending corneal rupture, surgery i.e. conjunctival flap may be indicated.

CAPNOCYTOPHAGA

An unusual etiology for keratomalacia has been identified in dogs that share a common history of long term antibiotic and corticosteroid therapy for various diseases including KCS and phacolytic uveitis among others.

These individuals are presented with acute keratomalacia. Prior to presentation, they were previously well controlled. The etiologic agent of 'dog bite sepsis', *Capnocytophaga, sp.,* has been isolated from severe corneal ulcerations in the canine. This thin, gram-negative rod has a characteristic and distinguishing long fusiform appearance. The organism is a facultative anaerobe and grows best on blood agar in a 5%-10% CO2 environment. Colonies on blood agar are non-hemolytic but often pit the agar. Growth on the plate may take 2-4 days to form a flat, spreading pattern with irregular edges. If a portion of the colony is removed with a spatula, it has a yellow coloration. All of these findings separate the organism from other gram-negative rods but biochemical tests can positively identify this bacterium. There are three species that are found in the oral cavity of man and these are the leading cause of periodontal disease in teenagers. *C. canimorsus and C. cynodegmi* may be found as part of the oral flora of dogs and cats. These species are the etiological agent of dog bite sepsis, a potentially life-threatening disease in especially the immunocompromised patient. Isolates to date have not been speciated. Therefore, we do not know if the organism originated from human or canine contaminant. The drugs of choice are penicillin V potassium, amoxicillin, clindamycin, erythromycin, ciprofloxacin, and imipenem.

These cases are treated topically the same as keratomalacia which is described above. Erythromycin is applied every 2-4 hours initially, along with fluoroquinolones. Clindamycin is given orally and the prior ocular disease must also be concurrently managed.

Table 1 Anti-Protease Drugs

Compound	Inhibitory Activity	Inhibitory Mechanism
Serum α-2-macroglobulin α -1-proteinase inhibitor	MMPs and serine protease	Entrapment of protease
Tetracycline Terramycin® Roerig Lab. Terak® Akorn Doxycycline oxytetracycline	MMPs	Chelating agent Ca and Zn
N-Acetyl-cyctein 5-10% Mucomyst® Roberts Pharmaceutical Mucosil® Dey, Inc.	MMPs	Chelating agent Ca and Zn
EDTA ointment 1% Wedgewood Pharmacy	MMPs	Chelating agent Ca and Zn
Synthetic MMP Inhibitor Galardin™ (Ilomostat), Glycomed, Inc.	MMPs	Chelating agent Ca and Zn

MYCOPLASMA FELIS

Mycoplasma spp was first described as a pleuropneumonia-like organism in 1932. By 1956, 15 species of this organism were identified and the genus *Mycoplasma* was assigned. Today, *Mycoplasma felis* is one of over 150 different species of *Mycoplasma* that has been identified. The organism is believed to be part of the normal flora in the upper airway in cats and other species. *Mycoplasma felis* has also been found in the conjunctiva in asymptomatic cats.

In one study, it was difficult to reproduce the infection without prior immunosuppression, i.e. corticosteroids. Many consider *Mycoplasma felis* to be an opportunistic organism, secondary to feline herpes virus. *Mycoplasma* involves the lower respiratory tract only in animals with additional underlying diseases.

Diagnosis of *Mycoplasma* conjunctivitis in the past has been based on clinical signs and the finding of epithelial cell intracytoplasmic basophilic inclusion bodies located near the level of the cell membrane. Inclusion bodies caused by *Chlamydophila felis* are located paranuclear in the epithelial cells. P.C.R. techniques have been used to identify *Mycoplasma felis* in 'normal' conjunctiva and in cases of conjunctivitis. It is difficult to culture these single cell organisms in the laboratory. Growth of *Mycoplasma* usually is not recognized in many routine clinical cultures because *Mycoplasma* are fastidious, grow more slowly than bacteria (often only as difficult-to-see, clear, pinpoint colonies after two days of incubation), do not stain with Gram's stain, and are not usually considered to be common bacterial pathogens. If *Mycoplasma* was suspected, based on initial findings, it was confirmed by 16S rRNA gene sequencing. This procedure is a useful diagnostic method because only minute amounts of *Mycoplasma* growth was required, viable organisms were not necessary, and rRNA gene sequences for *Mycoplasma* were available. This procedure is not commercially availabl.

Mycoplasma lack a rigid cell wall present in most bacteria. Instead, they have a thin flexible membrane containing its cytoplasma. The lack of a cell wall accounts for *Mycoplasma*'s resistance to penecillins and cephalosporins. The organism is sensitive to tetracyclines, doxycycline, fluoroquinolones, chloramphenicol, erythromycin, clindamycin, and azithromycin.

Mycoplasma felis has recently been cultured from the cornea in cats with deep stromal ulcers and/or keratomalacia. Although possibly not the primary microorganism in these cases, it is believed to be the greatest threat to vision.

In the past, over a dozen cases of deep stromal ulcerative keratitis and malacia have yielded a positive culture for *Mycoplasma*. The cats ranged in age from 7 weeks to 15 years. There was no breed or sex predisposition. Unilateral and bilateral cases have been identified. One cat 15 years of age was on chemotherapy drugs at the time of presentation. Additional cats had recently received systemic or topical corticosteroids prior to presentation. Most cats had a history of recent feline herpetic keratitis or concurrent corneal ulceration typical of feline herpetic keratitis. All cats had prior treatment with either topical or systemic antibiotics which would be ineffective for *Mycoplasma*. Other cats have been presented with acute stromal ulcers and/or keratomalacia. However, *Mycoplasma* has never been cultured from the cornea of a case that did not have a history of topical treatment for an ocular disease.

All cases have been treated with topical erythromycin or fluoroquinolones and systemic doxycycline or azithromycin. If indicated, they were treated also for feline herpetic keratitis with topical and/or systemic anti-viral medication. Response to therapy has been excellent in all cases.