CHRONIC CORNEAL DISEASES
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KCS – KERATOCONJUNCTIVITIS SICCA – CANINE
Clinical Presentation – This disease is much more common in the dog than in the cat. Mucoid to mucopurulent discharge may be present that is tenacious, profuse, and chronic. There may also be chemosis, hyper trophy, hyperemia, and keratinized plaques on the conjunctiva. Discomfort or pain may be present evidenced by rubbing eyes or blepharospasm or an elevated 3rd eyelid. Keratinization of the cornea is marked by superficial vascularization, surface hyper trophy, pigmented and/or leucomatous opacities and recurrent or nonhealing (indolent) corneal ulcers may be present. Blindness may occur due to scarring, pigmentary keratitis or corneal rupture.

Diagnosis - Schirmer Tear Test 1 (STT) should be evaluated even when cornea doesn’t appear dry. This test should be measured before any drops are added and after cleaning the discharge. The normal result is 15 to 25 mm/min., and it is diagnostic for KCS if the result is < 10 mm/min. In cases where the STT is over 20 in less than a minute, it is not necessary to continue timing unless relative response to medication is being evaluated. Symptomatic cases usually are < 5 mm/min. Other causes of low STT values include artificially low values from atropine, fear-induced sympathetic stimulation (often in cats), topical anesthetic prior to measurement. Cytology of conjunctival impression smears or cotton swab rolling may have results that include keratinization of epithelial cells and increased numbers of lymphocytes. Immunostaining for abnormal cytokeratins and B and T cells can be helpful in difficult cases as can immunostaining for MHC II.

Incidence - The absolute incidence of this disease is unknown. In evaluating VMDP data it was found to be the etiology or a contributing factor in 1.52% of all eye disease and 50% of all conjunctivitis cases. There are limitations in evaluating this data group, and this data is not necessarily accurate for private practice.

Pathogenesis - Lesions in dogs are much more severe than in humans, and this may be related to delayed diagnosis and inability to self medicate. Many dogs also have severe tear deficiencies compared to humans. The severity of the disease and its development are also related to underlying anatomic abnormalities including lagophthalmos and exophthalmos. The decrease in amount of tears causes corneal desiccation, the increased surface area in brachycephals increases rate of evaporation, and increased osmolality of tear film results and desiccates the cornea further. In addition, there is a nutritional deficiency (from decreased tear film Vit A) that causes vascularization. Mononuclear cell invasion into conjunctiva causes squamous metaplasia. Blinking then causes large shearing forces on the cornea when it is dry producing chronic epithelial damage exposing new antigens, and autoantibodies are formed. This initiates an escalating inflammatory cycle.

Etiology - Immune mediated KCS is thought to be the most common type of dry eye. The mechanism causing lacrimal gland tissue destruction is poorly understood. It is associated with a proliferation of invading lymphocytes which may release local hormones and inflammatory intermediates that damage the gland and suppress acinar production of tears. Neutering may be a predisposing factor, however, old age decreases lacrimation levels much more than neutering.

Other etiologies of KCS include: 1.) acute canine distemper conjunctivitis with PMN infiltration of the lacrimal gland; 2.) congenital KCS, may be unilateral, gland abiotrophy or aplasia; 3.) secondary to drug therapy i.e. atropine (temporary), phenazopyridine, sulphas, and EtoGesic® (etodolac) which can be irreversible; 4.) neurological xerosis from facial trauma, ear infections; 5.) blockage of ductules from chemosis from conjunctivitis or cicatriztion post infection (may be temporary); 6.) removal of third eyelid gland (cherry eye surgery); 7.) intermittent conjunctivitis causing intermittent KCS, such as in seasonal allergies.

Treatment – 1) Artificial tears may be used to replace normal tears. These do not have many of the constituents of normal tears, thus the nutrition of the cornea is compromised. Ointments have longer contact time, which is an advantage in KCS, however, eyedrops are easier to apply. Do not use saline or eyewash as tear replacements, because they will break up the tear film that is present. Gentle has a long contact time for a drop and ophthalmic petrolatum is a good choice for ointment unless antibiotics are needed.

Lacrimogenic drugs include pilocarpine (cholinergic stimulation) which is most effective when used orally (2 drops of 2% PO BID in food (25#). The second drug is Cyclosporine A which has direct anti-inflammatory effects directly on the lacrimal gland, and indirect neurohormonal effects, both stimulating tearing. Normal dogs and humans have been shown to have increased tearing when treated with topical CsA. The commercial preparation is 0.2% ointment, (Optimmune®) – which minimizes the amount of drug needed to achieve optimal clinical effects. It is a sterile preparation because it is anhydrous and does not support microbes: Stability is excellent with 90-105% of label strength for at least 24 months after manufacture. Compounded preparations can be irritating, are not FDA approved, and use concentrations which are higher than necessary for most animals. Compounded CsA has also been shown to cause systemic changes in lymphocyte activity in dogs, and the preparation can support bacterial growth (Klebsiella 46%, Pseudomonas 31%, and Staph 27%). Once or twice daily treatment is needed to produce the direct lacrimogenic effect. Dogs should be treated in the morning of their reevaluation, or the tear production may be lowered. Life-long treatment will be necessary unless the KCS is transient. Cyclosporine is also effective for KCS in the cat.

Anti-inflammatory drugs such as corticosteroids, suppress clinical signs including decreasing vessels and resolving conjunctivitis. They will not increase tear production, unless the KCS is secondary to chemois or transient inflammation. Complications from topical corticosteroid use include ulceration and iatrogenic Cushing’s disease. In the cat, Herpes symptoms may be initiated with topical or systemic steroids.

Topical antibiotics are used for the treatment of secondary bacterial infections. Topical use is indicated when the discharge is purulent instead of mucoid, or if cultures are
positive. Topical antibiotics should always be used when ulceration is present. Transient improvement of conjunctivitis with intermittent antibiotic ointment treatment should trigger suspicion of underlying KCS as the primary etiology. Systemic antibiotics are often needed in animals that also have otitis externa and chronic pyoderma. Broad spectrum bacteriocidal ointments should be used such as triple antibiotic or gentamicin. Ointments have longer contact time than drops, and are therefore indicated in KCS.

Surgical treatments include canthoplasty and parotid duct transposition.

**CHRONIC SUPERFICIAL KERATITIS (CSK, PANNUS), CANINE**

**Clinical Presentation** - This disease is most commonly seen in German Shepherd, Belgian shepherd, shepherd crosses, and greyhounds. Geographical predisposition to this disease is at high altitude where the disease starts at a younger age (3-6 years). In dogs with more sunlight exposure than typical, it has the same early age of onset. With less sunlight exposure and at sea level, the disease is seen at 6-7 years of age. Clinical signs are that the disease is usually bilateral, occasionally unilateral especially with a trauma etiology. The ventralateral cornea is the most typical location for initial lesion and the conjunctiva adjacent to corneal lesion is inflamed (redness, pigmentation). Corneal lesion development has a typical pattern of cellular infiltration into the cornea from the limbus, neovasculization follows the cellular involvement, formation of granulation tissue in the epithelium and superficial stroma, and pigmentation quickly invades the granulation tissue. The disease will slowly progress to blindness over the years. More rapid progression may be seen at high altitude. Animals can be very different in their individual response. This disease may also have an associated third eyelid mononuclear cell infiltrate.

**Diagnosis** - This disease is usually diagnosed from its typical clinical appearance and breed association. Cytological examination of a corneal scraping may be helpful. Histopathology is diagnostic in unusual cases.

**Pathogenesis** - Ultraviolet light damages the cornea. Immune complexes form secondary to the damage and stimulate a cellular reaction. Genetics is an important component of the disease.

**Treatment** - Corticosteroids are anti-inflammatory and immunosuppressive, and therefore are very effective for the treatment of this disease. Moderate disease may be treated initially with corticosteroids and then maintained on CsA. More severe disease can be treated and reversed initially with corticosteroids, and then maintained on a combination of steroids and CsA. Life-long treatment with some topical AI drug is necessary. Decreasing the dose to maintenance level usually takes 3-4 months. The pigment will clear very slowly after an initial dramatic improvement in the appearance of the cornea. Since most of these dogs are large breeds, iatrogenic Cushing’s disease is rarely a problem. Choices of treatments include the following drugs: Subconjunctival (triamcinolone - 4-10 mg/1/4 ml injection site or methylprednisolone acetate - 4-8 mg/1/4 ml) -should be used initially in severe or moderate disease and for patients where topical treatment is difficult. It cannot replace topical treatment entirely. Topical corticosteroids (prednisolone acetate 1% or dexamethasone phosphate 1%) are used in most cases as the initial treatment.

Cyclosporine study results show that pannus treated with CsA improved 80% vs Dex with 93% improvement. Cyclosporine will not thin the cornea or predispose to ulceration like steroids do. CsA will clear granulation tissue, vascularization, and pigment. It was not as effective with corneal inflammatory cells, although it did clear them over a longer period of time. It caused epiphora in some dogs. Beta irradiation with Strontium-90 source – this surgical technique can be used in addition to topical medical treatments to clear pigment more rapidly. Use 4500 to 7500 rads over 4-6 applications. It is difficult to get the source and maintain it because of regulations. It may cause mild to severe ulceration in some cases, and should be used with caution in patients that have treated with topical corticosteroids for years. It requires general anesthesia and is relatively expensive.

**FELINE OCULAR HERPES**

Feline conjunctivitis with or without corneal ulcers is one of the most frustrating ocular diseases to diagnose and treat. Unfortunately, it is also quite common. It is most frequently caused by the feline herpesvirus (FHV-1). Relatively new diagnostic techniques have not improved our ability to definitively diagnose this disease and in some cases may be a waste of a client’s money. Often, it is better to make a diagnosis based on clinical signs and begin frequent topical treatments without delaying until a definitive diagnosis is made.

**Clinical Signs** - The severity of the presenting conjunctivitis can be mild to extremely severe. The most common presenting signs include blepharospasm, serous to mucopurulent discharge, conjunctival hyperemia and chemosis. Symblepharon is the adhesion of conjunctiva to itself or to the cornea. A corneal ulcer does not have to be present for symblepharon to occur. If the disease is acute, the symblepharon may respond to treatment, however, if the disease has already become chronic, the symblepharon is usually permanent. Corneal ulceration may accompany the conjunctivitis. The patterns are described as dendritic, geographic, or deep ulceration that may be “melting.” The appearance of ulcers following chronic or intermittent conjunctivitis is suggestive of herpesvirus as the etiology. Many adult cats will present with unilateral or bilateral conjunctivitis without ulceration. Coughing and sneezing may or may not be present. Recurrence occurs because the herpesvirus establishes a latent infection in the trigeminal ganglia. Stressful situations or treatment with systemic corticosteroid drugs may trigger recurrent episodes of the disease. Recurrent corneal ulceration in adult cats may follow episodes of conjunctivitis. Some ulcers become indolent and cats may develop sequestra in the area of ulceration. Deep corneal vascularization is usually the result of stromal keratitis and may be accompanied by deep pigment. These cats usually do not have concurrent ulceration. The surface of the cornea is smooth, no stain uptake is present, and the cat does not appear to be painful, unless conjunctivitis is occurring at the time of presentation. The scarring from stromal keratitis does not respond to treatment.

**Presumptive diagnosis** based on clinical signs remains the most reliable way to diagnose FHV-1 infection in both kittens and older cats. Specific tests may produce a positive
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diagnosis, however, many of these diagnostic methods produce high numbers of false positives and negatives, and therefore are not useful for confirmation of the etiology in a specific clinical case.

**Treatment** - Therapy for the older cat with recurring attacks of FHV-1 conjunctivitis should be based on the severity, duration, and frequency of outbreaks. Topical antibiotic ointments such as erythromycin and Terramycin® may be sufficient in mild cases to provide lubrication and some cushioning to partially relieve ocular pain. Their benefit is that they are economical and may provide some relief for the cat until the disease again becomes dormant as part of its natural cycle. More severe conjunctivitis, with or without ulceration, should be treated with topical antivirals, which include idoxuridine, and trifluridine, 2-8x/day depending on severity. Ulcers that become indolent while they are being medically treated may heal quicker after debridement or keratectomy. They should not be treated with grid surgeries or chemical cautery due to the potential to stimulate sequestra formation. Oral L-lysine has been shown to be effective for treating and preventing further outbreaks of feline herpesvirus. L-lysine can be purchased in health food and drug stores and the tablets should be ground (coffee grinders work well), before adding it to canned cat food. This minimizes GI side effects. The dosage is 250 mg BID for kittens and small cats and 500mg BID for larger adult cats. If gastric upset is noticed (vomiting), the lysine should be discontinued for several days and then a lower dose should be tried. This side effect is uncommon if the supplement is administered with food. Interferon has also been discussed as a drug that suppresses feline herpesvirus, and it can be used orally, nasally or topically in the eye. Mucosal absorption of the drug is recommended to prevent digestion of the drug by the GI tract. Topical steroidal anti-inflammatory drugs should not be used because steroids activate the latent. Topical NSAIDs or cyclosporine have been shown to improve inflammation and scarring in human, rabbit, and mouse herpes studies with and without concurrent antiviral therapy. The most prudent and defensible therapeutic regime when anti-inflammatory drugs are necessary would be to use a topical NSAID or cyclosporine and an anti-viral.

**FELINE PROLIFERATIVE (EOSINOPHILIC) KERATITIS**

This disease occurs as a distinct entity in the cat. The cause is undetermined, but some have suggested another manifestation of the eosinophilic granuloma complex (rodent ulcer, etc.) The clinical appearance may be a focal plaque, or the entire cornea may be involved. It is white, proliferative, and has superficial blood vessels invading the lesion. It is not painful or ulcerated and does not retain stain. It is slowly progressive, infiltrating more of the cornea over time. The lesion may feel gritty when it is scraped to obtain cells for cytology, and granules may even be evident on the surface of the cornea at examination. Cytologic evaluation of corneal scrapings reveal predominantly eosinophils and mast cells in the acute disease state, and lymphocytes and plasma cells in more chronic disease. Diagnosis is based on clinical appearance, the species, and cytology. The eye will respond dramatically to topical steroid therapy, but it tends to recur. Topical prednisolone (1%) or dexamethasone (0.1%) are both effective. They may trigger an acute Herpes outbreak if the cat is a carrier. Frequent administration is necessary in the beginning (4-6x/day) and decreasing over 6 weeks to 2x/day therapy. After treating for 2 months, and weaning the dose to every other day, the medication can be discontinued. Recurrence may be a problem, either at that time or in the future. Some cats need life long therapy, but most can be treated intermittently as needed. Megestrol acetate is an effective systemic treatment and may be used to get the lesion under control initially. It should not be used continuously due to the serious systemic side effects including diabetes mellitus. It is very useful intermittently and in cats that are Herpes carriers. Megestrol acetate is not approved for use in cats. Cyclosporine may be useful after the condition has been initially treated with corticosteroids.