Extraocular Disease

The most common cause of extraocular feline disease is Herpesvirus infection. Population studies indicate that the disease has 95% prevalence and of this population, 80% of cats develop a latent infection in the trigeminal nerve ganglia that supplies the eye. Approximately 45% of these cats shed the virus throughout their lifetime. The disease is most commonly transmitted from ocular or nasal secretions in cats actively shedding the disease. It is most commonly seen unilaterally (88%) but can be seen bilaterally.

The disease most commonly causes conjunctivitis and keratitis in cats, but has also been implicated as a possible cause of anterior uveitis. Dendritic corneal ulcers are pathognomonic for the disease but punctate and geographic ulcers are also commonly seen. Diagnosis can be made with a positive PCR result, but false negatives are commonly reported. It develops after reactivation of the virus and this is most commonly due to stress, illness, or use of steroids. In fact, many cats on chronic steroids for IBD or stomatitis or on chemotherapy for Lymphoma develop Herpes ocular infections. I have also seen worsening of ocular disease after conjunctivitis is treated with topical steroids.

Common complications of the disease include symblepharon, corneal sequestrum, and eosinophilic keratitis. Symblepharon occurs when both the conjunctiva and cornea are ulcerated at the same time and adhere to each other during healing. It is often permanent and surgical correction seems to be only temporary as the adhesions recur a few weeks after surgery. Most commonly symblepharon is seen in kittens.

Corneal sequestrum occurs most likely as a result of chronic indolent geographic ulceration, but is also seen more commonly in brachycephalic cats with chronic corneal exposure or entropion. The clinical appearance is of a dark brown to black deposit in the cornea and histopathology reveals necrotic corneal stroma. Treatment usually requires superficial keratectomy with or without conjunctival graft, and these can be recurrent.

Eosinophilic keratitis is due to an immune response to the herpes virus infection and its clinical appearance is that of corneal neovascularization with yellow-tan plaques on the corneal surface. The diagnosis can be made by corneal scraping and cytology of the plaques and demonstration of even one eosinophil is diagnostic. This is one instance in which treatment with topical steroids is indicated. Other treatments include use of Megesterol acetate, which can quickly result in clearing of the deposits. Side effects of this drug include development of diabetes mellitus and behavior change.

Treatment of herpesvirus keratoconjunctivitis depends on the severity. Mild conjunctivitis cases are often self-limiting and don’t require therapy. More severe conjunctivitis and keratitis are best treated with topical anti-virals and antibiotics if ulcerations are present. In geographic corneal ulceration, debridement of the cornea is often necessary to speed healing. Under no circumstances should a grid keratotomy be performed due to its association with the development of corneal sequestrums.
Topical antivirals that are most commonly used include Idoxuridine, Cidofovir, and Vidarabine. The antivirals only kill the virus when it is outside of the cells, therefore frequent administration (TID-QID) is often necessary. In addition, topical interferon has been anecdotally reported to be beneficial.

Oral medications to aid in treatment include Lysine at 500mg PO BID in adults and 250mg BID in kittens. This amino acid reduces the uptake of Arginine, which the virus needs in order to make more viral particles. It is often good for adjunctive therapy or preventative therapy but usually does not control the infection alone. Famciclovir has shown lots of promise in treating resistant infections. This drug has been reported to be much more safe than previous oral antivirals, but a few reports of non-regenerative anemia have been seen. Recommended doses vary considerably as research suggests the best dose to be 90mg/kg PO BID for 1 week, then 90mg/kg SID for 2 weeks. However, ophthalmologists have seen good success at lower doses (30mg/kg BID for 1 week, then 30mg/kg SID for 2 weeks), which may end up being safer in cats. Pre- and post-medical therapy bloodwork is recommended to watch for non-regenerative anemia, which has only been anecdotally reported at this time.

Another common cause of conjunctivitis in cats (albeit less common than Herpes), is Chlamydophila (Chlamydia). The conjunctivitis may start out in 1 eye but then progresses to the other eye in a few days. Diagnosis can be made with ELISA antigen or PCR tests, or demonstrating the organism on cytology. The conjunctivitis usually resolves with treatment with either Erythromycin (less irritating) or Terramycin 2-3 times daily for 2-3 weeks. In chronic cases, systemic treatment with Azithromycin or Doxycycline has been successful. Chlamydophila does cause corneal disease, therefore if corneal disease is occurring concurrently with the conjunctivitis, the most likely disease is Herpes.

Eyelid disease can be a result of a congenital abnormality (eyelid agenesis), inflammatory/infectious, or neoplasia. Cats are the most common veterinary species to be born with eyelid agenesis in which the upper lateral portion of the eyelid margin did not develop. The cause is unknown but has been seen in kittens born from a cat given griseofulvin. This can result in trichiasis and exposure, leading to a neovascular keratitis and irritation. Treatment depends on the amount of defect. If the defect is small and the eyelids can close most of the way, then cryoepletion can be performed to prevent the trichiasis. If the defect is large, then there are several different surgical methods of recreating the upper eyelid to reduce the irritation and trichiasis and aid in eyelid closure.

Dermatophytosis causes periocular alopecia and eyelid ulceration. Diagnosis is made with use of DTM. Treatment for this disease involves clipping the periocular hair and applying miconazole or enilconazole or systemic treatment of itraconazole or griseofulvin.

Nodular growths on the eyelid can be either infectious or neoplasia. Infectious nodules are uncommon, but the two most common diseases seen causing these are Leishmania and Histoplasma. Leishmania infections are most commonly seen in cats from Texas, but Histoplasma is a relatively common cause of infection in cats in the Midwest. Treatment involves treating the underlying disease.

Tumors of the eyelids are less frequent than dogs, but are more likely to be cancerous. The most common tumor is squamous cell carcinoma, followed by lymphosarcoma, fibrosarcoma, and mast cell tumor. SCC accounts for up to 65% of
eyelid neoplasia. Treatment depends on the size but these tumors can respond to topical 5-fluorouracil or to surgery. Surgery includes cryotherapy, wide surgical excision with reconstruction, or radiation. Recurrence is common but metastasis is rare.

 Conjunctival neoplasia is rare but generally associated with high mortality rates. The most common neoplasms include melanoma and lymphosarcoma. Melanoma has been reported to be very aggressive with up to a 100% mortality rate. Lymphosarcoma is usually associated with systemic disease.

**Intraocular Disease**

The most common intraocular disease seen in cats is uveitis, which can be caused by many different diseases. Uveitis can be anterior, posterior, or both. Anterior uveitis symptoms include blepharospasm, corneal edema, corneal neovascularization, keratic precipitates, aqueous flare or fibrin or hypopyon or hyphema, miosis, and iritis. Most cats with anterior uveitis have near normal vision but may be limited due to inflammation. By contrast, posterior uveitis usually causes near complete loss of vision with a relatively quiet anterior chamber. Symptoms of posterior uveitis include retinal detachment, retinal vascular tortuosity and/or retinal edema.

Differential causes for uveitis in cats includes trauma, infectious (FeLV, FIV, FIP, Toxoplasma, Bartonella, Cryptococcus, Histoplasma, Coccidioides, Blastomyces, and Candida), neoplasia (melanoma, primary ocular sarcoma, lymphosarcoma, ciliary body adenoma, and metastasis), lens changes (cataract or lens luxation), hypertension or idiopathic or immune mediated disease.

Traumatic uveitis usually results from blunt or penetrating injuries. Blunt trauma usually results in intraocular hemorrhage. If the hemorrhage is confined to the anterior chamber (hyphema), topical and systemic anti-inflammatories can result in clearing and recovery of vision. Extensive hemorrhage in the posterior segment is often associated with retinal detachment and loss of vision. Penetrating injuries may be mild or severe but infection is common, so all cases should be treated with aggressive antibiotic (use those that penetrate the cornea, ie Ofloxacin, Tobramycin) and anti-inflammatory therapy. Bacterial endophthalmitis can develop rapidly and result in the need for enucleation. Open wounds or lacerations may need surgical repair and lens capsule ruptures need immediate removal of lens material.

FeLV is most commonly associated with causing lymphosarcoma, which can cause uveitis. FIV can cause a par planitis with white anterior vitreal debris being most commonly seen. FIV appears to often be associated with Toxoplasmosis. FIP causes a bilateral granulomatous uveitis with thick mutton fat keratic precipitates.

Toxoplasmosis is a protozoal infection that is most often associated with systemic disease such as anorexia, fever, hepatitis, myositis, pneumonia, diarrhea, and neurological dysfunction. Ocular disease includes anterior and/or posterior uveitis. Focal bullous retinal detachments are possible as well. Cats with active ocular disease often have concurrent FIV infection. Diagnosis is made by serology and treatment includes topical and oral steroids and oral Clindamycin. Uveitis may become chronic or recurring. Bartonella is usually transmitted from fleas and causes an anterior uveitis. Diagnosis is based upon positive serology and response to therapy. Treatment is use of Azithromycin 10mg/kg once daily for 21 days, along with appropriate use of anti-inflammatories.
Granulomatous anterior uveitis, often associated with chorioretinitis, may be associated with cryptococcosis, blastomycosis, histoplasmosis, and coccidiomycosis. Demonstrating the organism on cytology or histopathology samples results in a diagnosis, but serology can be helpful as well. Treatment involves topical therapy with anti-inflammatory medication and Itraconazole appears to be most effective for anti-fungal therapy.

The most common primary intraocular tumor is melanoma, which can cause a secondary uveitis. This disease usually starts off as a benign appearing iridal color change, which becomes progressively more dark and thickened and can invade the ciliary body and drainage angle. This invasion is often associated with secondary glaucoma and an increased risk for metastasis. Metastasis rates have been reported to be as high as 67%.

Diagnosis is difficult without cytology or histopathology so the biggest dilemma is to determine when to remove the eye. Enucleation is usually performed based upon increases in size and amount of pigment as well as elevation in IOP. Alternatively laser therapy is being evaluated as a means of treatment to save the eye in which early lesions are lasered with a Diode laser to prevent further growth or spread.

Feline ocular sarcomas are the second most common primary tumor and very aggressive and malignant. They have been associated with lens injury, chronic uveitis, and intraocular surgery (especially pharmacologic ablation of ciliary body with Gentamicin). They usually present as chronic uveitis, secondary glaucoma, hyphema, and white to pink masses. As these tumors tend to spread up the optic nerve to the brain, early enucleation with exenteration is recommended.

Primary ciliary body adenomas are much more rare in cats than in dogs, and usually appears as non-pigmented to pink masses near the pupil or iris root. As most of these tumors do develop secondary glaucoma, enucleation is recommended.

Lymphosarcoma is the most common cause of metastatic neoplasia to the eye in the cat. Symptoms include profound iridal thickening with uveitis and hypopyon is commonly present in the anterior chamber. Chorioretinitis with retinal detachment is also seen, causing loss of vision. Glaucoma is a common complication of the uveitis. Ocular disease can commonly precede other clinical symptoms associated with the cancer. Diagnosis is made on cytology. Aggressive therapy with topical steroids and systemic chemotherapy is necessary. Secondary glaucoma may need to be treated as well and usually consists of topical carbonic anhydrase inhibitors and beta-blockers.

Metastasis of carcinomas is also a cause of uveitis in cats. The most common tumors reported include mammary gland adenocarcinoma, uterine adenocarcinoma, and pulmonary carcinoma. Multiple myeloma causes secondary ocular disease due to the hyperviscosity syndrome, which can lead to retinal detachment and intraocular hemorrhage.

Cataract formation causes anterior uveitis as a result of changes of lenticular protein that elicits an immune response. This is most profound in rapidly developing cataracts and hypermature cataracts in which resorption is commonly seen. In addition, chronic uveitis can lead to lens luxation in cats. This can cause mechanical irritation from chronic movement inside the eye. Treatment includes anti-inflammatory therapy and/or removal of the cataract or lens luxation.

Hypertension is one of the most common causes of posterior uveitis and retinal detachment in older cats. It is often associated with chronic renal insufficiency,
hyperthyroidism, and hypertrophic cardiomyopathy. Ocular symptoms include serous bullous retinal detachment with intra- and pre-retinal hemorrhages, vitreal hemorrhage, and hyphema. Most cats have very elevated BPs of well over 200mmHg. In the majority of cases, lowering the BP will result in retinal reattachment and recovery of vision, especially if the retina is reattached within 1 month. Complications can occur leading to permanent vision loss and usually include retinal tearing with disinsertion or secondary glaucoma. Amlodipine is considered the treatment of choice.

Idiopathic or immune-mediated uveitis is seen in approximately 40% of cats with uveitis and is diagnosed by the exclusion of other causes of uveitis. This type of uveitis is often chronic and is associated with secondary changes, such as glaucoma.

Treatment of the uveitis involves treating the underlying disease as well as use of topical and/or systemic anti-inflammatories. Chronic changes include posterior synechia, cataract formation or lens luxation, and secondary glaucoma. Glaucoma in cats is usually due to chronic uveitis and is rarely reported to be primary in origin.

Non-inflammatory retinal diseases that are most commonly seen are taurine deficiency, PRA, or toxic damage. Since taurine is essential for photoreceptor survival, deficiency of taurine causes retinal degeneration. It begins as a granular appearance to the area centralis, which then develops into a hyperreflective focus, and then can progress to a horizontal streak, and then to an overall diffuse retinal degeneration. This can cause loss of vision. Since most commercial foods contain adequate taurine, this disease is most commonly seen in cats fed inappropriate diets or those with intestinal disease resulting in altered protein absorption.

PRA is seen in cats but much less commonly than in dogs. It has been reported in the Abyssinian and is associated with vision loss at a much earlier age in cats, with vision loss usually complete by 3-5 years of age. The most retinal toxin is enrofloxacin and is most commonly associated with parenteral administration and higher doses. In almost all cases, the blindness has been permanent and develops very rapidly. Although enrofloxacin has been most reported, all fluoroquinolones are considered potentially retinotoxic and should be used with caution in cats with decreased renal or hepatic function. The dose of enrofloxacin should never exceed the current recommended dose of 2.5mg BID and should be administered the least amount of time possible.

**Orbit**

Orbital disease most commonly presents as progressive exophthalmos, with resultant exposure keratitis. Retropulsion of the globe is restricted and may or may not be associated with pain. In general, orbital inflammation or abscesses are consistent with a higher amount of pain and variable fever, whereas orbital neoplasia is generally nonpainful.

The most common cause of orbital inflammation is from tooth root abscesses or upper premolar or molar teeth. This leads to a ventral orbital infection and pain. Treatment involves oral examination and dental radiographs if possible. If an abscess is present, then removal of the tooth and/or draining the abscess is necessary. Treatment with Clindamycin and pain and anti-inflammatory medications are necessary.

The most common orbital disease in cats is neoplasia. Approximately 90% of all orbital neoplasms in the cat are malignant, with about 2/3 of these being squamous cell
carcinoma. Orbital SCC is often associated with oral extension of the tumor as well. Therefore an oral exam is necessary and can be an easier location to obtain a biopsy or fine needle aspirate. Depending on the type of tumor diagnosed, therapeutic options include surgery, radiation therapy, and chemotherapy. However, most cases are euthanized within 1 month of diagnosis due to the poor prognosis.