

Feline Herpes Virus and other Feline Phenomena

Brady Beale, VMD, DACVO

*University of Pennsylvania, Ryan Hospital, Philadelphia, PA
Pet Emergency and Specialty Treatment Services, Lancaster, PA*

While cats have many similarities to other species, there are unique aspects of both anatomy and pathology that make a feline-focused discussion worthwhile. Striking differences exist for feline diseases including infection and neoplasia. Responses to treatment can also be species-specific.

Feline Herpes Virus

Feline herpes virus (FHV-1) is the most common disease state in the domestic cats and has varied clinical manifestations ranging from mild chronic ocular discharge to more dramatic symptoms including the plaques of eosinophilic keratitis or the brown scabs of corneal sequestrum.

Feline Herpes Virus commonly causes upper respiratory infection and conjunctivitis. In more advanced cases, ulceration of the cornea and associated complications such as eosinophilic keratitis and corneal sequestrum can occur. Diagnosis of FHV1 is most commonly made based on clinical signs and a complete history. Studies show that PCR for DNA is more sensitive than Viral Isolation or Fluorescent antibodies. However, testing for Feline Herpes virus is of limited use due to the prevalence of FHV-1 in a clinically normal population.

Many treatment options exist, and may vary depending on the severity of the disease. If a corneal ulcer is present, debridement (removal of diseased tissue) may be necessary to promote healing of the cornea. The classic FHV-1 ulcer is a focal dendritic ulcer but the affected area often enlarges to greater surface area. Bacteria often invade diseased tissues and worsen the effect of a viral condition, therefore, topical antibiotics are prescribed to treat or prevent secondary bacterial infections. First-line therapy includes erythromycin and terramycin applied twice daily. Triple antibiotic combinations should be avoided in cats as they contain neomycin which has now been implicated in rare anaphylactic reactions in cats. If the clinical signs are severe or worsen in the face of supportive antibiotic therapy, antivirals are recommended. Recommended compounded topical therapy would include Idoxuridine 0.1% (1 drop QID) which is well tolerated but requires a 3-4 times daily dosing or Cidofovir 0.5% (1 drop BID) which can be irritating and more expensive.

Several oral medications are also available. Oral L-lysine is an amino acid used to decrease viral replication and is recommended at 250 -1000mg per day for life as a maintenance regimen to decrease frequency and severity of flare-ups. Oral antivirals such as Famciclovir may also be used to decrease viral replication when dealing with FHV-1 complications. Famciclovir is typically reserved for more advanced cases including eosinophilic keratitis and sequestrum. Famciclovir studies demonstrate safety testing up to 90mg/kg but 62.5 mg per cat BID appears to produce clinical improvement and cost savings are dramatic.

Signs and symptoms of FHV-1 can be apparent at birth as kittens infected in utero will show abnormal ocular development. **Eyelid agenesis** describes a condition in which portions of the feline eyelids failed to form. The absence of eyelids can lead to complications of exposure (keratitis, ulcers and scarring) and can require surgical correction to protect the eyes. Several techniques have been described and most involve a rotational flap of an adjacent healthy area of eyelid.

When young kittens battling FHV-1 or other severe ocular infections that cause mucopurulent **neonatal conjunctivitis**, corneal ulceration can be so severe that globes rupture or extensive scarring persists. **Symblepharon** describes a condition of extensive adhesions over the conjunctiva or cornea. In severe cases, this leads to blindness. While medication may be recommended if active ulceration or inflammation exists, surgical removal of the corneal scarring is often unrewarding and does not yield significant improvement.

Eosinophilic proliferative Keratitis is a disease in cats in which eosinophils invade the cornea and conjunctiva creating plaques and ulcers. Viral and immune-mediated etiology processes likely play a role and diagnosis can be confirmed by noting eosinophils on a cytology sample. The treatment involves topical steroids (Tobramycin/Dexamethasone or Prednisolone acetate initiated at 1 drop BID) to suppress the immune reaction. However, steroids can have harmful effects on the healing of corneal ulcer so steroids should be stopped if the eye appears to worsen rather than improve. In many cases of Eosinophilic Keratitis, there is often an underlying Herpes Virus infection so treatment with topical and oral antiviral medications is initiated. As mentioned previously, topical antiviral choices include compounded Idoxuridine 0.1% (QID) and Cidofovir 0.5%(BID) and the most common oral antiviral is Famciclovir. The recommended dose ranges from 32.5 mg PO BID to 90mg/kg with lower doses showing clinical efficacy.

It may also be necessary to treat Eosinophilic Keratitis with oral steroids if the topical steroids are not entirely effective but the introduction of Famciclovir to the treatment regimen has decreased this need.

Corneal sequestrum describes a dark, necrotic lesion in the feline corneal stroma. Sequestra appear with 1.) chronic battles with non-healing FHV-1 ulcers or 2.) chronic corneal exposure in cats like Persians and Himalayans. It is possible for the body to extrude the sequestrum on its own with medical support including topical antivirals and antibiotics and oral antivirals. However, this process can take greater than six months and there are cases in which the cat is never free of the sequestrum. It is imperative that blood vessels grow into the cornea to elevate the dead corneal tissue. The path to success will look like an organized island of granulation tissue growing under the sequestrum. The decision to pursue surgical keratectomy to remove the sequestrum is made if the cat is uncomfortable, the pigmented lesion is greater than 50% deep and threatens rupture, or there is no sign of vascular ingrowth suggestive of pending resolution.

Acute Bullous Keratopathy is characterized by a sudden edematous or melting round lesion of the cornea, possibly involving a perforating rupture. Medical therapy is often insufficient to prevent a rupture. Surgery such as a conjunctival graft can be frustrating as additional bullous lesions often arise adjacent to the grafted area. Treatment can include third eyelid flaps for 14 days to stabilize the fragile area but if the condition is severe enough, enucleation may be required.

If a cat presents with a unilateral conjunctivitis characterized by chemosis and serous ocular discharge, **Chlamydia (*Chlamydophila felis*)** should be considered. Diagnosis can be made by cytology (looking for inclusion bodies inside the epithelial cells), fluorescent antibodies or PCR. *C. felis* should be considered a zoonotic but transmission rates are low and recommendations are generally limited to hand washing. Treatment recommendations are topical terramycin or erythromycin or oral tetracyclines or azithromycin in severe cases.

Diffuse Iridal Melanoma describes a progressive pigmentation of the feline iris that causes changes in the iris thickness and pupil mobility. Metastatic rates are reported as high as 65% of the cases. However, as there are not definitive clinical parameters for deciding when to remove an eye, this can be a difficult discussion for owners. Rapid increase in pigmentation, raised areas, free-floating pigment cells in the anterior chamber, and dyscoria (distortion of pupil movement) are all prognostic indicators that pigment has changed from benign melanosis. Cats who have developed secondary glaucoma from pigment cells clogging the iridocorneal angle are considered an advanced stage and enucleation is recommended for comfort and to decrease the chance of metastasis. One study noted metastasis to the liver and lungs 1-3 years after enucleation so radiographs of the chest and abdominal ultrasound are recommended prior to any surgery. Attempts are being made to correlate histopathology findings with a longterm prognosis (i.e. aggressive deep infiltration of the iris or the ciliary body behind it are linked to shorter survival rates) but this data is only useful to make recommendations to owners regarding future health after the eye has been removed. Diode laser ablation can be used to annihilate tumor cells if the pigment is contained within small discreet lesions in the iris.

Feline Ocular Sarcoma is the second most common neoplasia in the feline eye. This tumor is both locally invasive (often extending to the optic nerve) and highly metastatic. It is believed that a traumatic injury to the lens causes a malignant transformation of the lens epithelium. Average time from the trauma to the time of tumor detection is 5 years. If a cat presents with a penetrating ocular trauma involving the lens, early enucleation should be offered. If a cat presents with a mass-like lesion involving the lens, enucleation should be recommended after a metastatic check including chest radiographs, abdominal ultrasound and lymph node aspirates.

Uveitis describes inflammation inside the eye that originates in the uvea (ciliary body, iris and choroid.) The most common causes in cats included trauma, infection (FIP, Bartonella, Fungal, Toxoplasmosis, FIV, FeLV), or neoplasia (lymphosarcoma commonly.) If the inflammation is unilateral, acute, and severe, including a large flocculent clot of fibrin in the anterior chamber, trauma should be high on the differential list. While the large immune-mediated category is not as commonly implicated in feline uveitis, an idiopathic diagnosis is thought to occur in almost 80% of feline uveitis cases.

Medical management of uveitis targets the underlying cause as well as the acute inflammation to minimize damage to the intraocular structures. Topical anti-inflammatory medications drops (Prednisolone acetate or Tobra-Dexamethasone 1 drop 3-4 times daily) will decrease risks of posterior synechia and secondary glaucoma. Topical non-steroidals (Diclofenac, Flurbiprofen, or Ketorolac 1 drop 2-3 times daily) can also be used. Oral steroid

or NSAIDs may also be prescribed at anti-inflammatory doses, particularly if the inflammation occurs in the posterior aspect of the eye where topical medications are not as effective. Topical atropine (1/4 inch strip 1-2 times daily) may also be given to alleviate pain by decreasing ciliary spasm of miosis, prevent posterior synechia and stabilize the blood-aqueous barrier that is leaking and creating aqueous flare (prostaglandins with fibrin and white blood cells). In cats, the ointment form of atropine is preferable to minimize hypersalivation. Oral and topical antibiotics may be given if the cause of the uveitis is an infection or corneal ulcer.

While primary **glaucoma** is uncommon in the cat, elevated pressures of **secondary glaucoma** can result from a feline-specific glaucoma called aqueous misdirection syndrome or chronic inflammation from anterior uveitis or intraocular neoplasia.

Aqueous misdirection syndrome describes a unique scenario in which aqueous humor is directed backwards into the vitreous and then pushes the lens forward in the globe, collapsing the iridocorneal angle. Clinical signs will include a shallow anterior chamber, dilated pupil, and elevated intraocular pressure and with an average age of detection around 12 years of age, Eyes may remain visual for years with medical therapy and the progression of the disease is slow. Occasionally, surgery including a lens removal and anterior vitrectomy will be recommended but most cats are managed medically.

Treatment for feline glaucoma involves topical beta-blockers (timolol or levobunolol 1 drop BID) and carbonic anhydrase inhibitors (dorzolamide or brinzolamide 1 drop TID-QID). As most feline glaucoma is secondary to anterior uveitis, concurrent treatment with topical anti-inflammatories (Tobramycin/Dexamethasone or Prednisolone acetate) can be appropriate. Unfortunately, the rescue prostaglandin analogs (i.e. latanoprost) are not effective in cats as cats lack the appropriate receptors.

A note about **cataracts**: In contrast to canine patients, primary inherited cataracts and cataracts secondary to diabetes are quite rare. Cataracts in cats are typically secondary to trauma or chronic inflammation from uveitis.

Hypertensive Retinopathy Acute blindness caused by a retinal detachment should be considered hypertensive until proven otherwise, so systemic blood pressure measurement should be obtained immediately if a cat presents with sudden-onset blindness and retinal detachment. It is commonly associated with advanced age, chronic renal failure and hyperthyroidism.

While it is important to determine the underlying cause, treatment with Amlodipine (starting dose of 0.625mg PO SID) should be initiated as soon as possible and blood pressure rechecked in 3-5 days to increase medication to BID or as needed. Control of the blood pressure within the first 2 weeks will provide the greatest chance for retinal reattachment and vision return. Unless there is an associated uveitis caused by a retinal vessel bleed, topical ocular medications are generally not needed.

Enrofloxacin-associated Retinal Toxicity has been shown to cause a sudden and often complete toxic effect on the retina leading to acute blindness. While this is generally associated with doses higher than the manufacturer's recommend dose of 2.5 mg/kg PO every 12 hours, other factors can increase the risk of toxicity including old age, renal or hepatic impairment, and IV route of administration. Cat receiving enrofloxacin should be

monitored closely for pupil dilation, decrease in vision, or grey changes to the retina. Should any of these signs appear, enrofloxacin administration should be stopped immediately. When possible, alternative antibiotics should be chosen based on sensitivity studies.