Someone once suggested that feline ocular diseases should be considered using a different side of the brain than that used for studying ophthalmic problems in the dog. Nowhere is that statement more appropriate than when reviewing the unique disorders of the feline conjunctiva and cornea. The majority of the following feline ocular surface diseases simply have no counterpart in the dog.

**Conjunctivitis**

A red eye accompanied by ocular discharge is a common complaint made by cat owners. Unlike the dog, in which infectious conjunctivitis is almost always secondary to an adnexal or lacrimal disorder, the cat is plagued by primary conjunctival pathogens that do not require a predisposing injury to establish infection. Consequently, the etiology of feline conjunctivitis is presumed to be infectious until proven otherwise. Historically, more than one cat may be affected in multiple cat households, or a history of grooming, boarding, or travel to cat shows may indicate the contagious nature of the disease. The stress associated with these same activities is commonly implicated in reactivation of herpetic ocular disease.

In the naïve neonatal or adolescent cat, feline herpesvirus-1 (FHV-1) causes an acute conjunctival-respiratory infection. Characteristic features of the conjunctivitis are its bilateral nature and pronounced hyperemia, accompanied by sneezing and ocular/nasal discharge. The ocular discharge is first serous, then mucopurulent in nature. The dendritic corneal ulcers pathognomonic for herpesvirus occur more often in adults without concurrent upper respiratory infection (URI). However, in the very young kitten, herpetic conjunctivitis may be accompanied by keratitis so severe that adjacent raw epithelial surfaces adhere to one another, producing symblepharon. These conjunctival adhesions can cause permanent prominence of the third eyelid, epiphora from obstruction of the lower nasolacrimal punctum and lacrimal lake, and permanent corneal opacity. Herpetic conjunctivitis in the adult cat typically occurs without respiratory signs and is more often unilateral, with intermittent blepharospasm, mild conjunctival hyperemia, and serous discharge.

Cats infected with *Chlamydophila felis* usually present with negligible upper respiratory disease and a unilateral purulent conjunctivitis. Second eye involvement occurs 5 to 7 days later. Chemosis is more severe but hyperemia milder than that seen in herpes-infected cats. Unlike herpesvirus, chlamydophila does not affect the cornea. Conjunctival follicles have been described in chlamydial infections but probably represent chronicity of the infection rather than etiology. Basophilic intracytoplasmic inclusions in conjunctival scrapings performed during the first 2 to 9 days after the onset of clinical signs are diagnostic for the organism. In chronic cases, IFA or PCR testing is more sensitive than culture for detecting chlamydial infection.

Mycoplasma has historically been implicated as an agent in feline conjunctivitis, but controversy exists over the true pathogenesis of the organism since conjunctivitis cannot be experimentally established in the absence of other ocular pathogens. Mycoplasma-associated conjunctivitis may be unilateral or bilateral, with nonspecific blepharospasm, tearing, and serous discharge. The conjunctiva develops either a velvety texture due to epithelial hypertrophy or a thick white pseudomembrane within 10 to 14 days. Diagnosis may be confirmed by the presence of coccoid basophilic organisms found in clusters on the epithelial cell membrane.

Symptomatic therapy is often recommended in the acute conjunctivitis patient, based on the most likely pathogen involved. Specific antiviral therapy is seldom used for acute conjunctivitis due to the self-limiting nature of the initial viral ocular-respiratory syndrome and the inconsistent efficacy of topical antivirals. Topical antivirals are also irritating, potentially worsening conjunctival hyperemia. If conjunctivitis is particularly severe or persistent, antiviral options are similar to those recommended for herpes-related corneal disease. Although the use of topical or oral corticosteroids may initially decrease clinical hyperemia and swelling, such therapy will ultimately result in prolonged virus shedding, increased risk of herpetic ulceration, and increased likelihood of stromal keratitis, a particularly refractory corneal manifestation of herpesvirus infection. Topical tetracycline 3 to 4 times daily is the drug of choice for *Chlamydophila* and *Mycoplasma*, but erythromycin ointment or a fluoroquinolone solution may be substituted if the tetracycline is too irritating. In kittens with persisting conjunctivitis or in the adult cat with chronic conjunctivitis, a 3-week course of oral doxycycline (5 mg/kg b.i.d.) or azithromycin (5 mg/kg daily for 5 days, then q 72 hours for a total of 3 weeks) will effectively address both *Chlamydophila* and *Mycoplasma*. Elimination of the carrier state is more likely with doxycycline therapy. Noninfectious causes for feline conjunctivitis include eosinophilic conjunctivitis, tear film disorders, allergic conjunctivitis, and lymphosarcoma.
Herpetic Keratitis
Feline herpesvirus type-1 (FHV-1) is ubiquitous in the world’s cat population. Serologic surveys document that as many as 97% of cats are seropositive for FHV-1. Approximately 80% of cats become latently infected upon recovery from the initial infection, as evidenced by the presence of FHV-1 in the trigeminal ganglia of experimentally infected cats. Since the virus will spontaneously reactivate in 45% of these animals, this latently infected population serves as a major reservoir of virus from which FHV-1-naive cats become infected. Stressors such as relocation, surgery, pregnancy, lactation, feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV) associated immune suppression, and corticosteroids often precipitate subclinical viral shedding or recrudescent clinical disease.

Viral reactivation within the cornea creates linear or branching epithelial defects referred to as dendritic ulcers. These early lesions are considered pathognomonic for herpesvirus infection but are often subtle and easily overlooked. The epithelial irregularities can be highlighted by retroilluminating the tapetum and visualizing the corneal surface against the bright reflection. Rose bengal stain may delineate the lesions better than fluorescein since the initial cytopathic effect seldom disrupts the entire epithelial thickness. The dendritic lesions quickly coalesce into larger geographic ulcers that retain fluorescein dye and are often rimmed by ragged, poorly adherent epithelium. *Viral ulcers may be extensive but only disrupt corneal epithelium.* FHV-1-induced ulcers are quite painful. Herpetic ulcers may heal spontaneously or may persist for long periods, regardless of therapy.

Diagnosis
Diagnosis is based on clinical judgment (taking into account the history and clinical signs), on lack of response to antibacterial therapy and on improvement with antiviral therapy. Although the polymerase chain reaction (PCR) test is sensitive enough to identify minute quantities of viral DNA, it cannot distinguish between natural infection and vaccination. Many normal cats shed FHV-1 and most cats are seropositive because of widespread vaccination and establishment of latency. When virus is detected in a cat with disease, its presence may be coincidental or causative. Consequently no test is diagnostically reliable. FIV and FeLV are detected in a higher percentage of cats with chronic keratoconjunctivitis compared with the general population and should be routinely screened.

Treatment
*As a general rule, corticosteroids should be avoided in the treatment of feline conjunctivitis until an infectious cause is ruled out.* Antiviral agents should be considered when ocular signs are severe, persistent, or recurrent, or when corneal ulceration is present. Antivirals are unable to prevent or eradicate latent viral infection. No antiviral agent has been developed specifically for FHV-1. Agents used in the treatment of closely related human herpes simplex virus (HSV-1) are not predictably effective against FHV-1, nor do safety profiles of the drugs reliably translate from humans to cats. Antiviral agents tend to be more toxic than antibacterials, even when applied topically, potentially limiting therapeutic tolerance and duration. Currently available drugs are virostatic and most require frequent administration to retard viral growth. The relative in vitro potency of available antivirals tested against FHV-1, in decreasing order, is trifluridine >> idoxuridine = ganciclovir >> cidofovir = famciclovir/penciclovir > vidarabine >> acyclovir >> foscarnet.

Table 1: Summary of Available Antivirals

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade Name</th>
<th>Formulation</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idoxuridine</td>
<td>Compounded</td>
<td>0.1% solution</td>
<td>Apply at least 5 times daily.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5% ointment</td>
<td></td>
</tr>
<tr>
<td>Vidarabine</td>
<td>Compounded</td>
<td>3% ointment</td>
<td>Apply at least 5 times daily.</td>
</tr>
<tr>
<td>Trifluridine</td>
<td>Viroptic, generic</td>
<td>1% solution</td>
<td>Apply at least 5 times daily.</td>
</tr>
<tr>
<td>Cidofovir</td>
<td>Compounded</td>
<td>0.5% solution</td>
<td>Apply twice daily.</td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>Zirgan</td>
<td>0.15% gel</td>
<td>Undetermined.</td>
</tr>
<tr>
<td>Acyclovir</td>
<td>Zovirax</td>
<td>Tablets, capsules</td>
<td>Effective plasma concentrations not reached</td>
</tr>
<tr>
<td>Valacyclovir</td>
<td>Valtrex</td>
<td>Tablets</td>
<td>Fatal in cats. DO NOT USE.</td>
</tr>
<tr>
<td>Famciclovir</td>
<td>Famvir, generic</td>
<td>Tablets</td>
<td>Undetermined. Safe at 90 mg/kg t.i.d. for 21 days.</td>
</tr>
</tbody>
</table>

Selection of an antiviral against FHV-1 is not necessarily a straightforward decision. An agent seemingly effective in one cat may have limited benefit in another. Topical irritation is common (especially with trifluridine) and
frequently misinterpreted as a treatment failure when conjunctival inflammation worsens. Patient cooperation and drug toxicity can limit duration of therapy. The stage of infection, severity of the clinical disease, owner finances, and likelihood of compliance are additional considerations. With no ideal antiviral to offer, treatment recommendations vary widely among ophthalmologists. The following summarizes a regimen I often use in the initial management of feline herpetic keratoconjunctivitis. It should be considered no more than a starting point from which an antiviral regimen can be tailored for your own feline patients.

- **Spontaneous recovery from primary FHV-1 infection occurs within 3 weeks. Antiviral therapy is seldom used in this instance, unless the conjunctivitis is particularly severe or accompanied by corneal ulceration.** A topical antibacterial ointment such as tetracycline or erythromycin, with efficacy against *Chlamydophila felis*, is applied 3 to 4 times daily for 2 to 3 weeks to eliminate other primary conjunctival pathogens and discourage secondary bacterial infection.

- **Antiviral therapy is the mainstay of treatment in adult cats with recrudescence conjunctivitis or keratitis.** Treatment may be optional in patients with mild conjunctivitis, as the reactivation can be self-limiting. In patients with severe discomfort, inflammation, and/or ulceration, treatment begins with either oral famciclovir or topical cidofovir, the route based on the owner’s ability to administer the drug reliably. Famciclovir is empirically dosed at 20 to 30 mg/kg q 8 to 12 hours for 2 to 3 weeks. Alternatively, 0.5% cidofovir is applied to the affected eye q 12 hours for 2 to 3 weeks. In either instance, treatment is continued for 1 week beyond resolution of clinical signs. If negligible response is seen, then a second 2- to 3-week regimen is prescribed using the alternative antiviral. If clinical signs have improved but not resolved, a second 2-week regimen continues with the same antiviral as originally prescribed. Famciclovir and cidofovir are expensive, even in generic form. If cost is a factor, then topical idoxuridine is my recommended alternative.

- **L-lysine inhibits *in vitro* FHV-1 replication, presumably by competitive inhibition of arginine during viral nucleocapsid assembly.** It has been advocated to reduce severity and/or frequency of recrudescence episodes. Recent evidence brought lysine’s benefits into question, after a study in shelter cats fed diets formulated with lysine showed increases in disease severity and viral shedding. These results may disprove lysine’s benefits or may simply expose the limitations of lysine in shelters with factors such as group housing, variable food consumption, and viral transmission by contaminated utensils and personnel. A primary investigator in one of the shelter studies continues to recommend an oral bolus of 500 mg L-lysine twice daily to client-owned cats.

- **Interferons (IFNs) are released by host cells in response to viral infection.** Although these cytokines have no effect on infected cells, they are thought to limit infection of healthy cells and shorten the disease course. Although anecdotal clinical improvement is seen in cats with conjunctivitis treated solely with a compounded topical IFN-α2β solution (3000 U/ml) t.i.d., a recent study showed no improvement in clinical disease or viral shedding in naturally infected cats treated b.i.d. for 14 days.

- **As a general rule, corticosteroids should be avoided in the treatment of feline conjunctivitis until an infectious cause has been ruled out.** Ample evidence exists warning against the use of corticosteroids in herpes-infected individuals. It is not uncommon to see reactivation of herpesvirus conjunctivitis or ulceration when using steroids in the treatment of other ocular disorders such as anterior uveitis. Careful consideration is also warranted regarding use of topical cyclosporine or nonsteroidal anti-inflammatory drugs (NSAIDs) to manage surface inflammation in herpes-infected cats. Contradictory reports of the safety of these medications in nonfeline species describe either substantial improvement (with or without antivirals), maintenance of the status quo, or exacerbation of clinical signs comparable to that of steroid use. Jean Stiles advocates adding 0.03% flurbiprofen or 0.2% cyclosporine to the conventional antiviral regimen when marked inflammation persists despite a 2-week course of antivirals.

- **Give the eye a break.** If a prolonged topical regimen of antiviral +/- antibiotic fails to improve clinical signs, stop treatment for a few days. Topical antivirals are not only toxic to viruses but also to epithelial cells! A preservative-free artificial tear such as Celluvisc provides soothing lubrication during the washout period.

- **Poorly adherent epithelium at the margins of geographic ulcers should be debrided with a sterile cotton-tipped swab following topical anesthesia.** Normal epithelial migration improves and the cornea’s viral load decreases. The cat’s loose epithelial margin should be not confused with the indolent-type ulcer commonly seen in middle-aged and older dogs. **Keratotomy is contraindicated in herpes-infected cats due to the risk of corneal sequestration following this procedure.**
• Conjunctival/intranasal vaccination has been recommended for cats with chronic herpetic disease to boost local antiviral immunity. No experimental evidence exists to indicate this method is beneficial in reducing persistent infections. Perhaps the best use of topical vaccine is in the management of endemic disease in catteries where exposure to the virus occurs early and often.

**Corneal Sequestrum**

Corneal sequestration is characterized by a brown to black plaque that develops in the central or paracentral feline cornea. The lesion represents coagulation necrosis of the corneal stroma. The mechanism underlying the lesion’s bronze to black color remains a mystery. Retrospective studies indicate an anatomical predisposition to sequestrum formation in brachycephalic breeds of cat and a relationship with herpesvirus infection in non-brachycephalics. The problem is most often unilateral. In addition to the characteristic color change of the affected cornea, clinical signs include varying degrees of ocular discharge and blepharospasm. With time, corneal edema and vascularization are seen in response to the necrosing tissue. The presence of inflammatory cells surrounding the necrotic collagen has been attributed to a foreign body reaction. With luck, a sequestrum may slough spontaneously after several weeks to months.

Topical antibiotic therapy may be used to prevent secondary bacterial infection of the associated corneal erosion, but such therapy will have negligible effect on resolution of the sequestrum itself. Topical corticosteroids are generally contraindicated. Topical lubricants may symptomatically decrease discomfort by providing a barrier over exposed corneal nerve endings. In patients with a stubborn sequestrum, in those with notable discomfort, or in cats with progressive vascularization and scarring, a keratectomy may be indicated to remove the sequestrum, followed by a thin conjunctival graft or lamellar corneal graft to reduce the likelihood of recurrence of the sequestrum. Recurrence is possible, as is second eye involvement.

**Eosinophilic Keratitis**

Eosinophilic keratitis is a progressive, infiltrative corneal disease of unknown etiology that usually affects young adult mixed breed cats. Cell types found in affected tissues suggest an immunologic basis for the disease. Herpesvirus infection has been documented concurrently in some patients. Unilateral lesions predominate, with bilateral involvement in only 25% to 33% of patients. The typical lesion appears as a raised, irregular, white to pink vascularized mass affecting the superior temporal or inferior nasal corneal quadrants. Chronic disease is more likely to involve multiple corneal quadrants. Rule-outs include squamous cell carcinoma, chronic ulceration with secondary granulation tissue, foreign body granuloma, and fungal keratitis. Diagnosis is based on clinical signs and cytology. Scrapings of the lesion contain mixed inflammatory cells, eosinophils, and occasional mast cells; biopsies often include lymphocytes and plasma cells.

Treatment includes topical corticosteroids (1% prednisolone acetate or 0.1% dexamethasone q.i.d.), gradually tapering the frequency as response to therapy occurs. Topical 0.02% tacrolimus solution has been effective in some patients. Rapid improvement is often seen with oral megestrol acetate (5 mg daily for 5 days, quickly tapering the dose to avoid endocrinologic complications). A topical antiviral should be included in patients infected with herpesvirus. Approximately 60% of patients with eosinophilic keratitis will relapse if therapy is discontinued.

**Keratoconjunctivitis Sicca**

KCS is rare in cats. Decreased tear production occurs occasionally in patients with chronic infectious conjunctivitis or keratitis. Schirmer tear test (STT) values are consistently less than 5 mm/minute. Feline herpesvirus-1 is usually implicated in the pathogenesis of the problem owing to secondary ductal occlusion or lacrimal adenitis. Because the STT can decrease substantially in anxious cats, a single low reading may be insignificant. In contrast to canine KCS with marked corneal vascularization, pigmentation, and ocular discharge, feline KCS is characterized by variable conjunctival hyperemia and mild diffuse corneal opacification resulting from epithelial hyperplasia.

Response to cyclosporine or tacrolimus is usually poor owing to the viral rather than immunologic pathogenesis of the tear film deficiency. Some cats will respond to a regimen of oral famciclovir and topical lubricants. Topical corticosteroids should be used cautiously, if at all, in dry-eyed cats suspected of herpesvirus infection.

**References available upon request.**