

## FELINE INFECTIOUS CONJUNCTIVITIS

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Feline conjunctivitis is a common and often frustrating clinical problem. It is most frequently caused by feline herpesvirus-1 (FHV-1) or chlamydia, primary feline pathogens capable of infecting the healthy ocular surface. Chronic or recurrent episodes are attributed to the latent characteristics and carrier states of these organisms. Such primary infections are in contrast to infectious conjunctivitis in the dog, which is almost always a secondary bacterial complication of adnexal disease such as entropion or dry eye.

Owing to the frequent infectious nature of feline conjunctivitis, ***symptomatic therapy of feline conjunctivitis with topical and/or systemic corticosteroids is contraindicated*** until an infectious etiology is disproved. Clinical signs of inflammation may initially decrease with steroid therapy, but the immunosuppressive effects increase the risk of herpes-related corneal ulceration, lengthen the period of ocular virus shedding, and encourage deeper corneal infection. Many of the particularly refractory cases of ocular FHV-1 infection seen in our practice are preceded by corticosteroid use. Clients should also be educated regarding the chronic nature of feline conjunctivitis and prepared for the possibility of treatment failures, particularly in herpes-infected animals.

### Pathogenesis and Clinical Signs

Feline herpesvirus-1 and *Chlamydia psittaci* are relatively unstable outside the body, surviving less than 48 hours at room temperature. Because transmission requires intimate contact between infected and susceptible animals, chronic ocular infections tend to occur more frequently in catteries and multi-cat households. The limited ability of FHV-1 and chlamydia to stimulate long-lasting immunity no doubt contributes to the development of chronic disease and the difficulty of limiting infection in multi-cat environments. Some degree of immunity may nevertheless explain the absence of respiratory signs in adult cats with conjunctivitis.

Natural and exogenous stress factors have a proven role in reactivating latent ocular infections. Physiologic stressors include pregnancy, lactation, estrus, or concurrent systemic illnesses. Common external events that cause recurrence of clinical signs include relocation to a new home, introduction of new individuals (human or animal) into the household, participation in cat shows, and administration of corticosteroids.

### *Herpesvirus-1*

The typical patient with viral conjunctivitis is a neonatal or adolescent cat with an acute, conjunctival-respiratory infection. The acute ocular disorder is characterized by bilateral involvement, pronounced hyperemia and serous discharge. A mucopurulent discharge develops as the disease follows its typical 10 to 14 day course. In most cases, primary infections resolve with few residual ocular lesions, although conjunctival adhesions to adjacent tissues (symblepharon) frequently occur in very young kittens. Long term consequences of these adhesions include epiphora due to occlusion of the nasolacrimal puncta, third eyelid protrusion, reduced eyelid mobility, and permanent corneal opacity.

Following recovery from the initial viral episode, an estimated 80% of cats become latently infected; 45% of these will either shed the virus asymptotically or will develop recurrent clinical disease. Cats may have intermittent episodes of ocular disease, after which they appear clinically normal, or may have chronic clinical signs that do not regress naturally or do not respond to treatment. Unlike the acute disease, recurrent herpesvirus conjunctivitis is often unilateral and is characterized by intermittent blepharospasm, mild conjunctival hyperemia, and serous discharge, without signs of respiratory infection.

In patients with chronic conjunctivitis, decreased tear production (Schirmer tear test less than 5mm/min) can occur. FHV-1 is usually implicated in the pathogenesis of the problem, either as a consequence of ductal occlusion or lacrimal adenitis. Response to cyclosporine is frequently poor. Because Schirmer tear test values can decrease substantially in anxious cats, a single low reading in the absence of corneal dullness or vascularization may be insignificant.

## *Chlamydia psittaci*

In contrast to herpes-infected cats, patients with acute *chlamydia* rarely demonstrate signs of upper respiratory disease beyond a mild rhinitis. Conjunctivitis is initially unilateral, often characterized by marked conjunctival edema (chemosis), with serous to mucopurulent discharge. Clinical signs appear in the second eye 5-7 days later. Conjunctival follicles have been described as a feature of chlamydial infection but can also be seen in chronic herpes-infected patients. Chronic chlamydial conjunctivitis may be unilateral or bilateral, with mild blepharospasm, serous discharge and mild conjunctival hyperemia.

## *Other infectious agents*

Although *Mycoplasma spp* have been isolated from the cul-de-sacs of cats with chronic conjunctivitis, the organisms are also prevalent in the conjunctival sacs of normal animals. This ubiquitous nature, coupled with the difficulty of experimentally establishing mycoplasmal conjunctivitis in the absence of other organisms, suggests that mycoplasma is significant only as a secondary pathogen. Caliciviruses and reoviruses are considered insignificant ocular pathogens.

## **Diagnostics**

Since the initial herpesvirus conjunctivitis has a short clinical course and acute chlamydial conjunctivitis responds readily to antibacterial therapy, diagnostics are not usually performed in acute infectious conjunctivitis. Intracytoplasmic inclusions may be seen in conjunctival scrapings taken during the first few days of an acute chlamydial infection, but are unlikely to be found in chronic cases. Herpesvirus intranuclear inclusions are not identifiable in routinely prepared conjunctival scrapings.

Determination of the etiologic agent in chronic, recurrent conjunctivitis in the adult cat is especially difficult. A report by Nasisse et al suggested that an etiologic diagnosis cannot be made in the majority of chronically affected cats using aerobic bacterial and chlamydial cultures, viral isolation, immunofluorescent antibody techniques, serology or cytology. The reasons for this remain unclear, but it is theorized that the quantity of antigen present in chronic cases may be too low to be detectable by routine methods. Maggs, Lappin et al also concluded that serum neutralization, ELISA, virus isolation and IFA were of limited value in the diagnosis of chronic FHV-1 disease. Although polymerase chain reaction testing theoretically improves detection of viral or chlamydial DNA, most ophthalmologists doubt the validity of currently available tests due to poor correlation with clinical signs. These studies and perceptions may explain why only a handful of veterinary ophthalmologists attending a workshop on feline ocular disease at the 2001 ACVO scientific meeting indicated that they routinely perform one or more of these tests on FHV-1 suspects.

A clinical feature that clearly distinguishes herpesvirus infection from chlamydial infection is the presence of corneal ulceration. Linear branching epithelial ulcers termed dendrites are pathognomonic for herpetic keratitis, but these early indicators of viral replication within epithelial cells are usually subtle and may not be evident without use of rose bengal vital stain. Most dendritic lesions coalesce to form superficial ulcers that are geographic or amoeboid in shape.

A complete physical examination and diagnostic evaluation for concurrent diseases is indicated, as underlying systemic disease can predispose cats to chronic ocular infections. Because FIV and FeLV infections are detected in a higher percentage of cats with chronic conjunctivitis compared with the general population, it is recommended that the patients be routinely screened for these viral agents.

## **Therapy**

### *Acute conjunctivitis*

The usual approach to acute feline conjunctivitis is to “treat the treatable”. Symptomatic ocular therapy is directed against chlamydia and secondary bacterial pathogens, coupled with supportive systemic care for coexisting respiratory disease. Since the primary viral infection is self-limiting in 10-14 days, ocular antiviral therapy is rarely used during the initial infection. The exception would be in patients with concurrent corneal ulceration. There is no known way of preventing viral latency, even if antiviral therapy is initiated at this early stage of infection.

*Chlamydia* spp are resistant to many common topical ophthalmic antibiotics including bacitracin, neomycin, and gentamicin. The treatment of choice is topical tetracycline applied 4 times daily, but the ointment is often quite irritating. Alternative topical antibacterials that are better tolerated include erythromycin, chloramphenicol, and the fluoroquinolones such as ofloxacin. A 3-week regimen of therapy is recommended to discourage development of a carrier state.

In refractory or severe chlamydial infections, concurrent systemic therapy may be beneficial. Although tetracycline would be an excellent choice with respect to sensitivity of the organism, the risk of discoloration of dental enamel would preclude its use in young patients. Doxycycline is not as likely to produce such discoloration in the short term but the possibility still exists in the 3-week regimen recommended to eliminate the chlamydial carrier state (5mg/kg BID for 21 days). A macrolide antibacterial, azithromycin, has the advantages of a longer half-life and less frequent administration, but is substantially more expensive. The usual dosage is 5mg/kg daily for 5 days, then 5mg/kg every 72 hours for 5 doses. Anecdotal reports of efficacy are very encouraging, but there are no controlled studies documenting the efficacy of azithromycin for ocular chlamydia in the cat.

To summarize, a young kitten with conjunctivitis and upper respiratory disease will receive supportive care for the URI, coupled with topical and/or systemic therapy to address chlamydial infection. Herpesvirus will run its course, with development of latency likely.

### *Chronic conjunctivitis*

Therapy for the older cat with recurring bouts of conjunctivitis is first directed against *Chlamydia*, as described for the acute episode. Failure to respond to a 3-week course of oral doxycycline or azithromycin implicates herpesvirus as the inciting cause and subsequent treatment is based on the severity, duration, and frequency of the outbreaks.

In mild cases, oral L-lysine supplementation may alleviate clinical signs by suppressing arginine incorporation into viral proteins and limiting viral replication. The recommended lifelong dosage in adult patients with chronic conjunctivitis is 500mg twice daily. Lysine is readily available in health food and drug stores in 500-1000mg tablets that can be ground and administered in moist food to reduce the likelihood of gastric upset. The supplement is well tolerated in the vast majority of patients.

Topical antibiotic ointments or artificial tear supplements may provide symptomatic relief in mild viral conjunctivitis by providing lubrication and surface protection to partially relieve discomfort. Erythromycin ointment applied 2-4 times daily is commonly used for this purpose. Hylashield, a viscous preservative-free artificial tear solution available from I-Med Pharma (800-463-1008) can be applied 2-3 times daily for long lasting lubrication and a subjectively soothing effect on the inflamed conjunctiva. Obviously these products have no effect on the underlying viral etiology.

Topical antivirals, particularly trifluridine, may subjectively shorten the course and severity of the conjunctivitis but are generally reserved for patients with severe disease because of secondary irritation, expense, and the frequent application required for these virostatic compounds. Although in vivo efficacy studies in the cat are lacking, the dosage frequency recommended for the treatment of human herpetic keratitis appears appropriate: q1-2 hrs the first day, then 5 times daily for the course of therapy. Topical antivirals should not be applied for more than 3 weeks at a time due to epithelial cell toxicity. Available products are summarized below.

**Table 1. Topical antivirals for use in feline herpesvirus infections**

Active Ingredient	Brand Name	How Supplied	Comments
Vidarabine	Vira-A (Monarch)	3% ointment	Well tolerated in most cats. Low to medium efficacy against FHV-1
Idoxuridine	Pharmaceutically compounded	0.1% solution	Moderately irritating in some cats. Medium efficacy against FHV-1. Stable at room temperature.
Trifluridine	Viroptic (Monarch)	1% solution	Very irritating in most cats. Best in vitro efficacy against FHV-1. Very expensive. Refrigerate

Experimental studies of systemic antivirals in the treatment of FHV-1 have been disappointing. Effective systemic concentrations cannot be safely achieved with acyclovir in the cat. An acyclovir pro-drug, valacyclovir, is toxic to feline bone marrow, kidneys, and liver. The safety and efficacy of newer systemic antivirals such as famciclovir have yet to be established.

A variety of other products have been advocated in the management of refractory or recurrent herpetic conjunctivitis. Oral and topical interferon (IFN- $\alpha$ ) may protect uninfected cells from viral invasion. Slow oral administration of 30 IU once daily is recommended to facilitate pharyngeal absorption rather than gastric digestion. Topical application of 1 drop of a 25-50 IU/ml solution 4-6 times daily may be used alone or in combination with oral interferon. The stability of interferon may be limited when thawed and when compounded at low concentrations.

Topical povidone iodine (10% stock solution) may be clinically effective in dilutions of 1:10 (1%) or 1:20 (0.5%) applied 3-4 times daily in herpes-infected cats. The product is well tolerated at these concentrations and is an inexpensive option to other topical antiviral products. Rather than interfering with DNA synthesis as conventional antivirals do, povidone iodine interacts with the virus during its brief extracellular phase.

Topical cyclosporine has been shown to reduced inflammation and scarring in human, rabbit, and mouse herpes studies but the safety of this agent has not been determined in herpes-infected cats. If inflammation is so severe as to warrant anti-inflammatory therapy, the most prudent and defensible regimen would combine cyclosporine with an antiviral to minimize the risk of viral proliferation secondary to cyclosporine's immunosuppressive effects. Topical and systemic corticosteroids should never be used.

### **Prognosis**

Chronic feline conjunctivitis is a frustrating clinical problem, difficult to pinpoint etiologically and almost impossible to cure. Owners must be educated regarding the latent characteristics of the common pathogens, prepared for treatment failures, and willing to accept the possibility of lifelong ocular disease in their pet. Realistic expectations of antiviral efficacy should take into account the availability of drugs developed only for human herpes simplex rather than feline herpesvirus-1. The impact of physiologic and environmental stressors should be recognized and minimized. Control of infectious conjunctivitis in catteries may not be possible without strict quarantine, aggressive vaccination practices, uncompromising hygiene, and elimination of chronic carriers.

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