

# Conjunctivitis in Cats

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▲ **FIGURE 1** Rhinosinusitis, conjunctivitis, and mucopurulent ocular discharge in a patient with FHV-1 infection. *Photo courtesy of Michael G. Davidson, DVM, DACVO*

## PROFILE

### Definition

- ▶ Conjunctivitis is an inflammation of the conjunctiva, a tissue that lines the eyelids and covers the sclerae.
- ▶ The conjunctiva is an exposed mucous membrane that reacts to antigenic stimulation caused by contact with noxious stimuli.
- ▶ The superficial stroma of the conjunctiva is rich in lymphatic tissue, both diffuse and aggregated.
  - When aggregated tissue is stimulated, it forms lymphoid follicles, which produce effector cells. Conjunctival plasma cells produce specific immunoglobulins as part of the secretory component of the immune response.<sup>1,2</sup>

### Causes

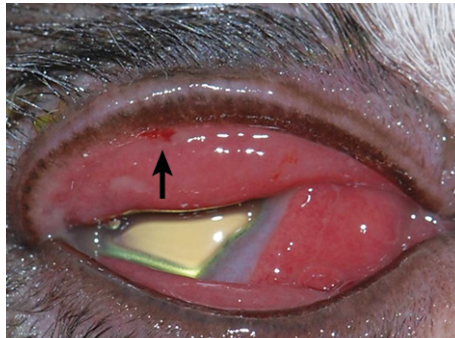
- ▶ Infectious primary pathogens
  - Cause of most cases of feline conjunctivitis<sup>1,3-6</sup>
- ▶ Feline herpesvirus type 1 (FHV-1)
  - Most common cause of conjunctivitis in cats
  - Studies suggest that 95% of cats worldwide have been exposed to the virus, and at least 80% of cats are latent carriers of the virus.<sup>7-11</sup>

- ▶ *Chlamydophila felis*
  - A common cause of conjunctivitis, especially in young kittens<sup>6,12-14</sup>
- ▶ Calicivirus
  - Primarily a respiratory tract pathogen that may cause mild and transient conjunctivitis
  - Most cats will recover spontaneously.<sup>15</sup>
- ▶ *Mycoplasma* spp
  - Can be present in healthy cats, however, and may thrive because of coinfection with FHV-1 or *C felis*, making its clinical significance questionable<sup>1,3-6,12-13</sup>
- ▶ Because of their epidemiologic prevalence, only FHV-1 and *C felis* will be discussed in this article.

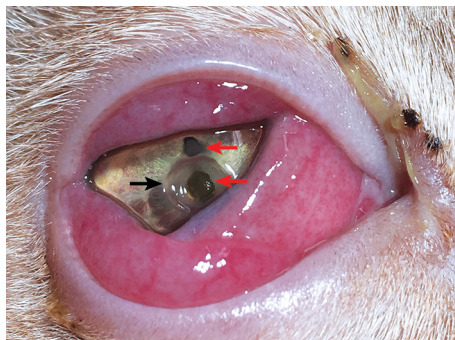
### Pathophysiology

- ▶ FHV-1 conjunctivitis
  - The primary disease commonly occurs in kittens and is caused by exposure to wild-type FHV-1, which is transmitted between cats by microdroplets (frequently from the queen) or fomites (possibly by the client).<sup>1,3</sup>
  - FHV-1 infection is characterized by conjunctivitis,

FHV-1 = feline herpesvirus type 1



▲ **FIGURE 2** Conjunctivitis and conjunctival ulceration (**black arrow**) in a patient with FHV-1 infection. Although *C felis* may cause conjunctivitis, presence of an ulcer indicates a viral disease. Photo courtesy of Michael G. Davidson, DVM, DACVO



▲ **FIGURE 3** A deep corneal ulcer (**black arrow**) partially obscuring the pupil (**red arrows**) in a patient with FHV-1 infection. Note the congested conjunctiva. Photo courtesy of Karin Berggren, DVM



▲ **FIGURE 4** Stromal keratitis in a patient with FHV-1 infection. Stromal keratitis is an immune-mediated reaction of the cornea to the viral particles. White-gray stromal infiltration is seen in the axial cornea surrounded by corneal blood vessels. Photo courtesy of Hebrew University of Jerusalem Seth Koch Slide Collection

respiratory tract signs (**Figure 1**), and, less frequently, corneal ulceration.<sup>4,5</sup>

- Following primary, and usually self-limiting, disease, FHV-1 establishes lifelong latency in the trigeminal ganglia.
  - The virus is cleared in only a limited number of cats.<sup>7</sup>
- Stress or treatment with steroids will induce subsequent reactivation and shedding of the virus and may result in recrudescence disease.<sup>8-9</sup>
  - Recrudescence disease is usually milder than the primary infection and can affect the cornea, conjunctiva, and/or respiratory system.<sup>9,11,16</sup>
- The recurrent disease may be cytolytic (because of viral replication) and cause conjunctival (**Figure 2**) or corneal (**Figure 3**) ulceration; it also may be immune-mediated and cause stromal keratitis (**Figure 4**) or chronic lymphoplasmacytic conjunctivitis.<sup>1,4,11</sup>
- ▶ *C felis* conjunctivitis
  - Cats are infected by airborne transmission or contact with infected cats or fomites.<sup>1,3</sup>
  - The infection initially may be unilateral.
    - It usually spreads to the other eye within a week, but some cases may remain unilateral.<sup>4</sup>
    - If untreated, chronic disease, characterized by membranous or follicular conjunctivitis, may occur, or the cat may become a subclinical carrier and contribute to the spread of the disease.<sup>5</sup>
  - Natural immunity may develop, and the disease is rarely seen in cats older than 5 years of age.<sup>17</sup>

### History & Physical Examination

- ▶ In cases of FHV-1 conjunctivitis, client questioning may reveal stressful events (eg, rehoming, traveling, introduction of a new pet or baby to the household) preceding the appearance of clinical signs.
- Pregnancy, parturition, lactation, concurrent illness, or treatment with glucocorti-

coids can also induce viral shedding and recrudescence disease.<sup>1,3-5,7,17</sup>

- ▶ In kittens with FHV-1 conjunctivitis, physical examination may show severe signs of upper respiratory disease, including fever, sneezing, rhinitis, and purulent nasal discharge.
- These signs are milder in cases of *C felis* conjunctivitis and in adult cats with FHV-1 conjunctivitis and may include nasal discharge and sneezing.<sup>1,3-5,11,16</sup>

### Clinical Signs

- ▶ Clinical signs are usually more severe in FHV-1 primary disease in kittens and milder in *C felis* and adult FHV-1 disease.
  - Clinical signs may help distinguish between the pathogens.<sup>1,3-5,7,11,16,17</sup>
- ▶ Hyperemia of conjunctival vessels (ie, red eye) is usually more marked in FHV-1 conjunctivitis than in *C felis* conjunctivitis.
- ▶ Conjunctival edema (chemosis), swelling, and thickening is usually more marked in *C felis* conjunctivitis than in FHV-1 conjunctivitis (**Figure 5**).
- ▶ Ocular discharge may be mucoid in *C felis* conjunctivitis and adult FHV-1 conjunctivitis and purulent in kittens with FHV-1 conjunctivitis (**Figure 1**).
- ▶ Conjunctival ulceration is more characteristic of FHV-1 disease, especially in kittens (**Figure 2**).
- ▶ Concurrent corneal involvement and ulceration may be seen in FHV-1 conjunctivitis but not in *C felis* conjunctivitis (**Figures 3 and 4**).
- ▶ Minimal ocular pain, but possible discomfort, expressed as blepharospasm, may be seen in conjunctivitis but is marked in cases of corneal ulceration.

### DIAGNOSIS

#### Clinical Diagnosis

- ▶ As compared with *C felis* infection, FHV-1 infection causes greater conjunctival hyperemia and ocular discharge, and respiratory



▲ **FIGURE 5** Chemosis and conjunctivitis without corneal involvement in a patient with *C felis* infection

signs are usually more severe, especially during the primary disease (**Figure 1**).

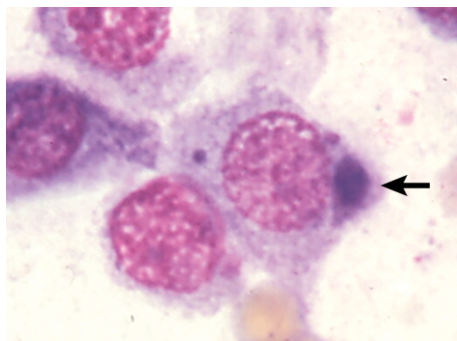
- Recurrent disease, keratitis, and corneal and conjunctival ulceration are definitive hallmarks of FHV-1 infection (**Figures 2-4**).
  - Presence of symblepharon, or adhesions between the cornea and conjunctiva, indicates previous FHV-1 infection.<sup>1,3-5,7,17</sup>
- ▶ Chemosis is more severe in *C felis* infection than in FHV-1 infection and is the most notable clinical sign (**Figure 5**).
  - Although infection with *C felis* is generally mild, chlamydial conjunctivitis can be persistent, especially if not treated.
  - In chronic stages, membranous or follicular conjunctivitis may develop.<sup>1,3-5,7-8</sup>
- ▶ Diagnosis may also be based on response to treatment.
    - FHV-1 involvement should always be suspected in patients with conjunctivitis.
    - *C felis* infection may be considered in patients with acute chemosis or chronic disease.<sup>1,4,11</sup>

### Differential Diagnoses

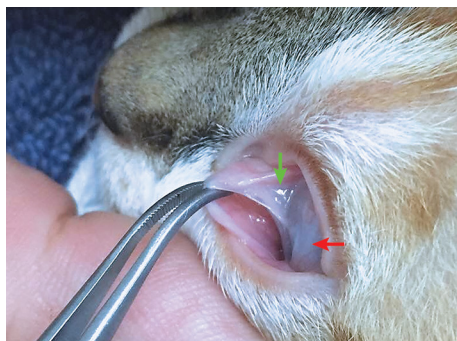
- ▶ Eyelid and eyelash disorders
  - Rare causes of conjunctivitis in cats
  - Dry eye (ie, keratoconjunctivitis sicca) is commonly a sequela of FHV-1 infection rather than a primary cause of feline conjunctivitis.<sup>1,4,11</sup>

FHV-1 = feline herpesvirus type 1

- ▶ Calicivirus, *Mycoplasma* spp, and *Bordetella bronchiseptica*<sup>1,4,12-13,15</sup>
- ▶ Lipogranulomatous, eosinophilic, and parasitic conjunctivitis<sup>1,3-5,17</sup>
- ▶ Red eye
  - Clinical sign of anterior uveitis and glaucoma
- ▶ Appropriate testing for these conditions should be performed.



▲ **FIGURE 6** Presence of an intracytoplasmic elementary body in an epithelial cell collected from a conjunctival scrape (**arrow**) is indicative of *C felis* infection. Photo courtesy of Michael G. Davidson, DVM, DACVO



▲ **FIGURE 7** Symblepharon, or adhesions between the cornea and conjunctiva, is a common complication of FHV-1 keratoconjunctivitis. In this case, most of the cornea is obscured because of adhesions of the bulbar conjunctiva (**red arrow**). Adhesions between the bulbar conjunctiva of the third eyelid and cornea (**green arrow**) are also present.

## Laboratory Findings

- ▶ Diagnostic tests for FHV-1 include immunofluorescent antibody testing, viral isolation of FHV-1 in feline cell cultures, and polymerase chain reaction (PCR).<sup>1,3,4</sup>
  - False-negative and false-positive test results are common because of subclinical shedding of FHV-1 by healthy animals, reduced shedding in recrudescence stages of the disease, and high prevalence of antibodies from vaccination and exposure.<sup>12-14</sup>
- ▶ Diagnostic tests for *C felis* include PCR and cytologic evaluation. Presence of intracytoplasmic elementary bodies in epithelial cells collected from conjunctival scrapes (**Figure 6**) is indicative of *C felis* infection.<sup>12-14,18</sup>
  - These bodies are transient and can be difficult to identify.
- ▶ As the utility of diagnostic testing is limited, treatment based on clinical signs without confirmation of the underlying disease is an acceptable approach to conjunctivitis in cats.<sup>1,3-5,7,11</sup>

## TREATMENT

### Inpatient or Outpatient

- ▶ Reducing stress is important in treating FHV-1 infection and may help determine the choice of therapy.
  - Some topical antiviral drugs require frequent administration, which can increase patient stress. In mild cases, no treatment may be preferable.<sup>1,3-5,7,11,17</sup>
- ▶ When possible, patients with conjunctivitis should receive treatment at home, where clients can provide a nurturing and less stressful environment.

### Medical

- ▶ Medical management includes use of topical and oral antivirals and antibiotics.
- ▶ *C felis* conjunctivitis
  - Treated with topical ointment containing 1% tetracycline q6-8h for 1 to 2 weeks
  - Recent studies suggest that topical treat-

- ment be supplemented, or even replaced, with oral doxycycline 10 mg/kg q24h for 3 weeks.
- Systemic treatment may be indicated in patients with concurrent respiratory disease.
  - Systemic treatment is also useful in preventing secondary ocular bacterial infection in FHV-1 conjunctivitis.<sup>19,20</sup>
  - Rapid resolution of signs during treatment may suggest that *C felis* is the causal agent.
- ▶ Topical antiviral drugs
- Usually administered 5 to 6 times a day, with treatment continuing for 10 to 14 days after resolution of signs<sup>21,22,25</sup>
  - Trifluridine 1%, idoxuridine 0.1%, and vidarabine 3%
    - Variably effective<sup>19,21-25</sup>
    - Trifluridine has the highest efficacy and provides transcorneal penetration but may be more irritating to cats.<sup>19-23</sup>
    - Idoxuridine and vidarabine are less irritating but may be difficult to obtain because they are not widely available commercially.
      - They can be ordered from compounding pharmacies.
  - Cidofovir 0.5%
    - Unavailable commercially as an ophthalmic preparation
    - Has strong in vitro and in vivo efficacy against FHV-1 infection, with treatment reducing severity of clinical signs and viral shedding<sup>26-28</sup>
    - Has beneficial effects when administered q12h, which is a significant advantage as compared with other topical antiviral medications.<sup>26-28</sup>
    - Less toxic than other antivirals because of its relatively high specificity for viral—rather than host—replication proteins<sup>26-28</sup>
- ▶ Systemic antiviral treatment
- Famciclovir
    - A prodrug of penciclovir
    - Safe and effective for treating FHV-1 conjunctivitis

- Recommended dose is 90 mg/kg q12h<sup>29-33</sup>
- ▶ All current systemic and topical antiviral drugs are virustatic and achieve their effect by interfering with active viral DNA replication.
- They are ineffective at eradicating latent infection.
  - Significant toxicity can occur with antiviral administration because of the intracellular location of the virus and the inability of available medications to selectively target viral—rather than host cell—replication.<sup>19,21-25</sup>
- ▶ Many commercially available antiviral drugs, notably acyclovir, are effective against human herpes simplex virus but ineffective against FHV-1.<sup>20-25</sup>
- Others, such as valacyclovir, may be toxic to cats and should not be used.<sup>19,23</sup>
- ▶ Most patients greatly benefit from frequent application of high-quality artificial tear (eg, hyaluronate) preparations, as FHV-1 infection reduces conjunctival goblet cells and causes qualitative tear film disorders.<sup>1,4,34,35</sup>
- ▶ Glucocorticoid use in cats should be considered carefully, as these drugs may also induce viral shedding.
- When glucocorticoid treatment is unavoidable (eg, in patients with eosinophilic keratitis or anterior uveitis), concurrent antiviral treatment should be provided and the patient monitored closely for recrudescence disease.
  - Because FHV-1 infection may be reactivated during immunosuppression, the prognosis is poor in immunosuppressed patients (eg, those with feline leukemia virus or feline immunodeficiency virus).<sup>1,3-5,7,11,17</sup>

### Client Education

- ▶ Clients should be advised that:
- Antiviral drugs are ineffective against latent FHV-1 infection.
  - Few cats will clear the virus, and it will

FHV-1 = feline herpesvirus type 1  
 PCR = polymerase chain reaction

remain latent in most patients.  
 • Even after clinical signs have resolved, recurrence of disease is possible, especially when cats experience stress.<sup>8,11,19</sup>

**FOLLOW-UP & COMPLICATIONS**

- ▶ Treatment should be continued for 2 weeks after resolution of clinical signs and the patient re-examined.<sup>8,19,23</sup>
- ▶ FHV-1 has been implicated in the pathogenesis of corneal sequestrum, eosinophilic keratitis, and dry eye.<sup>4,7,17</sup>
- These should be regarded as possible sequelae of infection.
- In kittens, FHV-1 keratoconjunctivitis may result in ulceration of both the cornea and conjunctiva.
- These ulcerated tissues may

adhere to each other and form symblepharon (**Figure 7**, page 98), which is challenging to treat and requires surgical intervention.<sup>4,7,17</sup>

**PROGNOSIS**

- ▶ Most patients with FHV-1 infection will remain carriers of the virus.
- Recurrence is possible, particularly for patients in a stressful environment.
- ▶ Cats also may be subclinical carriers of *C felis*.
- The carrier state is not characterized by recurrent disease, but it contributes to the spread of *C felis* infection to other cats.<sup>1,4,13,15</sup>

FHV-1 = feline herpesvirus type 1

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**TRIFEXIS® (spinosad + milbemycin oxime) Chewable Tablets**

**Caution:** Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.  
**Before using TRIFEXIS chewable tablets, please consult the product insert, a summary of which follows:**

**Indications:**  
 TRIFEXIS is indicated for the prevention of heartworm disease (*Dirofilaria immitis*), TRIFEXIS kills fleas and is indicated for the prevention and treatment of flea infestations (*Ctenocephalides felis*), and the treatment and control of adult hookworm (*Ancylostoma caninum*), adult roundworm (*Toxocara canis* and *Toxascaris leonina*) and adult whipworm (*Trichuris vulpis*) infections in dogs and puppies 8 weeks of age or older and 5 pounds of body weight or greater.

**Dosage and Administration:**  
 TRIFEXIS is given orally, once a month at the minimum dosage of 13.5 mg/lb (30 mg/kg) spinosad and 0.2 mg/lb (0.5 mg/kg) milbemycin oxime body weight. For heartworm prevention, give once monthly for at least 3 months after exposure to mosquitoes (see **EFFECTIVENESS**).

**Contraindications:**  
 There are no known contraindications to the use of TRIFEXIS.

**Warnings:**  
 Not for human use. Keep this and all drugs out of the reach of children. Serious adverse reactions have been reported following concomitant extra-label use of ivermectin with spinosad alone, a component of TRIFEXIS (see **ADVERSE REACTIONS**).

**Precautions:**  
 Treatment with fewer than 3 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention (see **EFFECTIVENESS**).

Prior to administration of TRIFEXIS, dogs should be tested for existing heartworm infection. At the discretion of the veterinarian, infected dogs should be treated with an anthelmintic to remove adult heartworms. TRIFEXIS is not effective against adult *D. immitis*. While the number of circulating microfilariae may decrease following treatment, TRIFEXIS is not indicated for microfilariae clearance. Mild, transient hypersensitivity reactions manifested as labored respiration, vomiting, salivation and lethargy, have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

Use with caution in breeding females. The safe use of TRIFEXIS in breeding males has not been evaluated.

Use with caution in dogs with pre-existing epilepsy (see **ADVERSE REACTIONS**). Puppies less than 14 weeks of age may experience a higher rate of vomiting.

**Adverse Reactions:**  
 In a well-controlled US field study, which included a total of 352 dogs (176 treated with TRIFEXIS and 176 treated with an active control), no serious adverse reactions were attributed to administration of TRIFEXIS. All reactions were regarded as mild.

Over the 180-day study period, all observations of potential adverse reactions were recorded. Reactions that occurred at an incidence >1% (average monthly rate) within any of the 6 months of observation are presented in the following table. The most frequently reported adverse reaction in dogs in the TRIFEXIS group was vomiting.

Average Monthly Rate (%) of Dogs With Adverse Reactions

Adverse Reaction	TRIFEXIS Chewable Tablets*	Active Control Tablets*
Vomiting	6.13	3.08
Pruritus	4.00	4.91
Lethargy	2.63	1.54
Diarrhea	2.25	1.54
Dermatitis	1.47	1.45
Skin Reddening	1.37	1.26
Decreased appetite	1.27	1.35
Pinnal Reddening	1.18	0.87

\*n=176 dogs  
 In the US field study, one dog administered TRIFEXIS experienced a single mild seizure 2 1/2 hours after receiving the second monthly dose. The dog remained enrolled and received four additional monthly doses after the event and completed the study without further incident.

Following concomitant extra-label use of ivermectin with spinosad alone, a component of TRIFEXIS, some dogs have experienced the following clinical signs: trembling/twitching, salivation/drooling, seizures, ataxia, mydriasis, blindness and disorientation. Spinosad alone has been shown to be safe when administered concurrently with heartworm preventatives at label directions. In US and European field studies, no dogs experienced seizures when dosed with spinosad alone at the therapeutic dose range of 13.5-27.3 mg/lb (30-60 mg/kg), including 4 dogs with pre-existing epilepsy. Four epileptic dogs that received higher than the maximum recommended dose of 27.3 mg/lb (60 mg/kg) experienced at least one seizure within the week following the second dose of spinosad, but no seizures following the first and third doses. The cause of the seizures observed in the field studies could not be determined.

For technical assistance or to report suspected adverse drug events, contact Elanco Animal Health at 1-888-545-5293. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or <http://www.fda.gov/AnimalVeterinary/SafetyHealth>

**Post Approval Experience (Mar 2012):**  
 The following adverse reactions are based on post-approval adverse drug event reporting. The adverse reactions are listed in decreasing order of frequency: vomiting, depression/lethargy, pruritus, anorexia, diarrhea, trembling/shaking, ataxia, seizures, hypersalivation, and skin reddening.

**Effectiveness:**  
**Heartworm Prevention:**

In a well-controlled laboratory study, TRIFEXIS was 100% effective against induced heartworm infections when administered for 3 consecutive monthly doses. Two consecutive monthly doses did not provide 100% effectiveness against heartworm infection. In another well-controlled laboratory study, a single dose of TRIFEXIS was 100% effective against induced heartworm infections.

In a well-controlled six-month US field study conducted with TRIFEXIS, no dogs were positive for heartworm infection as determined by heartworm antigen testing performed at the end of the study and again three months later.

**Flea Treatment and Prevention:**

In a well-controlled laboratory study, TRIFEXIS demonstrated 100% effectiveness on the first day following treatment and 100% effectiveness on Day 30.

In a well-controlled laboratory study, spinosad, a component of TRIFEXIS, began to kill fleas 30 minutes after administration and demonstrated 100% effectiveness within 4 hours. Spinosad, a component of TRIFEXIS, kills fleas before they can lay eggs. If a severe environmental infestation exists, fleas may persist for a period of time after dose administration due to the emergence of adult fleas from pupae already in the environment. In field studies conducted in households with existing flea infestations of varying severity, flea reductions of 98.0% to 98.8% were observed over the course of 3 monthly treatments with spinosad alone. Dogs with signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermitis and pruritus as a direct result of eliminating the fleas.

**Treatment and Control of Intestinal Nematode Infections:**  
 In well-controlled laboratory studies, TRIFEXIS was 100% effective in removing naturally and experimentally induced adult roundworm, whipworm and hookworm infections.

**Palatability:**

TRIFEXIS is a flavored chewable tablet. In a field study of client-owned dogs where 175 dogs were each offered TRIFEXIS once a month for 6 months, dogs voluntarily consumed 54% of the doses when offered plain as if a treat, and 33% of the doses when offered in or on food. The remaining 13% of doses were administered like other tablet medications.

NADA 141-321. Approved by the FDA  
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## LOOK FOR THESE ARTICLES IN FUTURE ISSUES

- ▶ Step-by-Step Basic Cardiology Examination
- ▶ Imaging Primary & Metastatic Bone Tumors
- ▶ Diagnosing & Treating Decreased Tear Production
- ▶ Pancytopenia in a Cat
- ▶ Step-by-Step Trichogram