**FOCAL POINT**

Although *Chlamyphila felis* infection is an important cause of feline conjunctivitis, much remains unknown regarding its pathogenesis, spectrum of clinical manifestations, and zoonotic potential.

**KEY FACTS**

- Chronic chlamydial infections may result from the ability of the organism to persist within tissue for prolonged periods, despite the host’s immune response, p. 232.
- The role of *C. felis* in reproductive disease and as a zoonosis remains unclear, p. 233.
- Diagnosis is most reliably made using cell culture or the polymerase chain reaction assay, p. 234.
- Completely eradicating the organism may be possible when all cats in the household are treated with oral doxycycline (5 mg/kg every 12 hours for 3 weeks), p. 234.
- Chlamydial vaccines have been associated with atypical reactions 7 to 21 days after vaccination in approximately 3% of cats, p. 235.

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**ABSTRACT:** *Chlamyphila felis* (previously *Chlamydia psittaci* var. *felis*) is a common cause of acute and chronic conjunctivitis in cats. However, knowledge of the pathogenesis of feline chlamydiosis is incomplete, and the involvement of *C. felis* in reproductive tract disease and its zoonotic potential are controversial. Molecular assays (e.g., polymerase chain reaction) are now routinely used to diagnose human chlamydiosis and are becoming increasingly available for diagnosing chlamydial infections in cats. This article reviews the current knowledge of the pathogenesis, epidemiology, clinical manifestations, diagnosis, and treatment of feline chlamydiosis. Vaccination, immunity, and the public health significance of the organism are also discussed.

*Chlamyphila felis* (previously feline *Chlamydia psittaci*) was first isolated in the United States from cats with respiratory disease in 1942. The causative organism was initially thought to be a virus, and the organism and its disease were named *feline pneumonitis.* Because *C. felis* was the first feline respiratory pathogen to be identified, most cases of feline upper respiratory tract disease (URTID) were initially believed to result from chlamydial infection. When feline calicivirus (FCV) and herpesvirus-1 (FHV1) were isolated in the late 1950s, the importance of *C. felis* was questioned. In the late 1970s, however, several studies reemphasized its importance, primarily as a conjunctival pathogen of cats. Because pneumonia caused by the organism is generally subclinical, the term *feline pneumonitis* is no longer considered appropriate. There is some evidence that *C. felis* may occasionally be associated with disease of other organs (e.g., the genital tract), but much remains to be learned about the significance of these conditions.

**CAUSE**

Chlamydiae are obligately intracellular gram-negative bacteria. Their developmental cycle involves an alternation between a predominantly extracellular infectious elementary body (EB) and an intracellular metabolically active reticulate body (RB). Only the RB can divide, which occurs in an intracellular vacuole.

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called an inclusion. The RBs then reorganize into EBs, which are subsequently released from the host cell and may enter a new, uninfected host cell where they reorganize into RBs. Chlamydiae have recently been reclassified into nine species belonging to two genera, *Chlamydia* and *Chlamydophila*, based on ribosomal gene sequences. The four new species derived from *Chlamydia psittaci* (i.e., *C. felis*, *Chlamydophila psittaci*, *Chlamydophila abortus*, *Chlamydophila caviae*) generally infect cats, birds, sheep, and guinea pigs, respectively.

Sero logic study results have been suggestive of the existence of multiple strains of *C. felis* that may differ in virulence. However, the exact sites of antigenic variation in *C. felis* are unknown.

Chlamydial EBs survive only a few days at room temperature, although survival for up to 1 month at 4°C may be possible. They are inactivated by lipid solvents and detergents but are somewhat resistant to acids and alkalis.

**PATHOGENESIS**

Much remains unknown regarding the pathogenesis of chlamydial infections in cats. Chlamydiae appear to have a predilection for conjunctival epithelial cells. Natural transmission of *C. felis*, like that of other respiratory pathogens, presumably occurs mainly by close contact with other infected cats and their aerosols and via fomites. Venereal transmission of chlamydiae occurs in several host species but has not been confirmed in cats.

Infections caused by chlamydiae tend to follow a chronic, insidious course, often progressing through asymptomatic stages. In cats, conjunctivitis associated with *C. felis* may persist for several months. Organisms have been isolated from the conjunctiva for up to 215 days after experimental infection, although most cats cease conjunctival shedding at around 60 days after infection. Persistent chlamydial infections are poorly understood, although RBs with atypical morphology have been identified in humans with chronic chlamydial diseases (e.g., reactive arthritis). Such infections are often culture negative and may be resistant to antimicrobial therapy. The intestinal tract may be a site of persistent infection in cats, as has been shown in birds and ruminants. In cats with experimentally induced chlamydial conjunctivitis, prolonged rectal and vaginal *C. felis* excretion have been documented. *C. felis* has also occasionally been found in the spleen, liver, and peritoneum of cats. The significance of the presence of organisms in these locations remains unclear.

Chlamydial disease may be exacerbated by superinfection with other microorganisms. In one study, 8% of cats had both chlamydial and either FCV or FHV1 infection. Cats with concurrent FCV infection usually have other signs (e.g., oral ulceration) in addition to conjunctivitis. Dual infection appears to be more common with FCV than with FHV1. Coinfection with feline immunodeficiency virus (FIV) prolongs conjunctivitis and chlamydial shedding; in cats with existing FIV infection, superinfection with *C. felis* may accelerate the clinical progression of FIV infection. Both *Mycoplasma* species and *Bordetella bronchiseptica* can complicate *C. felis* infections. Other bacteria, including those that normally colonize the healthy conjunctival sac, can also act as secondary invaders and worsen disease.

**EPIDEMIOLOGY**

The prevalence of *C. felis* infection has been examined using a variety of assays in several geographic locations. The prevalence of *C. felis* in cats with URTD as determined by culture has ranged from 23% to 31%. A prevalence of 14.3% (66 of 462) was determined using a variety of assays in several geographic locations. The prevalence of *C. felis* in asymptomatic cats is low. None of 50 cats was positive for the organism using culture, and 1 of 95 cats was positive for the organism using the PCR assay. Persistent chlamydial shedding after clinical signs have resolved may explain positive results in some asymptomatic cats.

Cats 2 to 6 months of age are most likely to be infected with *C. felis*. The prevalence is also high in cats 7 to 11 months of age. The prevalence of *C. felis* infection in kittens younger than 2 months of age is low, presumably because of passive immunity. Cats older than 5 years of age are least likely to be infected with *C. felis*. There is no clear breed or sex predilection.

**CLINICAL SIGNS**

**Respiratory and Ocular Disease**

*Chlamydophila felis* is primarily a conjunctival pathogen capable of causing acute to chronic conjunctivitis with blepharospasm, chemosis, congestion, and a serous to mucopurulent ocular discharge without dyspnea or coughing after approximately 3 to 5 days of incubation (Figure 1). Transient pyrexia and reduced appetite may occur shortly after infection, although many cats remain well and continue to eat. Clinical signs improve after a few weeks, but mild conjunctivitis frequently persists for several months (Figure 2). The strain or route of infection may influence the extent of respiratory tract involvement. Mild and clinically insignificant pulmonary lesions may result from aerosol exposure. Nasal discharge and sneezing occur in some cats. Signs of rhinitis without concurrent ocular in-
volvement are highly unlikely to be associated with C. felis infection, and involvement of other organisms (e.g., respiratory viruses) should be suspected.

Chlamydophila felis infection is rarely associated with corneal damage. Although corneal involvement has been reported, these reports did not always exclude the possibility of a mixed infection involving such pathogens as FHV1. One study showed that simultaneously inoculating a Streptococcus species isolate with C. felis was more likely to be associated with keratoconjunctivitis. The ability of the organism to cause corneal disease may also depend on strain or host factors.

Chlamydophila felis has occasionally been isolated from neonatal conjunctivitis in kittens, although maternal antibody seems to protect most kittens until they are 9 to 12 weeks of age.

Reproductive Tract Disease

Causal relationships between chlamydial infections and reproductive disease have been recognized in many host species. C. felis has been suspected as a cause of abortion, neonatal mortality, and infertility in catteries, but a definite causative link has not been reported. Intravaginal and intraurethral chlamydiae inoculation has been associated with vaginal discharge, bleeding, and swelling in females; urethritis and urethral discharge in males; and proctitis in both sexes. Directly inoculating C. felis into the oviducts led to salpingitis and growth of the organism in this location for weeks, with minimal systemic signs. Vaginal discharge and shedding of chlamydiae from the vagina occur in some cats infected via the conjunctivae. Placental tissue infection was demonstrated by PCR assay in a cat that was experimentally infected with C. felis by conjunctival inoculation during gestation. Placentitis was not observed histologically, and no evidence of infection was detected in the neonates. The queen experienced apparently normal parturition, but vaginal shedding of C. felis began immediately afterward. C. felis infection may be influenced by changes in the host’s endocrine environment, as has been shown for other host species.

Despite these findings, results of studies of naturally infected cats suggest that C. felis is unlikely to be an important cause of feline reproductive disease. Infertility and abortion have been equally distributed between infected and uninfected cat colonies, and many Chlamydia-infected colonies do not have reproductive problems. FHV1 may be responsible for many suspected cases of C. felis-induced genital and perinatal disease. FHV1 was detected in four of eight cats with combined reproductive disease and URTD in a large epidemiologic survey of cats with URTD, whereas C. felis was not detected. If there is an association, the ability of C. felis to cause reproductive disease may depend on such factors as the stage of pregnancy when infection occurs, coinfection with other organisms, concurrent immunosuppression, route of infection, and the strain involved.

Other Manifestations

Chlamydial infection has been associated with peritonitis in a mature female cat. Chlamydiae were also observed in the gastric mucosa of 12 young cats from five related research or commercial breeding colonies. Four of the cats showed signs of weight loss of undetermined cause. Administering the organism to cats by aerosol and oral inoculation resulted in conjunctivitis, rhinitis, and (in some cats) mild gastritis.

An association between chlamydial infection and lameness in cats has also been suggested. Further studies are required to determine whether C. felis is capable of causing lameness in cats.
Swabbing technique for collecting diagnostic samples of feline chlamydiosis.

**DIAGNOSIS**

Chlamydial infection needs to be differentiated from other causes of feline URTD. Accurate diagnosis requires some form of microbiologic assay. Unless the test of the assay is antibodies, most available diagnostic tests are designed to be conducted on conjunctival swabs (Figure 3).

Examining Giemsa-stained conjunctival smears for chlamydial inclusions is not recommended as a reliable means of diagnosing feline chlamydial infection. Inclusions are generally only visible early in the course of infection and sometimes not at all. False-positive results may be obtained when melanin granules in the cytoplasm of conjunctival cells are mistaken for organisms.

In unvaccinated cats, serum antibody titers detected using indirect immunofluorescence correlate well with recent infection. Ninety-six percent of cats infected with *C. felis* have titers greater than 32, whereas only 7.5% of uninfected cats have titers that high. However, the availability of this assay is limited, antibodies induced by vaccination may interfere with interpreting the assay, and acute and convalescent phase sera may be required to obtain a diagnosis in acute cases. The complement fixation test is unreliable in detecting recent *C. felis* infection.

Several ELISA antigen kits are available for diagnosing human *Chlamydia trachomatis* infection. Their sensitivities and specificities for detecting *C. felis* are extremely variable. One assay had a specificity of 90% and a sensitivity of only 79% when compared with cell culture for detecting *C. felis*, whereas another had very poor sensitivity (25%) and specificity (84%) when compared with fluorescent antibody testing.

The gold standard for chlamydial diagnosis is cell culture, which most commonly uses fluorescent antibodies to detect intracytoplasmic chlamydial inclusions after inoculating cell monolayers. This is more sensitive than is directly applying fluorescent antibody to smears of affected tissue. Conjunctival swabs must be placed in special transport media containing appropriate antimicrobials to preserve chlamydial viability. Isolation in cell culture is technically demanding, time consuming, and expensive. Transportation and storage problems can affect the sensitivity of cell culture. The sensitivity of culture may vary among laboratories depending on equipment and technical expertise.

Diagnostic PCR assays are now used routinely for diagnosing human chlamydial infections, and assays for *C. felis* are becoming increasingly available. PCR assays have been shown to have good sensitivity and specificity with proper sample collection and storage, although the sensitivity of PCR assays may vary among laboratories. Because *C. felis* does not need to be viable for detection, special transport media are not required. False-positive results may be obtained from contamination before or after sample submission to the laboratory. Veterinarians collecting samples for PCR assay should contact the laboratory for sample collection and handling guidelines to minimize contamination.

**TREATMENT**

The drug of choice to treat chlamydial infections in cats is doxycycline. Other tetracyclines are also effective. In experimentally infected cats, acute *C. felis* infection was successfully treated using oral doxycycline for 3 weeks (5 mg/kg every 12 hours). Topical treatment was not required. Rapid clinical improvement occurred within 2 days of the start of treatment. Organisms could not be detected using PCR assay and culture after day 6. Because of the long half-life of doxycycline, once-daily administration at 10 mg/kg is likely to be equally effective and more convenient for owners.

Despite these results, sometimes treatment for longer than 3 weeks has been necessary to resolve natural *C. felis* infections. Some authors have recommended combining systemic therapy with topical tetracycline ointments every 6 to 8 hours. A minimum of 6 to 8 weeks of treatment, especially in catteries, has also been suggested. Continuing treatment for 2 weeks after clinical signs have resolved is generally recommended. Cats in two catteries were successfully treated with immediate lincomycin–spectinomycin (55 and 111 mg/cat/day for 8 weeks, respectively). Chlamydiae are also susceptible to erythromycin, rifampin, fluoroquinolones, and the newer macrolide azithromycin, but these drugs have not been evaluated for treating feline chlamydiosis. Thus far, clinically significant antimicrobial resistance has not been reported. Sulfonamides and chloramphenicol are ineffective against *C. felis*. Penicillin is inhibitory at high doses but does not eliminate the organism.
Chlamyphila felis may be more difficult to eliminate in chronic infections, as occurs in humans with chlamydial arthritis. However, recurring cases often involve many cats and poor compliance; often, all cats are not treated and the owner fails to administer all doses. All cats must be treated with the full course of antimicrobials, and proper hygiene and quarantine must be maintained. This may be difficult to achieve when many cats must be treated. Clinicians must consider concurrent presence of the viral causes of URTD, which may show initial response to antimicrobial therapy because secondary bacterial infections may resolve. Use of a 1:32 bleach:detergent solution is recommended for general environmental disinfection when undiagnosed FCV infection remains a possibility.

There is a risk of permanent teeth discoloration in kittens if tetracyclines are used in pregnant queens in the last 2 to 3 weeks of pregnancy or in kittens in the first few months of life. Doxycycline has reduced calcium-binding avidity compared with other tetracyclines and therefore produces only minor discoloration. Little evidence suggests that such side effects occur in cats receiving doxycycline, but owners should be made aware of the possibility. In humans, erythromycin is substituted, but there have been no studies on the effect of erythromycin in cats with chlamydiosis. Of the tetracyclines, doxycycline also has a lower risk of other side effects (e.g., gastrointestinal disturbances, exacerbating or producing renal disease).

**VACCINATION AND IMMUNITY**

Immunity to chlamydial infection is generally weak or short-lived. Although protection from rechallenge occurs 3 months after initial challenge, further protection is only partial. However, the apparent age-related resistance of cats to C. felis infection is suggestive of some form of protective immunity eventually developing. Cell-mediated immunity appears essential for resolving infection.

Both modified-live and inactivated cell culture vaccines have been used, either alone or in combination with feline panleukopenia, FCV, and FHV1 components. C. felis vaccines have been associated with atypical reactions (fever, lethargy, anorexia, lameness) 7 to 21 days after vaccination in approximately 3% of cats. The chlamydial vaccine does not prevent infection or clinical signs, although the latter are generally reduced in severity. Both the chlamydial vaccine and the recently introduced intranasal B. bronchiseptica vaccine are only indicated for cats at demonstrable risk of acquiring infection and thus are considered noncore vaccines. This is in contrast to the FCV and FHV1 vaccines, which are considered core vaccines because of
the high prevalence of disease caused by these viruses and the relative refractoriness of viral URTD to treatment. The chlamydial and *B. bronchiseptica* vaccines are most beneficial as part of a control program in catteries or shelters where the disease is endemic. Because the maximum duration of immunity of these vaccines is not known, the recommendation is to administer booster vaccinations annually to cats that are at risk of acquiring these infections.

**Zoonotic Potential**

*Chlamydophila felis* has been implicated in conjunctivitis in humans, but evidence to support this association has not been strong. One report involved a man with unilateral follicular conjunctivitis. His 12-week-old kitten, which slept on his bed, also had a unilateral ocular discharge.\(^{36,37}\) The man lived in a crowded boarding house with several other humans, cats, dogs, and monkeys. Chlamydiae were isolated from the kitten and the affected human and distinguished from the human pathogen *C. trachomatis* by their failure to uptake iodine. However, in another report, only 19% (4 of 21) of cat owners with chlamydial conjunctivitis complained of recent itchy or sore eyes compared with 25% (2 of 8) of cat owners negative for *C. felis*.\(^{6}\) *C. felis* has also been associated with other diseases in humans, including hepatosplenomegaly, glomerulonephritis, and endocarditis.\(^{17,38}\) In all these cases, associations were made on the basis of serology, which is not species specific. The pathogen involved in some or all of these cases was possibly the recently discovered *C. pneumoniae*, which also fails to stain with iodine. If *C. felis* is zoonotic, maintenance of hygienic conditions is probably adequate to prevent human disease, although further investigation of the zoonotic potential of this organism is needed.

*Chlamydia* has also been implicated via serology in cat-scratch disease in humans,\(^{40}\) which is now known to be caused by *Bartonella henselae* and *Bartonella claridgeiae*. Recent studies have described serologic cross-reactions between *Bartonella* and *Chlamydia* species\(^{41}\) that may be responsible for the erroneous interpretations of *Chlamydia* in cat-scratch disease. In addition, bartonellosis cannot be ruled out as a cause of such clinical manifestations as endocarditis and glomerulonephritis in humans diagnosed with chlamydiosis on the basis of serology.

**About the Author**

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**REFERENCES**


5. Chlamydiosis is most likely to be documented in cats of age.
   a. younger than 5 weeks   d. 1 to 5 years
   b. 2 to 11 months   e. older than 15 years
   c. 5 to 10 years

6. Which of the following statements regarding clinical manifestations of feline chlamydiosis is true?
   a. *C. felis* commonly causes reproductive failure in cats.
   b. *C. felis* can cause rhinitis without signs of conjunctivitis.
   c. Cats with chlamydiosis commonly show signs of inappetence and lethargy throughout the course of illness.
   d. *C. felis* is rarely associated with keratitis in cats.
   e. Transient lameness occurs commonly in cats infected with *C. felis*.

7. In general, which of the following is the most unreliable diagnostic test for feline chlamydiosis?
   a. serology using indirect immunofluorescence
   b. conjunctival cytology
   c. direct fluorescent antibody test
   d. cell culture
   e. PCR assay

8. Which of the following statements regarding diagnosis of feline chlamydiosis is false?
   a. The gold standard for chlamydial diagnosis is cell culture.
   b. The main disadvantage of the PCR assay is the potential for false-positive results caused by contamination.
   c. Antigen-detection ELISA kits for detecting human *C. trachomatis* infections may cross-react with *C. felis* and can be used for diagnosing feline chlamydiosis.
   d. The complement fixation test is unreliable in detecting chlamydial infection.
   e. Samples for diagnosis via PCR assay must be shipped carefully in appropriate transport media to preserve chlamydial viability.

9. The treatment of choice for feline chlamydiosis is
   a. erythromycin. d. azithromycin.
   b. chloramphenicol. e. sodium penicillin.
   c. doxycycline.

10. Which of the following statements regarding *C. felis* is true?
    a. *C. felis* is frequently isolated from asymptomatic cats because of the carrier state.
    b. Cat-scratch disease may be caused by *C. felis* and *B. henselae*.
    c. *C. felis* infection can be prevented by vaccination.
    d. Several antibiotic-resistant strains of *C. felis* have been documented.
    e. Evidence to support a causal role for *C. felis* in human conjunctivitis is weak.