GUIDELINE for Chlamydia felis

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Chlamydophila (Chlamydia) guidelines were first published in the J Feline Med Surg 2009; 11: 605-609 by Tim Gruffydd-Jones et al. The present guideline was updated by Séverine Tasker.

Synopsis

Chlamydia felis is a Gram-negative bacterium that is an obligate intracellular parasite of cats. *Chlamydia felis* does not survive outside of the host so close contact between cats is required for transmission, usually via ocular discharges. Chlamydiosis typically affects young cats under 9 months of age. It causes ocular signs: initially unilateral then bilateral with conjunctivitis, hyperaemia of the nictitating membrane, blepharospasm, ocular discharge (initially serous then mucopurulent) and chemosis. The diagnostic method of choice is PCR performed on conjunctival or oropharyngeal swabs. Disease management comprises systemic antibiotics; doxycycline is usually used and should be given for at least 4 weeks to eliminate infection, and at least 2 weeks beyond resolution of clinical signs. Amoxycillin-clavulanate is an alternative antibiotic especially for young kittens. Prompt diagnosis and treatment are associated with a favourable outcome, with signs typically improving within 48 hours of starting appropriate treatment. Vaccination for *C. felis* is a non-core vaccine and is not indicated for all cats but may be recommended for those in multi-cat households (e.g., breeding catteries, shelters) at high risk of infection or if there has been a history of chlamydiosis.

Agent properties

ABCD follows a recent nomenclature proposal to classify all 11 currently recognized *Chlamydiaceae* species in a single genus, the genus *Chlamydia* (Sachse et al., 2015); these species include *Chlamydia felis*, *Chlamydia pneumoniae* and *Chlamydia psittaci*. *C. felis* is the species typically seen infecting cats.

Chlamydia felis, typical of the genus *Chlamydia*, is a Gram-negative rod-shaped coccoid bacterium; its cell wall is devoid of peptidoglycan. As an obligate intracellular parasite, it lacks the ability to replicate autonomously (Becker, 1978).

The genome of *C. felis* has been sequenced (Azuma et al., 2006). There is extensive nucleotide sequence homology between the genomes of various *Chlamydia* species. The membrane contains important families of proteins: the major outer membrane proteins (MOMPs) and polymorphic outer membrane proteins (POMPs). The organism attaches to sialic acid receptors of cells. It has a unique pattern of replication within cells, involving reticulate bodies and elementary bodies. The latter represent the infectious forms of the micro-organism that are released following cell lysis. Some *C. felis* isolates appear to contain plasmids, and this may be related to their pathogenic ability (Everson et al., 2003).

Epidemiology

Since *C. felis* has low viability outside the host, transmission requires close contact between cats; transfer of ocular secretions is probably the most important route of infection. Infection is most common in multi-cat environments, particularly breeding catteries, and therefore prevalence may be higher among pedigree cats (Wills et al., 1987). However, other studies have highlighted a high prevalence of *C. felis* in stray cats (Wu et al., 2013), including those with conjunctivitis (Halanova et al., 2011). One study of cats in Slovakia (Halanova et al., 2019) found that the risk of *C. felis* infection was significantly greater in cats with conjunctivitis and/or upper respiratory tract signs (30.4% positive by PCR) than healthy cats (4.2%); additionally, cats from shelters (31% positive by PCR) and street stray cats (35.7%) were significantly more at risk of infection than indoor only cats (0%). Most cases occur in young cats, particularly under one year of age. *C. felis* is the infectious organism most frequently associated with conjunctivitis in cats and is isolated from up to 30% of affected cats, particularly in those with chronic conjunctivitis (Wills et al., 1988) and is associated with more severe ocular disease and conjunctivitis (Fernandez et al., 2017) although another study of 60 shelter cats with ocular disease in the US found no evidence of *C. felis* infection by PCR (Zirofsky et al., 2018). Studies have shown variable results when investigating for any

association between gingivostomatis and *C. felis* (Fernandez et al., 2017; Nakanishi et al., 2019). Serological surveys have shown that 10% or more of unvaccinated household pets have antibodies (Lang, 1992; Gunn-Moore et al., 1995). Studies by PCR in cats with ocular or upper respiratory tract disease signs have shown prevalences of 12 to 20%. Prevalence in healthy cats is low, by PCR some studies show less than 2-3% in cats without clinical signs (Di Francesco et al., 2004; Fernandez et al., 2017).

Pathogenesis

Chlamydia spp. target mucosal tissues and the primary target for *C. felis* is the conjunctiva. The incubation period is generally 2-5 days. They primarily cause ocular disease and conjunctivitis, with ocular discharge, hyperaemia of the nictitating membrane, chemosis and blepharospasm can all occur. *Chlamydia* spp. persistently infect the epithelial cells of the ocular, respiratory, gastrointestinal and/or reproductive systems, although association with disease in some of these systems is poorly understood. Chlamydial organisms can be isolated from the vagina and rectum of cats, but it is unclear whether venereal transmission occurs although there is circumstantial evidence that *Chlamydia* may cause abortion (Graham and Taylor, 2012).

In most cats, conjunctival shedding ceases at around 60 days after infection, although some may continue to become persistently infected (O'Dair et al., 1994). *C. felis* has been isolated from the conjunctiva of untreated cats for up to 215 days after experimental infection (Wills, 1986).

Immunity

Passive immunity

Infected cats develop antibodies and kittens appear to be protected initially for the first one or two months of life by maternally derived antibodies (Wills, 1986).

Active immunity

The nature of the protective immune responses to *Chlamydia* infection is uncertain. However cellular immune responses are believed to play a crucial role in protection (Longbottom and Livingstone, 2006). The MOMPs and POMPs are important targets for protective immune responses in other species (Longbottom and Livingstone, 2006) and have been shown to exist in the cat (Harley et al., 2007).

Clinical signs

Unilateral ocular disease may be seen initially, but this generally progresses to become bilateral. There can be intense conjunctivitis with extreme hyperaemia of the nictitating membrane, blepharospasm and ocular discomfort (Fig. 1). Ocular discharges are initially watery but later become mucoid or mucopurulent (Fig. 2). Chemosis of the conjunctiva is a characteristic feature of chlamydiosis. Respiratory signs are generally minimal with *Chlamydia* infections. In cats with respiratory disease but without concurrent ocular signs, *C. felis* infection is unlikely. Ocular complications such as adhesions of the conjunctiva, may occur but keratitis and corneal ulcers are not generally associated with infection. Transient fever, inappetence and weight loss may occur shortly after infection, although most cats remain well and continue to eat.

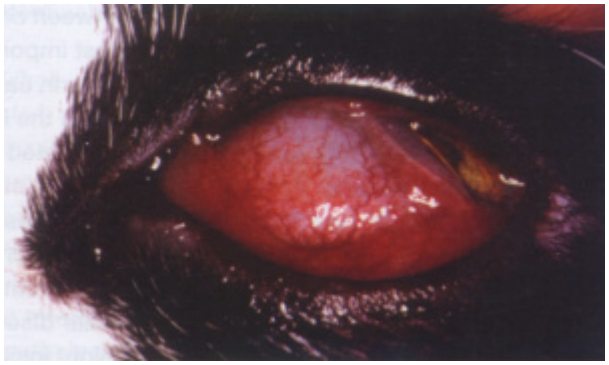

Fig. 1. Conjunctivitis in a cat with Chlamydia felis infection. Courtesy of The Feline Centre, Langford Vets, University of Bristol, UK

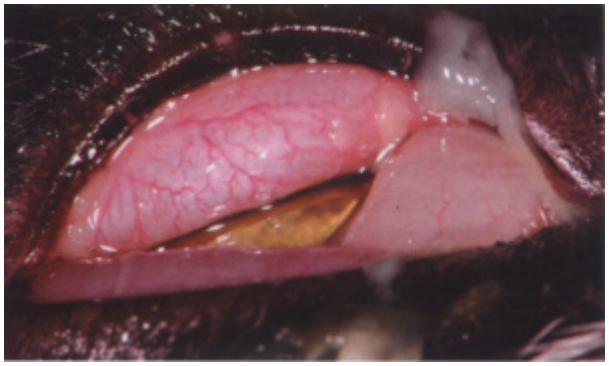

Fig. 2. Purulent conjunctivitis and chemosis in a cat with Chlamydia felis infection. Courtesy of Eric Déan

Diagnosis

Direct detection methods

It is possible to identify infection by culture, but PCR techniques are now the preferred option for diagnosing *Chlamydia* infection. Such techniques are extremely sensitive and avoid problems with poor viability of the organisms. Ocular swabs are generally used as samples (Fig. 3), although a recent study did not find a significant difference in the ability to detect *C. felis* by PCR from ocular, oropharyngeal, nasal and tongue swabs, suggesting that other sampling sites can be used (Schulz et al., 2015). Additionally, organisms may also be detected in vaginal swabs, aborted foetuses and rectal swabs, although these are seldom used diagnostically. Since the organism is intracellular, it is necessary to obtain good quality swabs that include cells. It has been shown that the topical anaesthetic proxymetacaine does not appear to affect PCR amplification of chlamydial DNA from ocular swabs (Segarra et al., 2011).

Other techniques for demonstrating the organism are less sensitive and less reliable than PCR. Chlamydial antigen tests based on detecting group specific antigen using ELISA or similar techniques are available. Also, conjunctival smears can be Giemsa-stained to check for inclusions, but chlamydial inclusions are easily confused with other basophilic inclusions (Streeten and Streeten, 1985).

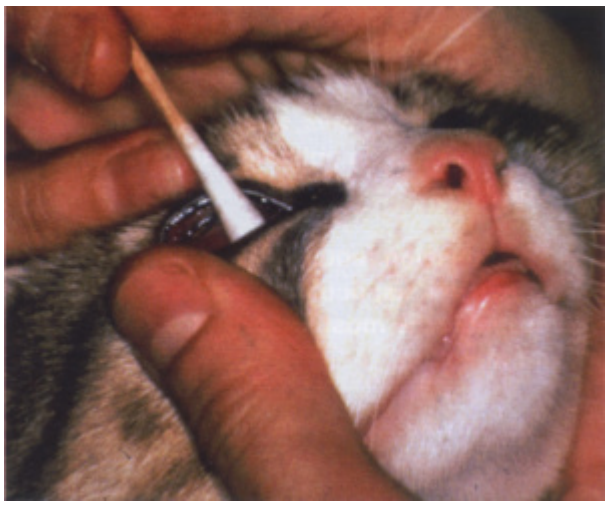

Fig. 3. Collecting a conjunctival swab; the sample must contain enough cells for PCR diagnosis. Courtesy of The Feline Centre, Langford Vets, University of Bristol, UK

Indirect detection methods

In unvaccinated cats, antibody detection can confirm the diagnosis of *C. felis* infection. Immunofluorescence (IF; Fig. 4) and ELISA techniques are used for determining antibody titres. Some cross reactivity with other bacteria occurs, and low IF titres (≤32) are generally considered as being negative. Established active or recent infections are associated with high titres, often of ≥512. Serology can be particularly useful to establish whether infection is endemic in a group. It can also be of value in investigating cases with chronic ocular signs. A high titre suggests that *Chlamydia* may be an aetiological factor, whereas a low titre discounts likely chlamydial

involvement.

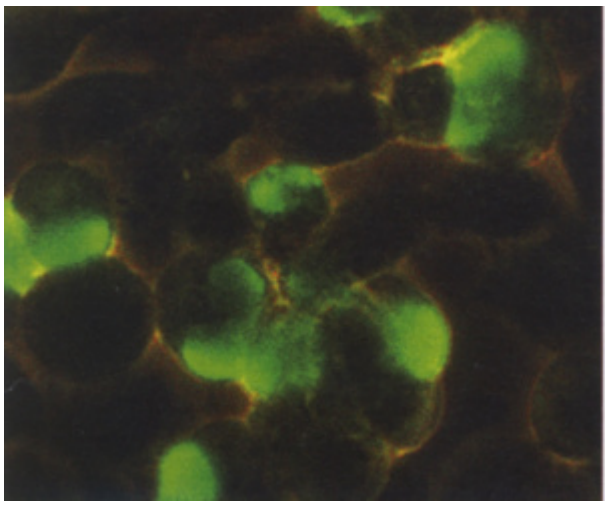

Fig. 4. Indirect immunofluorescence test to titrate antibody directed against Chlamydia felis; infected cell culture serves as the antigen substrate. Courtesy of The Feline Centre, Langford Vets, University of Bristol, UK

Treatment

Chlamydia infection in cats can be treated very effectively with antibiotics. Systemic antibiotics are more effective than local topical treatment (Sparkes et al., 1999). Tetracyclines are generally regarded as the antibiotics of choice for chlamydial infections (Dean et al., 2005). Doxycycline has the advantage of requiring only a single daily dose and is most frequently used at a daily dosage of 10 mg/kg orally, although 5 mg/kg orally twice daily can be used if vomiting occurs with single day dosing. Administration of the hyclate preparation of doxycycline should always be followed by food or water because of the possibility of it inducing oesophagitis in cats with incomplete swallowing. Studies have shown that treatment must be maintained for 4 weeks to ensure elimination of the organism (Dean et al., 2005). In some cats, recrudescence may be noted some time after discontinuation of therapy. Continuation of treatment for two weeks after resolution of clinical signs is recommended. Tetracyclines have potential side effects in young cats although these appear to be less common with doxycycline than oxytetracycline. Alternative antibiotics may be considered if this is a concern. Both enrofloxacin and pradofloxacin have shown some efficacy against *Chlamydia* spp. (Gerhardt et al., 2006; Hartmann et al., 2008), although pradofloxacin would be preferred over enrofloxacin in view of the diffuse retinal degeneration and acute blindness that has been reported following enrofloxacin treatment in cats, albeit very rarely. A 4-week course of therapy with clavulanic acid potentiated amoxicillin may represent the safest choice of alternative to doxycycline in young kittens (Sturgess et al., 2001).

Vaccination

Chlamydia felis vaccines are non-core. Both inactivated and modified live (attenuated) vaccines, based on whole *Chlamydia* organisms, are available, but only as components of multivalent vaccine preparations. Vaccines are effective in protecting against clinical manifestation of the disease, however, not against occurrence of infection (Wills et al., 1987). No reliable data are available to compare the efficacy of inactivated versus modified live vaccines.

Vaccination should be considered for cats at risk of exposure to infection, particularly in multicat environments, and if there has been a previous history of *Chlamydia* infection.

Vaccination of kittens generally begins at 8-9 weeks of age with a second injection 3-4 weeks later at around 12 weeks of age. Limited information is available about the duration of immunity. There is some evidence that previously infected cats can become vulnerable to re-infection after a year or more. Annual boosters are recommended for cats that are at continued risk of exposure to infection.

Disease control in specific situations

Shelters

Chlamydia infection can be a significant cause of disease in rescue shelters but is generally a less significant problem than respiratory viruses (McManus et al., 2014). Vaccination should be considered if there has been a previous history of Chlamydial disease in the

shelter. Since close contact is necessary for transmission and the organism has low viability outside the host, single housing of cats and routine hygiene measures should avoid cross infection. Whenever cats are maintained together longer term, they should be vaccinated regularly.

Breeding catteries

In catteries with endemic *Chlamydia* infection, the first step is generally treatment of all cats in the household with doxycycline for at least 4 weeks to attempt to eliminate the infection. In some cattery cats a minimum of 6 to 8 weeks of treatment has been shown to be necessary to eliminate natural infection. Once clinical signs have been controlled, cats should be vaccinated to provide protection against disease should re-infection of the cattery occur.

Immunocompromised cats

Immunocompromised cats should only be vaccinated when it is deemed absolutely necessary, and then an inactivated vaccine should be used.

Zoonotic risk

There is no epidemiological evidence for a significant zoonotic risk although conjunctivitis caused by *C. felis* was reported in an HIV-infected patient (Hartley et al., 2001) and, more recently, in an immunocompetent female (Wons et al., 2017) in which the source of infection was her pet kitten. Additionally, *C. pneumoniae*, a well-recognised human pathogen, has been identified in a small number of cats (Sibitz et al., 2011), although transmission from cats to humans has not been documented. *C. psittaci* primarily infects birds and is an important zoonotic agent which causes atypical pneumonia in humans. Occasionally, infection in cats is reported (Lipman et al., 1994). A case report of fatal *C. psittaci* infection in a 7-week old kitten has been reported (Sanderson et al., 2021); this kitten showed Gram negative sepsis with acute necrosuppurative hepatitis and nonsuppurative pneumonia and mild leptomeningitis, and infection of the kitten's mother via bird hunting during pregnancy was suspected.

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