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CHLAMYDOPHILA FELIS INFECTION
ABCD guidelines on prevention and management

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Bacterial properties

Chlamydophila felis is a Gram-negative rod-shaped coccoid bacterium with a cell wall that lacks peptidoglycan. It is an obligate intracellular parasite that cannot replicate autonomously.[1] *Chlamydophila* is a genus within the family *Chlamydiaceae* of the order Chlamydiales. The genome of *C felis* has recently been sequenced.[2]

There is extensive homology between chlamydial species. The membrane contains major outer membrane proteins (MOMPs) and polymorphic outer membrane proteins (POMPs). The organism enters the host cell after attachment to sialic acid receptors. It has a unique replication cycle within host cells, involving reticulate bodies and elementary bodies, the latter representing the infectious forms of the microorganism that are released upon cell lysis. Some *C felis* isolates contain plasmids and phages, which may be related to their pathogenicity.[3]

Epidemiology

Since *C felis* does not survive outside the host, transmission requires close contact between cats; ocular secretions are probably the most important body fluid for infection. *Chlamydophila felis* disease is most common in multi-cat environments, particularly breeding catteries, and the prevalence of infection may therefore be higher among pedigree cats.[4] Most cases occur in cats under 1 year of age. *Chlamydophila felis* is the infectious organism most frequently associated with conjunctivitis and is isolated from up to 30% of affected cats, particularly those with chronic conjunctivitis.[5] Serological surveys have shown that 10% or more of unvaccinated household pets have antibodies against *Chlamydophila*.[6,7]

In studies using PCR, 12–20% of cats with ocu-

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The European Advisory Board on Cat Diseases (ABCD) is a body of experts in immunology, vaccinology and clinical feline medicine that issues guidelines on prevention and management of feline infectious diseases in Europe, for the benefit of the health and welfare of cats. The guidelines are based on current scientific knowledge of the diseases and available vaccines concerned.

An extended version of the *Chlamydophila felis* infection guidelines presented in this article is available at www.abcd-vets.org

Overview *Chlamydophila felis* is a Gram-negative bacterium and its primary target is the conjunctiva. The bacterium does not survive outside the host.
Infection Transmission requires close contact between cats; ocular secretions are probably the most important body fluid for infection. Most cases occur in cats under 1 year of age. *Chlamydophila felis* is the infectious organism most frequently associated with conjunctivitis.
Disease signs Unilateral ocular disease generally progresses to become bilateral. There can be intense conjunctivitis with extreme hyperaemia of the nictitating membrane, blepharospasm and ocular discomfort. Transient fever, inappetence and weight loss may occur shortly after infection, although most cats remain well and continue to eat.
Diagnosis PCR techniques are now preferred for diagnosing *C felis* infection. Ocular swabs are generally used. In unvaccinated cats, antibody detection can be used to indicate infection.
Disease management Tetracyclines are generally regarded as the antibiotics of choice. Doxycycline has the advantage of requiring only single daily administration and is given at a dose of 10 mg/kg orally. Vaccination should be considered if there is a history of confirmed chlamydial disease in a shelter. Single housing and routine hygiene measures should suffice to avoid cross-infection. Cats maintained together for longer terms should be vaccinated regularly. In breeding catteries where *C felis* infection is endemic, the first step should be to treat all cats with doxycycline for at least 4 weeks. Once clinical signs have been controlled, the cats should be vaccinated.

Vaccination recommendations
Vaccination should be considered for cats at risk of exposure to infection. Vaccination generally begins at 8–10 weeks of age, with a second injection 3–4 weeks later. Annual boosters are recommended for cats at continued risk of exposure.

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lar or upper respiratory tract disease signs were found to be chlamydia-positive; in cats without clinical signs, the prevalence was <3%.[8]

Conjunctivitis caused by *C felis* was reported in a human immunodeficiency virus-infected patient.[9] However, there is no epidemiological evidence that *C felis* represents an appreciable zoonotic risk.

Pathogenesis and clinical signs

Chlamydia target mucosal tissues, and the primary target for *C felis* is the conjunctiva. The incubation period is generally 2–5 days.

In the first day or two after clinical signs develop, unilateral ocular disease may be seen, 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 and subsequently become mucoid or mucopurulent (Fig 2). Chemosis of the conjunctiva is a characteristic feature of chlamydiosis. Respiratory signs are generally minimal; in cats with respiratory disease, but without concurrent ocular signs, *C felis* infection is unlikely. Ocular complications, such as adhesions of the conjunctiva, may develop, but keratitis and corneal ulcers are not generally associated with infection. Transient fever, inappetence and weight loss may be seen shortly after infection, although most cats remain well and continue to eat.

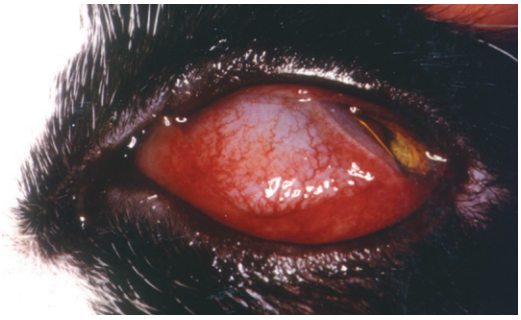

FIG 1 Conjunctivitis in a cat with *Chlamydophila felis* infection. *Courtesy of The Feline Centre, University of Bristol, UK*

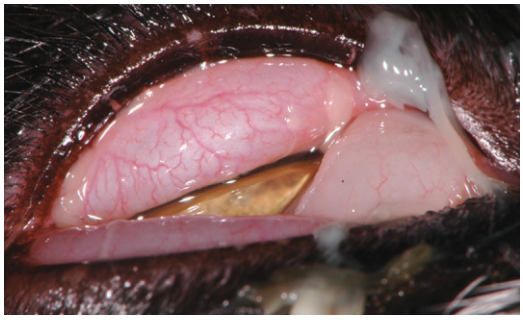

FIG 2 Purulent conjunctivitis and chemosis associated with *Chlamydophila felis*. *Courtesy of Eric Déan*

Chlamydial organisms can be isolated from the vagina and rectum of cats, but it is unclear whether venereal transmission occurs. There is circumstantial evidence that *C felis* may cause abortion, but not for a link with gastrointestinal disease.

Conjunctival shedding generally ceases at around 60 days after infection, although in some cats a persistent infection may develop; *C felis* has been isolated from the conjunctiva for up to 215 days after experimental infection.[10,11]

Immunity

Passive immunity

Infected cats develop antibodies, and kittens are protected for the first 1–2 months of life by maternally derived antibodies.[11]

Active immunity

The precise nature of the protective immune response to *C felis* infection is uncertain, but cellular immune responses are believed to play a crucial role.[12] The MOMPs and POMPs are important targets for protective immune responses in other species and exist also in the cat.[12,13]

Diagnosis

Direct detection methods

It is possible to culture *C felis*, but PCR techniques are now preferred for diagnosing infection [EBM grade III]. PCR is extremely sensitive and avoids problems associated with the poor viability of the organism. Ocular swabs are generally used (Fig 3); although chlamydia may be detected in aborted fetuses, vaginal and rectal swabs, these are seldom used diagnostically. Since the organism is intracellular, it is important to obtain conjunctival swabs that contain a sufficient number of cells.

Other diagnostic techniques are less sensitive and less reliable than PCR. Chlamydial antigen tests based on detecting the group-specific antigen using ELISA or similar techniques are available. Also, conjunctival smears can be Giemsa stained to look for inclusions, but chlamydial bodies are easily confused with other basophilic inclusions.[14]

Indirect detection methods

In unvaccinated cats, antibody detection can confirm the diagnosis of *C felis* infection. Immunofluorescence (Fig 4) and ELISA techniques are used for determining antibody titres. Because of some cross-reactivity with other bacteria, low immunofluorescence reciprocal titres (≤32) are

Conjunctival shedding generally ceases at around 60 days after infection, although in some cats a persistent infection may develop; *C felis* has been isolated from the conjunctiva for up to 215 days after experimental infection.

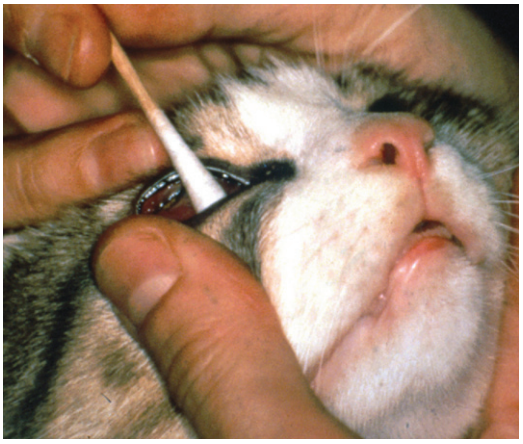

FIG 3 *Chlamydophila felis* infection is generally diagnosed using PCR on ocular swab samples. Since the organism is intracellular, it is important that conjunctival swabs contain a sufficient number of cells. *Courtesy of The Feline Centre, University of Bristol, UK*

generally considered as being negative. Active or recent infections are often associated with reciprocal titres ≥512. Serology can be particularly useful for establishing 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 *Chlamydophila* is an aetiological factor, whereas a low titre discounts its likely involvement.

Treatment

Antibacterial therapy

Chlamydophila infection in cats can be effectively treated with antibiotics – systemic application being more efficacious than local treatment [EBM grade II].[15] Tetracyclines are generally regarded as the antibiotics of choice [EBM grade III].[16] Doxycycline has the advantage of requiring only single daily administration and is given at a dose of 10 mg/kg orally. Doxycycline treatment must be maintained for 4 weeks to ensure elimination of the organism – recrudescence may occur if therapy is stopped earlier [EBM grade III].[16] Continuation of treatment for 2 weeks after resolution of clinical signs is recommended.

Tetracyclines may have side effects in young cats, although they appear to be less common with doxycycline than with oxytetracycline. Alternative antibiotics may be considered if this is a concern. Fluoroquinolones are effective against chlamydia [EBM grade I], but a 4-week course with clavulanic acid-potentiated amoxicillin may represent the safest choice in young kittens [EBM grade III].[17–19]

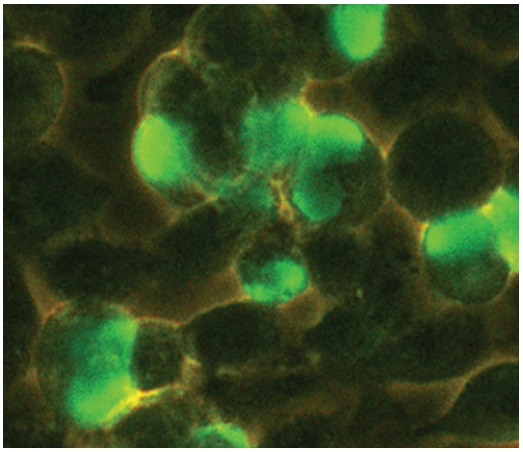

FIG 4 Indirect immunofluorescence in infected cell culture is used as a serological test to titrate the antibodies against *Chlamydophila felis*. *Courtesy of The Feline Centre, University of Bristol, UK*

EBM ranking used in this article

Evidence-based medicine (EBM) is a process of clinical decision-making that allows clinicians to find, appraise and integrate the current best evidence with individual clinical expertise, client wishes and patient needs (see Editorial on page 529 of this special issue, doi:10.1016/j.jfms.2009.05.001).

This article uses EBM ranking to grade the level of evidence of statements in relevant sections on diagnosis and disease management, as well as vaccination. Statements are graded on a scale of I to IV as follows:

- **EBM grade I** This is the best evidence, comprising data obtained from properly designed, randomised controlled clinical trials in the target species (in this context cats);
- **EBM grade II** Data obtained from properly designed, randomised controlled studies in the target species with spontaneous disease in an experimental setting;
- **EBM grade III** Data based on non-randomised clinical trials, multiple case series, other experimental studies, and dramatic results from uncontrolled studies;
- **EBM grade IV** Expert opinion, case reports, studies in other species, pathophysiological justification.

If no grade is specified, the EBM level is grade IV.

Further reading

Roudebush P, Allen TA, Dodd CE, Novotny BJ. Application of evidence-based medicine to veterinary clinical nutrition. *J Am Vet Med Assoc* 2004; **224:** 1765–71.

Doxycycline treatment must be maintained for 4 weeks to ensure elimination of the organism – recrudescence may occur if therapy is stopped earlier.

Vaccination recommendations

General considerations

Vaccines are effective in protecting against disease resulting from *C felis* infection, but not against infection itself [EBM grade III].[4] No reliable data are available to compare the efficacy of inactivated products with modified-live virus vaccines [EBM grade IV].

Non-core vaccine

The ABCD considers vaccine components that protect against *C felis* infections as being non-core.

Primary course

Vaccination generally begins in kittens at 8–10 weeks of age, with a second injection given 3–4 weeks later.

Booster vaccinations

The duration of immunity is unknown, but previously infected cats can become reinfected after 1 year. Annual boosters are therefore recommended for cats that are at continued risk of exposure.

Vaccination

Both inactivated and modified-live virus vaccines based on whole chlamydial organisms are available as part of multivalent preparations. Vaccination should be considered for cats at risk of exposure to infection, particularly in multi-cat environments, and if there has been a history of chlamydial infection (see box above).

Disease control in specific situations

Shelters

Chlamydophila felis can be an important cause of disease in rescue shelters, but it is generally less significant than the respiratory viruses. Vaccination should be considered if there is a history of confirmed chlamydial disease in the shelter. Since close contact is necessary for transmission, and the organism is poorly viable outside the host, single housing and routine hygiene measures should suffice to avoid cross-infection. Whenever cats are maintained together long term, they should be vaccinated regularly.

Breeding catteries

In situations where *C felis* infection is endemic, the first step should be to treat all cats with doxycycline for at least 4 weeks, in an attempt to eliminate the infection. Once clinical signs have been controlled, the cats should be vaccinated.

Immunocompromised cats

Immunocompromised cats should only be vaccinated if deemed necessary, in which case an inactivated vaccine should be used.

KEY POINTS

- *Chlamydophila felis*, a Gram-negative bacterium, is an obligate intracellular parasite.
- Transmission requires close contact between cats; ocular secretions are probably the most important body fluid for infection.
- The prevalence of infection may be more common among pedigree cats.
- Most cases occur in cats under 1 year of age.
- Chlamydia target mucosal tissues. The primary target for *C felis* is the conjunctiva.
- Ocular discharges are initially watery and become mucoid or mucopurulent later.
- Transient fever, inappetence and weight loss may occur shortly after infection.
- Kittens are protected for the first 1–2 months of life by maternally derived antibodies.
- Diagnosis of infection can be performed by PCR on ocular swab material, provided it contains enough cells.
- *C felis* infection in cats can be effectively treated with tetracyclines.
- Both inactivated and modified-live virus vaccines based on whole chlamydial organisms are available as part of multivalent preparations.
- Vaccination should be considered for cats at risk of exposure to infection, particularly in multi-cat environments, and if there has been a history of chlamydial infection.
- Vaccination generally begins at 8–10 weeks of age, with a second injection 3–4 weeks later. Annual booster vaccination is recommended for cats at risk of exposure.

Acknowledgements

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