Journal of Feline Medicine and Surgery (2009) 11, 610–614
doi:10.1016/j.jfms.2009.05.010

CLINICAL REVIEW

BORDETELLA BRONCHISEPTICA INFECTION IN CATS
ABCD guidelines on prevention and management

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Overview *Bordetella bronchiseptica* is a Gram-negative bacterium that colonises the respiratory tract of mammals and is considered to be a primary pathogen of domestic cats. It is sensible to consider *B bronchiseptica* as a rare cause of zoonotic infections. The bacterium is susceptible to common disinfectants.

Infection The bacterium is shed in oral and nasal secretions of infected cats. Dogs with respiratory disease are an infection risk for cats. The microorganism colonises the ciliated epithelium of the respiratory tract of the host, establishing chronic infections.

Disease signs A wide range of respiratory signs has been associated with *B bronchiseptica* infection, from a mild illness with fever, coughing, sneezing, ocular discharge and lymphadenopathy to severe pneumonia with dyspnoea, cyanosis and death.

Diagnosis Bacterial culture and PCR lack sensitivity. Samples for isolation can be obtained from the oropharynx (swabs) or via transtracheal wash/bronchoalveolar lavage.

Disease management Antibacterial therapy is indicated, even if the signs are mild. Where sensitivity data are unavailable, tetracyclines are recommended. Doxycycline is the antimicrobial of choice. Cats with severe *B bronchiseptica* infection require supportive therapy and intensive nursing care.

Vaccination recommendations
In some European countries an intranasal modified-live virus vaccine is available. The modified-live product is licensed for use as a single vaccination with annual boosters. Cats should not be routinely vaccinated against *B bronchiseptica* (non-core), since the infection generally causes only a mild disease.

Bacterial properties

Bordetella bronchiseptica is a primary pathogen of domestic cats, particularly in high population density conditions such as rescue shelters and multi-cat households.

Bordetella pertussis, *Bordetella parapertussis* and *B bronchiseptica* are closely related Gram-negative coccobacilli that colonise the respiratory tract of mammals. *Bordetella pertussis* is a strictly human pathogen and the primary aetiological agent of whooping cough, which can also be caused by *B parapertussis*. Being the least host-restricted member of this taxonomic cluster, *B bronchiseptica* causes chronic respiratory infections in cats, dogs, rabbits, pigs and humans. Sequence analysis has shown that *B parapertussis* and *B pertussis* are independent derivatives of *B bronchiseptica*-like ancestors. During their evolution, there was large-scale gene loss and inactivation; host adaptation seems to be a consequence of loss, not gain, of function, and differences in virulence may be related to loss of regulatory or control functions.[1]

Because of its role as a human pathogen, *B bronchiseptica* is becoming more and more important.[2,3] Most cases occur in immunocompromised patients, without clear evidence of exposure to animals. Zoonotic infections have been incidentally recorded in the literature: a possible human infection from a rabbit, and infections in paediatric lung transplant recipients, where dogs had been suspected as the origin of infection.[4,5] It is sensible therefore to consider *B bronchiseptica* as being a rare potential cause of zoonotic infections.

European Advisory Board on Cat Diseases
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 *Bordetella bronchiseptica* infection guidelines presented in this article is available at www.abcd-vets.org

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1098-612X/09/070610+5 $34.00/0

In a large survey of pathogens associated with respiratory disease in multi-cat (≥5 cats) households in nine European countries, *B bronchiseptica* was detected by PCR in 5% of cats from households with disease and in 1.3% without disease.

Epidemiology

The bacterium is shed in oral and nasal secretions of infected cats.[6] Direct and indirect contacts with such discharges are probably responsible for *B bronchiseptica* transmission, although this has not been experimentally confirmed. As with feline calicivirus (FCV) and feline herpesvirus (FHV), overcrowding and poor management predispose to infection and disease.

The physicochemical stability of *B bronchiseptica* is unknown. The mean environmental persistence of *B pertussis* is longer than 10 days, and *B bronchiseptica* is probably equally hardy, so indirect transmission must be assumed.[7] The bacterium is susceptible to common disinfectants.

In a large survey of pathogens associated with respiratory disease in multi-cat (≥5 cats) households in nine European countries, *B bronchiseptica* was detected by PCR in 5% of cats from households with disease and in 1.3% without disease. The larger the group, the more likely a cat was to be found positive. PCR will have underestimated the true prevalence since it was found to be less sensitive than bacterial culture. Seroprevalence was 61% and 41%, respectively, and the poor hygiene in rescue shelters was also associated with higher seroprevalence.[8]

In a cross-sectional survey of a convenience (non-random) sample (740 cats), *B bronchiseptica* was isolated from 19% of the cats in rescue catteries, from 13.5% in research colonies and not at all from household pets.[9] Dogs with respiratory disease are a risk factor for cats; the suggestion of dog–to–cat transmission of *B bronchiseptica* has been supported by molecular data.[10]

After experimental infection, the organism has been isolated for 19 weeks. It was also cultured from post-parturient queens that had been negative previously. Under these conditions, the kittens remained *B bronchiseptica*-negative and did not seroconvert.[11]

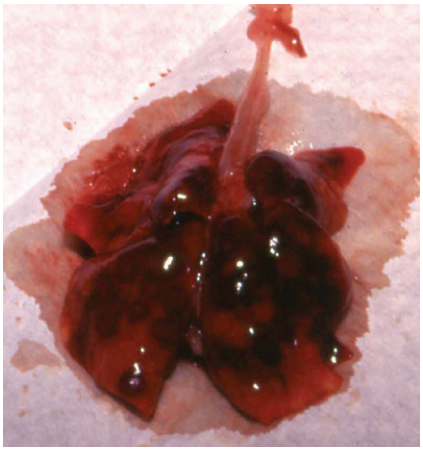

FIG 1 Lungs of a kitten that died of pneumonia. *Bordetella bronchiseptica* was isolated from the lungs. *Courtesy of Maria Grazia Pennisi, University of Messina, Italy*

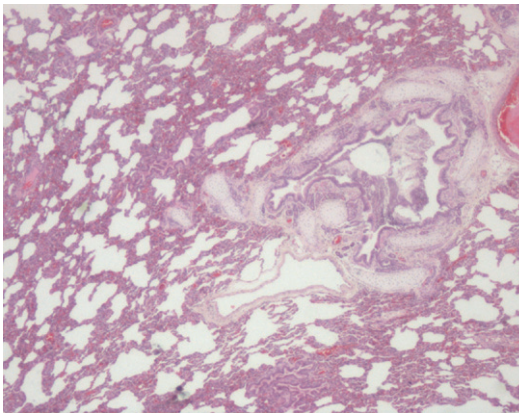

FIG 2 Lung section from a kitten that died of pneumonia caused by *Bordetella bronchiseptica* infection. *Courtesy of The Feline Centre, University of Bristol, UK*

Pathogenesis

Bordetella bronchiseptica is a primary pathogen of cats. Respiratory disease has been reproduced in specific pathogen-free cats after aerosol and nasal challenge, and field cases associated with *B bronchiseptica* have also been reported (Figs 1 and 2).[11–14] However, in the field, additional factors may be involved in disease development, including environmental conditions leading to stress (eg, overcrowding), or pre-existing viral infections.

Little information exists about the pathogenicity of *B bronchiseptica* in the cat, and much has to be inferred from infections in other species. Features responsible for *B bronchiseptica* acting as a primary pathogen in the feline respiratory tract are its motility (propulsion by flagella), the presence of adhesins and toxin production.

This microorganism colonises the ciliated epithelium of the respiratory tract of the host, establishing chronic infections. Bordetellae have evolved mechanisms, some of them shared, that allow them to colonise this site, a surface designed to eliminate foreign particles.[15] These include adhesins such as filamentous haemagglutinin, fimbriae and periactin. Fimbriae are required for efficient and persistent colonisation of the trachea. They also play an important role in the development of humoral immunity to *Bordetella* infection.[16] Once attached, toxins and *B bronchiseptica*-specific secreted proteins result in ciliostasis and destruction of the cilia.

Immunity

Antibodies play an important role in the immune response to *B bronchiseptica* and bacterial clearance.

Passive immunity

Little information is available on the transmission of maternally derived antibodies (MDA) to kittens. In one study of kittens born to *B bronchiseptica*-positive queens, MDA remained low and only detectable for 2 weeks.[11] In another study, low levels of MDA remained detectable for 8 weeks, but were not assayed for longer.[12]

Active immune response

After *B bronchiseptica* infection, serum antibodies rise rapidly, but it is unknown for how long they persist.[11] Immunoglobulin A (IgA) is the main class in mucosal secretions. Individuals deficient in IgA are more susceptible to certain sinopulmonary infections.[17] In mice it was shown that IgA is also essential for controlling *B bronchiseptica* in the upper respiratory tract. Transfer of IgA-containing convalescent serum effectively reduced *Bordetella* numbers in the trachea, but cleared only *B bronchiseptica* and not the human *Bordetella* pathogens.[18]

Clinical signs

Experimental infection of specific pathogen-free cats induced mild clinical signs consisting of fever, coughing, sneezing, ocular discharge and lymphadenopathy, which resolved after about 10 days.[11,12]

In the field, a wide range of respiratory signs has been associated with *B bronchiseptica* infection, from the mild ones described above to severe pneumonia with dyspnoea, cyanosis and death.[6,13,14] Pneumonia is usually seen in kittens younger than 10 weeks old, but older cats can be affected as well (Fig 3). *Bordetella bronchiseptica* infection should be considered in coughing cats (acute and chronic).

Diagnosis

Bacterial culture (isolation) and PCR are available, but both methods suffer from a lack of sensitivity. Samples for isolation can be obtained from the oropharynx (swabs) or via transtracheal wash/bronchoalveolar lavage. Cytological analysis of tracheal washes demonstrates polymorphonuclear leukocytes, macrophages and bacteria.[14]

The identification of *B bronchiseptica* from bronchoalveolar lavage samples of cats with lower respiratory signs is considered to be diagnostic.

Bacterial culture

For isolation, swabs should be placed into charcoal (or regular) Amies transport medium. *Bordetella bronchiseptica* should be cultured on a selective medium such as charcoal/cephalexin agar, which reduces overgrowth by other respiratory flora. The identification of *B bronchiseptica* from bronchoalveolar lavage samples from cats with lower respiratory signs is considered to be diagnostic. The significance of *Bordetella* in oropharyngeal swabs from cats with predominantly upper respiratory clinical signs is less clear-cut, but will usually be considered an indication for antibiotic treatment.

In cats from multi-cat households and other crowded environments, the prevalence of *B bronchiseptica* infection is higher and the bacterium may simply be present coincidentally; other causes for the presenting clinical signs must then be considered.

PCR

Sensitive real-time PCR methods are capable of discriminating between different bordetellae and can detect fewer than 10 genome copies of *B bronchiseptica* /µl.[19] Some laboratories have developed multiplex assays that allow the simultaneous detection of all common feline respiratory pathogens. Unfortunately, such assays are often less sensitive.[8]

Serology

Serology is of limited diagnostic value due to the high seroprevalence in the general cat population.

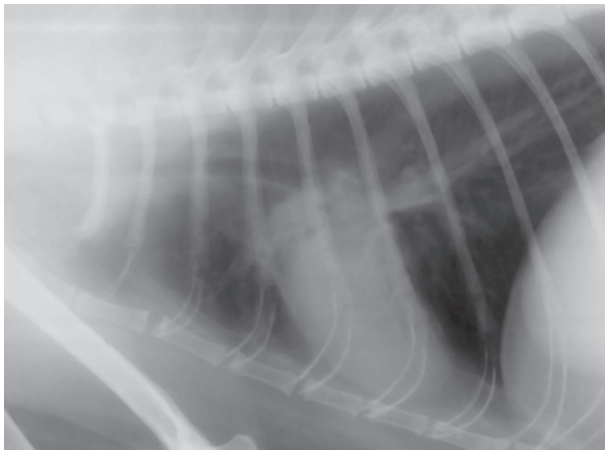

FIG 3 ***Bordetella bronchiseptica*** **infection in cats can sometimes lead to bronchopneumonia as a complication.** *Courtesy of Andy Sparkes*

In the field, a wide range of respiratory signs has been associated with *B bronchiseptica* infection, from mild (fever, coughing, sneezing) through to severe pneumonia with dyspnoea, cyanosis and death.

Disease management

Antibacterial therapy

Antibacterial therapy may be indicated, even when the signs are mild, because *B bronchiseptica* might progress to colonise the lower respiratory tract. Therapy should be based on the results of antibiotic sensitivity testing. Where sensitivity data are unavailable, tetracyclines are recommended, since most feline *B bronchiseptica* isolates have been found to be susceptible. Doxycycline is the antimicrobial of choice. Feline *B bronchiseptica* isolates are less susceptible to clavulanate-potentiated amoxicillin, and resistance has often been detected to ampicillin and trimethoprim [EBM grade III].[20] While antimicrobial therapy should help to alleviate clinical signs, short courses of antibiotic treatment in recovered carrier cats have little effect on shedding.[11]

Supportive treatment

Cats with severe *B bronchiseptica* infection require supportive therapy and intensive nursing care. The resolution of dehydration and restoration of electrolyte and acid–base disturbances, preferably by intravenous fluid administration, may be required.

Vaccination

In some European countries an intranasal modified-live virus vaccine is available. The ABCD recommends that cats should not be routinely vaccinated against *B bronchiseptica* (non-core), since the infection generally causes only a mild disease.

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 a statement relating to disease management. To put this into context, the grading exists 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.

In shelters, *B bronchiseptica* vaccination is encouraged, particularly if there is a history of microbiologically confirmed disease.

Disease control in specific situations

Control of *B bronchiseptica* in cat populations is aimed at minimising the exposure of naive cats. Stocking densities may need to be reduced and the environment cleaned and disinfected to minimise the risk of transmission. Otherwise, the measures advocated for the control of other common respiratory pathogens, such as FCV and FHV, in groups of cats will help to control infection and disease.

Shelters

Random source populations with largely unknown vaccination histories, continuous resident turnover, and a high risk of infectious disease characterise most shelters. In these, *B bronchiseptica* vaccination is encouraged, particularly if there is a history of microbiologically confirmed disease.

Breeding catteries

Vaccination schedules used for privately owned cats are appropriate for most breeding catteries. Again, *B bronchiseptica* vaccination should only be encouraged where the organism has been confirmed to be associated with disease.

Immunocompromised cats

Vaccination of immunocompromised cats is not recommended.

Vaccination recommendations

General considerations

Bordetella bronchiseptica vaccines containing viable bacteria should never be administered to kittens under 4 weeks of age. In addition, they are ineffective in cats on, or due to receive, antibiotics. Cats receiving live vaccines will shed bacteria and must be avoided where an owner is known to be immunocompromised. As in dogs, these vaccines may occasionally induce mild clinical signs in cats.

Primary course

Vaccination should be limited to cats living in or moving into high-density populations with a history of *B bronchiseptica* disease, and should be performed according to the manufacturer's recommendations.

Booster vaccinations

The modified-live virus vaccine is licensed for use as a single vaccination with annual boosters. A duration of immunity of at least a year has been demonstrated.[21]

Boosters should be continued as long as the cat remains in a high-risk situation.

Non-core vaccine

The ABCD considers vaccines that protect against *B bronchiseptica* infections as being non-core.

Acknowledgements

The European Advisory Board on Cat Diseases (ABCD) is indebted to Dr Karin de Lange for her judicious assistance in organising this special issue, her efforts at coordination, and her friendly deadline-keeping. The tireless editorial assistance of Christina Espert-Sanchez is gratefully acknowledged. The groundwork for this series of guidelines would not have been possible without financial support from Merial. The ABCD particularly appreciates the support of Dr Jean-Christophe Thibault, who respected the team's insistence on scientific independence.

KEY POINTS

- *Bordetella bronchiseptica* is a primary pathogen of domestic cats.
- Zoonotic infections have been incidentally recorded in the literature.
- The bacterium is shed in oral and nasal secretions of infected cats.
- The bacterium is susceptible to common disinfectants.
- Dogs with respiratory disease are an infection risk for cats.
- *B bronchiseptica* colonises the ciliated epithelium of the respiratory tract of the host.
- A wide range of respiratory signs has been associated with *B bronchiseptica* infection, from mild presentations through to severe pneumonia with dyspnoea, cyanosis and death.
- Where sensitivity data are unavailable, tetracyclines are recommended, since most feline *B bronchiseptica* isolates have been found to be susceptible.
- In some European countries an intranasal modified-live virus vaccine is available.

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