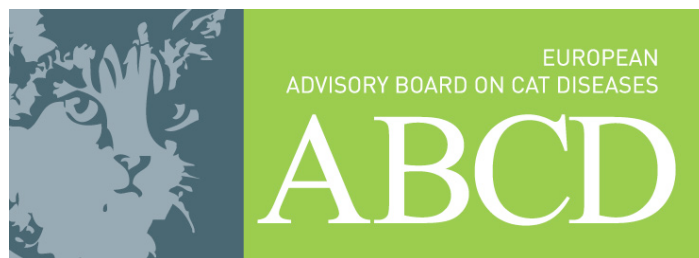


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The following recommendations have been formulated by the European Advisory Board on Cat Diseases.



The European Advisory Board on Cat Diseases is an independent panel of 17 veterinarians from ten European countries, with an expertise in immunology, vaccinology and/or feline medicine. The ABCD was set up to compile guidelines for the prevention and management of major feline infectious disease in Europe based on current scientific knowledge and available vaccines.

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## ABCD Panel members

### **Marian Horzinek**

Former Head, Dept of Infectious Diseases, div. Immunology & Virology, Faculty of Veterinary Medicine; Director, Graduate School Animal Health; Director, Institute of Veterinary Research; Utrecht, (NL). Founder President European Society of Feline Medicine. Research foci: feline coronaviruses, viral evolution.

### **Diane Addie**

Director, Feline Institute Pyrenees, France. Honorary Senior Research Fellow, University of Glasgow Veterinary School, UK. Research foci: eradication of feline coronavirus (FIP); cure for / prevention of chronic gingivostomatitis. Interested in all feline infectious diseases. [www.catvirus.com](http://www.catvirus.com)

### **Sándor Bélak**

Full professor, Dept of Virology, Swedish University of Agricultural Sciences (SLU) & The National Veterinary Institute (SVA), Uppsala (S); OIE Expert for the diagnosis of viral diseases (Sweden). Research foci: biotechnology-based diagnosis, vaccine development, the genetic basis for viral pathogenesis, recombination and virus-host interaction.

### **Corine Boucraut-Baralon**

Associate professor, Infectious Diseases, Toulouse Veterinary School; Head, Diagnostic Laboratory Scanelis, France. Research foci: poxviruses, feline calicivirus, feline coronavirus, and real-time PCR analysis.

### **Herman Egberink**

Associate professor, Dept of Infectious Diseases and Immunology, Virology division, Faculty of Veterinary Medicine, Utrecht; Member of the national drug registration board, the Netherlands. Research foci: feline coronavirus (FIP) and FIV, vaccine development and efficacy, antivirals.

### **Tadeusz Frymus**

Full professor, Head, Division of Infectious Diseases and Epidemiology, Dept of Clinical Sciences, Warsaw Veterinary Faculty, Poland. Research foci: vaccines, Feline leukaemia virus (FeLV), Feline immunodeficiency virus (FIV), Feline Coronavirus (FCoV/FIP) Bordetella bronchiseptica infection, and canine distemper.

### **Tim Gruffydd-Jones**

Head, The Feline Centre, Professor in Feline Medicine, Bristol University, UK; founder member European Society of Feline Medicine. Research foci: feline infectious diseases, in particular coronavirus and Chlamydia.

### **Katrin Hartmann**

Head, Dept of Companion Animal Internal Medicine & full professor of Internal Medicine, Ludwig Maximilian University Munich, Germany; AAFCP vaccination guidelines panel member. Research foci: infectious diseases of cats and dogs with special interest in diagnosis and treatment.

### **Margaret J. Hosie**

Institute of Comparative Medicine, Glasgow, UK. RCVS Specialist in Veterinary Pathology (Microbiology) Research focus: Feline immunodeficiency virus pathogenesis and vaccine development, feline calicivirus.

### **Albert Lloret**

Clinician, Veterinary Teaching Hospital, Barcelona University, Spain. Research foci: feline medicine, molecular diagnostics of feline disease, feline injection site sarcomas.

### **Hans Lutz**

Head, Clinical Laboratory, Faculty of Veterinary Medicine, University of Zurich, Switzerland. Research foci: feline retro- and coronaviruses (pathogenesis & vaccination), epidemiology and molecular diagnostics of feline infectious diseases.

### **Fulvio Marsilio**

Dept of Comparative Biomedical Sciences, Div. Infectious Diseases, University of Teramo (I). Research foci: PCR as diagnostic tool for upper respiratory tract disease in cats, recombinant feline calicivirus vaccine.

### **Maria Grazia Pennisi**

Professor, Clinical Veterinary Medicine. Head, Companion Animal Internal Medicine Clinic, Dept Veterinary Medical Sciences, University of Messina, (I). Research foci: clinical immunology, Bordetella bronchiseptica in cats, FIV.

### **Alan Radford**

Senior Lecturer & Researcher, Dept Small Animal Studies, Liverpool Veterinary School, UK. Research foci: FCV and FHV-1 virulence genes, Bordetella bronchiseptica in cats, parvoviruses and coronaviruses, immune-response variation.

### **Andy Sparkes**

Head, Feline Unit, Animal Health Trust; Chairman, Feline Advisory Bureau, UK; Editor, European Journal of Feline Medicine and Surgery; AAFCP vaccination guidelines panel member. Research foci: feline infectious diseases, lower respiratory tract disease, oncology.

### **Etienne Thiry**

Full professor, Head of Veterinary Virology, Dept Infectious Diseases and Virology, Liege Veterinary Faculty (B); Member, Committee of Veterinary Medicinal Products (B); Agencies for animal health and food safety (F, B). Research foci: herpesviruses, caliciviruses, emerging feline viruses, host-virus interactions.

### **Uwe Truyen**

Head of the Institute for Animal Hygiene & Veterinary Public Health, University of Leipzig, Germany, Head of the German standing vaccination committee Vet. Research foci: Animal Hygiene, epidemiology, parvoviruses, feline calicivirus.

## **8 Bordetella bronchiseptica infection in cats**

### **8.1 Bacterial properties**

*Bordetella bronchiseptica* (*Bb*) is a primary pathogen of domestic cats particularly in high population density conditions such as some rescue shelters and multicat households.

*Bordetella pertussis*, *Bordetella parapertussis* and *Bb* are closely related Gram-negative coccobacilli that colonize the respiratory tracts of mammals. *B. pertussis* is a strict human pathogen and is the primary etiologic agent of whooping cough. *B. parapertussis* can also cause whooping cough, and *B. bronchiseptica* is the most promiscuous member of this taxonomic cluster and causes chronic respiratory infections in a wide range of animals including cats, dogs, rabbits, pigs and humans. Sequence analysis indicates that *B. parapertussis* and *B. pertussis* are independent derivatives of *Bb*-like ancestors. During the evolution of these two host-restricted species 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 [Parkhill et al., 2003].

*Bb* is acquiring relevance because of its increased importance as a human pathogen [Woolfret and Moody 1991; Bauwens et al 1992]. Most cases in humans are in immunocompromised patients and lack a clear link with exposure to animals. There is no evidence to support zoonotic infection between cats and people. However, there is one report describing possible human infection from a rabbit [Gueirard et al 1995] and a report describing two *Bb* infections in pediatric lung transplant recipients. In the latter case pet dogs were suspected to be the origin of infection [Ner et al 2003]. Therefore, it seems sensible to consider *Bb* as a rare but potential zoonotic infection.

### **8.2 Epidemiology**

*Bordetella* is shed in oral and nasal secretions of infected cats [Speakmann et al 1999]. It is therefore likely that direct or indirect contact with such discharges is the main route of transmission, although no detailed studies have been carried out to confirm this. Some

cats may shed higher levels of the *Bb* and therefore be more likely to transmit it to other animals. As with the FCV and FHV, overcrowding and poor management may predispose to infection and disease.

Environmental persistence of *B. bronchiseptica* is unknown. However, the mean environmental persistence of *B. pertussis* is greater than 10 days [Weather & Ewald, 2004], so it would seem likely that *B. bronchiseptica* would be equally hardy, therefore we presume that indirect transmission is possible. However, it is susceptible to common disinfectants.

In a large survey of pathogens associated with respiratory disease in 1724 cats from 218 multicat (five or more cats) households in nine European countries, *Bb* was detected by PCR in 5% of cats from households with disease and 1.3% of cats from households without disease [Helps et al 2005]. The larger the group of cats the more likely a cat was to be positive. The PCR used in this study will underestimate true prevalence since it was shown to be less sensitive than bacterial isolation [Helps et al 2005]. Seroprevalence rates in 1463 cats from the same study for which blood samples were also available were 61% and 41% respectively with rescue shelters and poor hygiene also being associated with increased seroprevalence.

In a convenience study using isolation from 740 cats, *Bb* was isolated from 19% of cats in rescue catteries, 13.5% of those in research colonies and 0% of household pets. There was also evidence for dogs with respiratory disease being a risk factor for feline infection and suggesting dog to cat transmission, a possibility supported by molecular data in one case study [Dawson et al 2000].

In experimental infections the organism has been isolated for 19 weeks post infection and also from post-parturient queens that were negative before parturition perhaps suggesting that the physiological stress of giving birth may reactivate a previously undetectable infection [Coutts et al 1996]. However, under these experimental conditions, kittens remained *Bb*-negative suggesting transmission from mother to kitten does not always occur.

### **8.3 Pathogenesis**

In the past, *Bb* was considered to play only a secondary role in feline respiratory disease but it is now established as a primary pathogen in this species. Respiratory disease has been reproduced in specific pathogen free cats following both aerosol and nasal challenge [Jacobs et al., 1993; Coutts et al., 1996] and a number of field cases associated with *Bb* have also been reported [Willoughby et al., 1991; Welsh, 1996]. However, it is likely in the field that other factors may be involved in disease including environmental factors such as stress or overcrowding, or in some cases, pre-existing viral infection

There is little data available on the pathogenicity of *Bb* in the cat but much can be inferred from infections in other species. Features of *Bb* that are responsible for acting as a primary pathogen in the feline respiratory tract are its motility (mediated by flagellin), the presence of adhesins and production of toxins.

This microorganism colonizes the ciliated epithelium of the respiratory tract of the host, establishing chronic infections. *Bordetella* have evolved many often shared mechanisms that allow them to colonize this site, a surface designed to eliminate foreign particles [Mattoo et al., 2001]. These include adhesins such as filamentous hemagglutinin, fimbriae and periactin. Fimbriae are required for efficient establishment and persistent colonization of the trachea. They also play an important role in the development of humoral immunity to *Bordetella* infection [Mattoo et al., 2000].

Once attached, toxins such as a bifunctional adenylate cyclase/hemolysin, dermonecrotic toxin, tracheal cytotoxin, and *Bb*-specific type III secreted proteins result in ciliostasis and destruction of the cilia.

### **8.4 Immunity**

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

#### **8.4.1 Passive immunity**

There is limited data available on the transmission of maternally derived antibodies (MDA) to kittens. In one study of two litters of kittens born to *Bb* positive queens, MDA

remained low and was only detectable for two weeks [Coutts et al 1996]. In a second study, low levels of MDA remained detectable up to 8 weeks but were not assayed for longer [Jacobs et al 1993].

#### **8.4.2 Active immune response**

Following infection, serum antibodies rise rapidly [Coutts et al 1996]. There is no data on the duration of persistence of these antibodies.

IgA is the main immunoglobulin in mucus secretions. Clinical and experimental studies show that individuals deficient in the immunoglobulin A (IgA) isotype of antibodies, are more susceptible to certain sinopulmonary infections [Renegar et al 2004]. In mice it was shown that IgA is also essential for controlling *Bb* in the upper respiratory tract. Passive transfer of IgA-containing convalescent serum has also been shown to effectively reduce *Bb* numbers in the trachea. [Wolfe et al., 2007].

Adoptively transferred antibodies rapidly cleared only *Bb*, not the human *Bordetella* pathogens.

### **8.5 Clinical signs**

Experimental infection of SPF cats induced mild clinical signs consisting of pyrexia, coughing, sneezing, ocular discharge and lymphadenopathy [Jacobs et al 1993, Coutts et al 1996]. Signs resolved after about 10 days.

In the field, a wide range of respiratory signs have been associated with *Bb* infection of cats, ranging from the mild clinical signs described above, to severe respiratory signs caused by pneumonia including dyspnoea, cyanosis and death, [Willoughby et al 1991, Welsh 1996, Speakman et al 1999]. Cases of pneumonia are usually seen in young kittens less than 10-weeks-old but older cats can be affected as well. *Bb* infection should be considered in coughing cats (acute and chronic).

### **8.6 Diagnosis**

Both isolation and PCR tests are available but both suffer from a lack of sensitivity. Samples for isolation can be obtained from the oropharynx (swabs) or through

transtracheal wash/ broncho-alveolar lavage. Cytological analysis of tracheal washes show polymorphonuclear leucocytes, macrophages and bacteria [Welsh 1996].

### **8.6.1 Bacterial culture**

For isolation, swabs should be placed into charcoal Amies transport medium, although ordinary Amies transport medium can also be used. *Bb* should be cultured on an appropriate selective medium such as charcoal/cephalexin agar, which reduces overgrowth by other respiratory flora. The identification of *Bb* from bronchoalveolar lavage samples from cats with lower respiratory signs can be considered to be diagnostic. Interpretation of the significance of the identification of *Bordetella* in oropharyngeal swabs from cats with predominantly URT signs is less clearcut but will usually be considered as an indication for appropriate antibiotic treatment. Positive culture from oropharyngeal swabs from cats from multicat households have to be interpreted with the awareness that the prevalence of infection is higher in cats from crowded environments and that the bacterium may simply be present co-incidentally and other causes of presenting clinical signs must be considered.

### **8.6.2 PCR**

Sensitive real-time PCR assays have been described that are capable of discriminating between different *Bordetella* and detecting less than 10 genome copies of *Bb* per  $\mu\text{l}$  [Koidl et al., 2007]. Some laboratories have developed multiplex assays that allow the detection of all common feline respiratory pathogens in one assay. Unfortunately, such assays often have a negative impact on the sensitivity of such assays [Helps et al 2005].

### **8.6.3 Serology**

Serological diagnosis is of limited diagnostic use due to the high seroprevalence in the general cat population.

## **8.7 Disease management**

In cases of a *Bb* infection, antibacterial therapy is indicated even if signs are relatively mild because it can not be excluded that *Bordetella* might colonize the lower respiratory

tract. If possible this should be based on results of antibiotic sensitivity. However, this is not likely to be available in all cases.

Where sensitivity is not available, almost all isolates of *Bb* from cats are sensitive to tetracyclines. Doxycycline is the antimicrobial of choice for treating *Bb* infections. Feline isolates of *Bb* are less susceptible to clavulanate-potentiated amoxicillin (CPA) and a high level of resistance has been detected to ampicillin and trimethoprim [Speakman et al., 1997]. Whilst antimicrobial therapy should help alleviate clinical disease, short courses of antibiotics in clinically recovered carrier cats may have little effect on shedding [Coutts et al., 1996].

Cats severely affected by *Bb* 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.

## **8.8 General recommendations on vaccination**

In some European countries an intranasal modified live vaccine against *Bb* is available. Modified live (ML) *Bb* vaccines should never be administered to kittens under 4 weeks of age. In addition, they are unlikely to be efficacious in cats on, or due to receive, antibiotics. Cats receiving a live vaccine will shed post-vaccination. They are perhaps best avoided where an owner is known or suspected to be immunocompromised. As with *Bb* vaccination in dogs, ML vaccines may induce mild clinical signs in occasional vaccinated animals.

### **8.8.1 Primary vaccination course**

Since *Bb* is generally a mild disease of low prevalence in the small populations that pet cats typically live in, ABCD recommends that cats are not routinely vaccinated against *Bb* (non-core). Rather vaccine should be limited to those cats living in or moving into high density populations of cats with a history of *Bb* disease.

Where vaccine is deemed appropriate, cats should be vaccinated according to manufacturer's recommendations.

### **8.8.2 Booster vaccinations**

The live vaccine is licensed for use as a single vaccination with annual boosters. A duration of immunity of at least a year has been demonstrated [Williams et al. 2002] Boosters should only be performed as long as the cat remains exposed to high risk situations.

## **8.9 Disease control in specific situations**

Control of *Bb* in cat populations is aimed at minimizing the exposure of naïve cats. Stocking densities may need to be reduced and the environment cleaned and disinfected to minimize 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 control infection and clinical disease.

### **8.9.1 Shelters**

Random source populations with largely unknown vaccination histories, continuous resident turnover, and high risk for infectious disease characterize most shelters.

*Bb* vaccination should be encouraged when there is a history of confirmed disease.

### **8.9.2 Breeding catteries**

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

### **8.9.3 Vaccination of immunocompromised cats**

It is not recommended to vaccinate immunocompromised cats .

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