



PEER REVIEWED

VITAL VACCINATION SERIES

KENNEL COUGH REVISITED

Richard B. Ford, DVM, MS,
Diplomate ACVIM & ACVPM (Hon)
North Carolina State University

Kennel cough—it is one of the oldest descriptors of canine disease that appears in the veterinary literature. Aliases include canine cough, canine croup, infectious tracheobronchitis (ITB) and, most recently, canine infectious respiratory disease (CIRD), also known as canine infectious respiratory disease complex (CIRDC).

No matter the name, kennel cough is one of the most common canine respiratory infections. As a clinical syndrome, it has undergone changes in etiology, treatment recommendations, and options for prevention. The causes are many and include a growing list of pathogenic bacteria and viruses.¹⁻⁷ The most notable changes, however, are found in vaccine options and claims of efficacy.

The controversies in this area include:

- Roles of vaccination in treating active infections
- Onset of immunity following vaccination
- Duration of immunity
- Public health implications of *Bordetella bronchiseptica*, including risk associated with human exposure to live avirulent (intranasal and oral) vaccine.

This article provides an overview of CIRD from the perspective of clinical manifestations and prevention, including vaccines and vaccination protocols. Turn to page 30 to read Dr. Laura Nafe's article, **Diagnostic & Therapeutic Approach: Dogs Infected with *Bordetella bronchiseptica* & Canine Influenza Virus (H3N8)**, for in-depth information on diagnosis and treatment of CIRD.

PATHOGENIC AGENTS

CIRD is well recognized as a contagious upper respiratory infection of dogs resulting from bacterial or viral infection. Because clinical manifestations vary according to the primary infecting agent, or combination of agents, CIRD is appropriately referred to as a respiratory syndrome. *B bronchiseptica* is commonly implicated as the principal cause of kennel cough;⁸ however, it is by no means the exclusive, nor is it the most virulent, pathogen implicated.

Bacteria

Bacteria recovered from dogs exhibiting signs consistent with CIRD include:

- *B bronchiseptica*
- *Streptococcus equi* subspecies *zoepidemicus* (sometimes called *strep zoo*)
- *Mycoplasma* species (to a lesser extent), particularly *M cynos*.

***B bronchiseptica*.** *B bronchiseptica* is a gram negative bacterium capable of infecting multiple species, including humans, and it can potentially be transmitted from dogs (and possibly cats) to humans.

Simply recovering *B bronchiseptica* from the respiratory tract of a coughing dog/cat does **not** define its role as causative. This pathogen has the unique ability to reside on epithelial cells of the upper respiratory tract as a commensal organism; hence, *B bronchiseptica* is commonly recovered from the respiratory tract of healthy dogs and cats.

For reasons not fully understood, these "innocent" bacteria are able to transition into highly pathogenic organisms. *Bor-*

detella virulence is linked to a gene complex (Bvg) capable of expressing multiple, well defined virulence factors (toxins) that cause serious, rapid injury to respiratory epithelium.⁹

***Streptococcus equi* subspecies *zooepidemicus*.** Recently, *S. equi* subspecies *zooepidemicus*, a gram positive bacterium, has gained attention as a zoonotic infection of horses. Although **not** a commensal organism in dogs/cats, *S. zooepidemicus* is capable of colonizing upper respiratory epithelial cells of dogs and cats. It appears to be a significant cofactor in upper respiratory infections of dogs and cats and has been attributed to fatal necrohemorrhagic pneumonia in outbreaks of CIRDC in shelters.³

Viruses

Primary pathogens in CIRDC include:^{5,7}

- **Canine parainfluenza virus (CPIV)**
- **Canine adenovirus-2 (CAV-2)**
- **Canine influenza virus (CIV)**
- **Canine distemper virus (CDV).**

Additional viruses recovered from dogs with CIRDC include:

- **Canine respiratory coronavirus (CRCoV):** Shelter/kennel-housed dogs with CIRDC in Europe, Japan, and the U.S.⁶
- **Canine pneumovirus (CnPnV):** Recovered from respiratory tract of coughing dogs in the U.S.⁴ These dogs were found to carry other known pathogens involved in CIRDC; however, the significance of CnPnV in causing, or contributing to, CIRDC is still unknown.

SPECTRUM OF CLINICAL MANIFESTATIONS

Clinical signs vary based on the individual agent responsible for infection in clinically affected dogs.

Viral pathogens tend to be associated with clinical signs ranging from acute onset, highly contagious cough with expectoration of mucus that typically lasts 1 to 2 weeks to mild or no clinical signs (seroconversion only). Although coughing may persist for several weeks, dogs tend to effectively clear infectious viruses within 2 weeks following onset of signs.

Bacterial pathogens tend to be associated with not only cough, but systemic illness characterized by mucoid to mucopurulent nasal and ocular discharge, fever, and loss of appetite. Other clinical findings include orthopnea, dyspnea, and even life-threatening pneumonia, particularly in young animals. Clinical signs can persist for several days or longer depending on treatment administered.

Clinical illness associated with individual pathogens, however, does not necessarily represent the spectrum of clinical manifestations encountered in practice. For example, reports of dogs with confirmed CIV infection indicate that some simply seroconvert without developing significant respiratory signs, while others die.

However, it is unlikely that CIV, acting alone, causes such dramatic variation in clinical outcomes; CIRDC likely results from the complex interaction between:

- Host
- Multiple respiratory pathogens acting together (viral and bacterial)

- Environmental factors.

The occurrence of co-infection explains, at least in part, why predicting clinical outcomes of CIRDC in individual dogs can be difficult, and it explains why well vaccinated dogs still develop kennel cough.

TABLE 1. CIRDC Pathogens for Which Vaccines Are Available in the U.S.

- *B. bronchiseptica*
- CPIV
- CAV-2
- CDV
- CIV

PREVENTION

Vaccination

Routine vaccination of dogs at risk for exposure is indicated and generally effective in reducing severity of cough in challenged dogs, despite the inability to immunize dogs against each of the known CIRDC pathogens. **Table 1** lists the pathogenic viruses and bacteria associated with CIRDC for which vaccines are available in the U.S.

Several types of vaccine (**Table 2**, page 74) are available for administration to dogs by the intranasal, oral, and parenteral (subcutaneous) route. The constituents and the routes of administration of commercially available vaccines vary. The route of vaccine administration indicated by the manufacturer must be strictly followed.

Prophylactic Use of Antibiotics

Although not indicated for the prevention of signs of CIRDC in individual pets, I have utilized **doxycycline, 5 mg/kg PO Q 24 H for 5 days**, administered to all dogs entering a large animal shelter experiencing high rates (> 50%) of acute onset cough. Follow-up over a 30-day period indicated:

- Rapid and substantial reduction in incidence of CIRDC within the population
- Higher placement rates
- Reduced euthanasia rates
- Lower operating costs.

Anecdotal observations suggest that empirical, daily administration of a broad-spectrum antibiotic may be of benefit in managing endemic respiratory disease associated with bacteria among shelter-housed dogs. While the cost of doxycycline may prohibit implementing programmatic treatment of all dogs entering a shelter, other less expensive, broad-spectrum antibiotics are available and may augment attempts to reduce the frequency or severity of CIRDC in populations of co-housed dogs.

Nosodes

Nosodes are liquid homeopathic preparations, sometimes called *homeopathic vaccines*, containing minute amounts of infectious material (tissue/discharge) collected from actively infected, unvaccinated animals. Intended for oral administration, proponents of nosodes claim efficacy in, not only preventing, but also treating infectious diseases in dogs and cats.

TABLE 2. Types of Vaccines Available for Immunizing Dogs Against CIRDC

ANTIGEN(S)	PREPARATION	INITIAL VACCINATION	REVACCINATION (BOOSTER)
Parenteral (subcutaneous)			
<i>B bronchiseptica</i>	<ul style="list-style-type: none"> • 1-mL single dose vial • Inactivated, antigen cell extract 	<ul style="list-style-type: none"> • 2 doses, 2–4 weeks apart • ≥ 8 weeks of age 	Annual single dose in dogs with sustained risk for exposure ^{a,b}
CDV + CPiV and CAV-2	<ul style="list-style-type: none"> • Commonly 1-mL dose in combination with CPV • Modified-live virus 	<ul style="list-style-type: none"> • 3-dose series recommended (initial puppy core vaccination series) • Between ≥ 6 weeks of age and 14–16 weeks of age 	Single booster recommended within 1 year of initial 3-dose series; thereafter, triennial vaccination recommended for all dogs
CIV	<ul style="list-style-type: none"> • 1-mL single dose vial • Killed virus 	<ul style="list-style-type: none"> • 2 doses, 2–4 weeks apart required regardless of age 	Annual single dose in dogs with sustained risk for exposure
Intranasal (mucosal)			
<i>B bronchiseptica</i>	<ul style="list-style-type: none"> • 0.5-mL total volume • Attenuated, avirulent bacteria 	<ul style="list-style-type: none"> • Single dose recommended • ≥ 3 weeks of age 	Revaccinate annually
<i>B bronchiseptica</i> + CPiV	<ul style="list-style-type: none"> • 1 mL total volume^c • Attenuated, avirulent live bacteria with modified live virus 	<ul style="list-style-type: none"> • Single dose recommended • ≥ 3 weeks of age 	Revaccinate annually
<i>B bronchiseptica</i> + CPiV and CAV-2	<ul style="list-style-type: none"> • 0.5-mL total volume • Attenuated, avirulent live bacteria with modified live virus 	<ul style="list-style-type: none"> • Single dose recommended • ≥ 3 weeks of age 	Revaccinate annually
Oral (mucosal)			
<i>B bronchiseptica</i>	<ul style="list-style-type: none"> • 1 mL total volume (the entire dose should be administered at the same time) • Attenuated, avirulent live bacteria 	<ul style="list-style-type: none"> • Single dose recommended • ≥ 8 weeks of age 	Revaccinate annually ^a

a. Manufacturer recommendation
 b. Duration of immunity studies have not been published
 c. May be reduced to 0.5 mL total volume by reducing volume of diluent used

Nosodes are **not** recommended for the treatment or prevention of CIRDC because:

- Values for composition, concentration, and purity of ingredients are not standardized.
- Nosodes are not subject to regulatory oversight.
- No studies have been published documenting either safety or efficacy.

VACCINATION PROTOCOL

There is no definition of a universal vaccination protocol applicable to all dogs. In fact, the availability of a diverse

The overall quality of protection a dog derives from vaccination against CIRDC is most likely correlated to the route of administration and the number of antigens administered.

selection of vaccines against one or more agents of CIRDC (Table 2) continues to raise the questions:

- Which vaccines should be administered?
- When should vaccines be administered?
- At what intervals should vaccines be administered?

Core & Noncore Vaccines

- **Core:** Parenteral vaccines against CDV and CAV-2 are considered core and indicated in **all** dogs.¹⁰
- **Noncore:** Vaccines for *B bronchiseptica*, CPiV, and CIV are considered noncore, or optional, and indicated in dogs with known or likely risk for exposure to other dogs, especially in kennels or co-housed environments; most dogs fall into this category. Vaccination is **not** indicated for dogs with strictly limited, or no, exposure to other dogs.
- **Note:** The canine (enteric) coronavirus vaccine is **not** effective against the antigenically distinct canine respiratory coronavirus.

Vaccines should only be administered to healthy animals. For example, administering a live, avirulent *B bronchiseptica* vaccine (intranasal or oral) to a dog concurrently receiving an antibiotic may exert an antibacterial effect on the vaccine antigen, resulting in reduced to no immunity.

Factors Applicable to Selection

While manufacturer advertisements and claims of vaccine efficacy can lead to confusion regarding vaccine selection, veterinarians recommending vaccination against CIRDC must base selection on several factors:

1. Age

Intranasal vaccines can be administered as a single dose as early as 3 to 4 weeks of age (see manufacturer label instructions) because maternally derived antibody (IgG) does not interfere with mucosal immune responses (secretory IgA). Although impractical among individual household pets, puppies housed in high-risk environments (animal shelters) may benefit from early vaccination (ie, at 3–4 weeks of age). In this case, intranasal vaccine may need to be repeated at 2 to 4 week intervals until 12 weeks of age.

It is not known whether the **oral *B bronchiseptica* vaccine**, which also induces local immunity, has efficacy in puppies less than 8 weeks of age. The **parenteral *B bronchiseptica* vaccine** requires 2 initial doses, at a minimum interval of 2 weeks, with the first dose administered to dogs 8 weeks of age or older.

2. Exposure Risk

Assessment of exposure risk is particularly important when selecting a vaccine. For dogs with limited risk for exposure, administration of any combination of parenteral, oral, or intranasal vaccines is indicated. In high-risk environments, however, administering either the **oral or parenteral *B bronchiseptica* vaccines alone limits** the scope of protection to *B bronchiseptica*; neither product contains vaccine against CPiV or CAV-2.

3. Onset of Immunity

Following a single dose of **intranasal *B bronchiseptica* vaccine**, dogs have shown protection against aerosol challenge by 48 to 72 hours.^{11,12} Vaccination with **oral *B bronchiseptica* vaccine** is expected to induce rapid-onset mucosal immune response similar to the intranasal vaccine.^{13,14}

Dogs initially vaccinated with **parenteral *B bronchiseptica* vaccine** are **not** expected to derive protective immunity until 5 to 7 days following administration of the second dose, that is, not earlier than 19 to 21 days following administration of the first dose.

4. Ease of Administration

Reports from veterinarians indicate that **parenteral and**

oral vaccines are easiest to administer and best tolerated by individual dogs. A small number of dogs will aggressively resist **intranasal vaccination**; resistance to intranasal vaccination may warrant changing to oral or parenteral administration (see **Change of Administration Route**).

5. Route of Vaccination

The most recent studies (see **Studies on *B bronchiseptica* Vaccine Administration**, page 76) assessing routes of administration center on *B bronchiseptica* vaccination. These studies highlight the role of mucosal immunity in protecting dogs against exposure to *B bronchiseptica*. Similar comparative studies assessing the quality of protection derived from intranasal versus parenteral CPiV and CAV-2 vaccine administration have not been published.

Administration Considerations

1. Vaccine Loss Following Administration

Following intranasal administration of vaccine to dogs, subsequent sneezing and head shaking is likely to result in a small volume of vaccine dose being expelled from the nose; however, it is unlikely that this degree of vaccine loss reduces efficacy due to:

- High antigen concentration per dose
- Affinity of avirulent live *B bronchiseptica* for respiratory epithelium.

2. Reduction of Diluent Volume to Reduce Volume/Dose

When administering intranasal vaccine to small breeds, particularly small brachycephalic breeds, the volume of diluent may be arbitrarily reduced when reconstituting lyophilized vaccine antigen. Doing so reduces the volume of vaccine that reaches the nasopharynx without reducing antigen concentration or vaccine efficacy.

3. Vaccine Mixed with Food

Due to the absence of published studies, administering a dose of oral *B bronchiseptica* vaccine by mixing the dose with food is **not** recommended. Doing so may result in significantly reduced antigen contact with mucosal surfaces and, thus, ineffective immunization.

4. Change of Administration Route

When administering an intranasal vaccine, veterinarians may encounter sufficient resistance in some dogs to warrant switching to a parenteral or oral vaccine.

Switching from Intranasal to Parenteral. Intranasal vaccination may not consistently result in significant levels of serum IgG. Therefore, administration of 2 **parenteral** doses, 2 to 4 weeks apart, is recommended, regardless of the dog's age when the dosing route is changed. The dog may be revaccinated annually thereafter.

Switching from Intranasal to Oral. If switching from intranasal to oral vaccination, a single **oral** dose is indicated to effectively protect against *B bronchiseptica* infection.

5. Inappropriate Route of Administration

Vaccines indicated for protecting dogs against CIRDC must be

Studies on *B bronchiseptica* Vaccine Administration

A study published in 2002¹⁵ advanced the notion that mucosal administration of vaccine would be less effective in stimulating secondary (versus primary) immune responses. This study popularized a vaccination protocol that involves initially administering an intranasal vaccine; then administering all subsequent vaccines parenterally in order to effectively booster serum antibody titers.

A study published in 2007¹⁶ highlighted immunologic and clinical advantages of intranasal vaccination over parenteral vaccination. Dogs vaccinated with intranasal vaccine:

- Developed local immunity (*B bronchiseptica*-specific IgA titers in nasal secretions)
- Developed significant serum antibody titers
- Following challenge, had significantly lower shedding and lower cough scores compared to dogs vaccinated parenterally.

A 2013 study¹⁴ compared the quality of protection in dogs vaccinated against *B bronchiseptica* by intranasal, oral, and parenteral routes. Following challenge, cough scores in all dogs were reduced when compared to control dogs. However, dogs vaccinated by intranasal and oral routes had significantly lower cough scores compared to those vaccinated parenterally.

administered in accordance with the manufacturer's recommendations. See **The Do Nots of Vaccine Administration**.

6. Simultaneous Administration of Multiple Vaccine Types

Parenteral CDV + canine parvovirus (CPV) + CAV-2 vaccine combined with CPiV is among the multivalent vaccines most commonly administered to dogs in the U.S. and Canada.

Because intranasal *B bronchiseptica* vaccine may also include vaccine against CPiV or CPiV + CAV-2, dogs can receive both parenteral and intranasal vaccine for the same virus. There is no risk associated with doing so, even if administered during the same appointment.

Immunologically, dogs vaccinated against *B bronchiseptica*, CPiV, and CAV-2 by both parenteral (circulating IgG) and mucosal (secretory IgA) routes (oral and intranasal) at the same time may derive a greater degree of protection than those vaccinated either parenterally or mucosally. However, no scientific studies exist that confirm this.

PUBLIC HEALTH CONSIDERATIONS

Published reports document the role of *B bronchiseptica* as a primary respiratory pathogen in humans, and it can be transmitted from dogs, cats, and rabbits to humans and other animals.

The Do Nots of Vaccine Administration DO NOT ADMINISTER:

1. An intranasal *B bronchiseptica* vaccine by the oral route because concentration of *B bronchiseptica* in an intranasal vaccine is less than that in an oral vaccine.
2. The intranasal vaccines containing modified-live viruses (CPiV and CAV-2) by the oral route because an intranasal vaccine, if administered orally, is not expected to induce protective immunity.
3. The parenteral *B bronchiseptica* vaccine by the oral or intranasal route; the parenteral vaccine is an inactivated cell culture extract and not effective if administered orally or intranasally.
4. An oral or intranasal (attenuated) *B bronchiseptica* vaccine by the parenteral route because some dogs may develop injection-site granulomas or abscesses (Figure).
5. The oral or intranasal (attenuated) *B bronchiseptica* vaccine by the parenteral route; rarely, may lead to nonseptic hepatic necrosis and death.¹⁷



Figure. Spontaneous rupture of a subcutaneous abscess in a dog 5 days following parenteral administration of an intranasal vaccine containing avirulent live *B bronchiseptica*.

Infection Risks

When exposed to an infected dog or cat, humans are at low risk for infection. However, greater risk for infection exists in immunocompromised individuals, children, and individuals working in high-density animal facilities (eg, shelters, rescue kennels).^{18,19}

Postvaccinal sneezing and/or coughing are commonly reported in dogs that recently received intranasal vaccines. Reports of human infection with *B bronchiseptica* have raised concerns about administration of avirulent live (oral or intranasal) vaccine to dogs owned by immunocompromised individuals and families with young children (see **Was It the Vaccine?**).

The intricacies of systemic versus mucosal immunity are rather complex, and few studies are available that even attempt to “measure” mucosal immune responses. Mucosal immunity to *B bronchiseptica* does appear to involve mechanisms other than secretory IgA. However, further discussion of this topic is outside the scope of this article.

Scientific Studies

To date, there are no published studies confirming human infection and illness associated with exposure to recently vaccinated dogs. Special precautions to avoid human contact with recently vaccinated dogs (oral or intranasal route) do not appear warranted.

Anecdotal Concerns

Although anecdotal, I have voiced concern about the risks associated with veterinarians being directly exposed to intranasal (attenuated) vaccines at time of administration. To date, despite the large number of veterinarians reporting exposure, there is no evidence suggesting development of respiratory signs among those exposed to intranasal or oral vaccines.

Was It the Vaccine?

One unpublished case report described the case of a 14-year-old boy who was inadvertently sprayed in the face with a dose of intranasal *B bronchiseptica* + CPIV vaccine that was intended for the child’s pet dog.²⁰ Five days later, the boy developed a pertussis-like cough that persisted for 3 to 4 months. However, confirmation that the illness was causally associated with vaccine exposure was never accomplished.

SUMMARY

Canine infectious respiratory disease is still among the most frequently encountered respiratory infections reported in dogs. Despite the availability and widespread use of vaccines for many of the viral and bacterial pathogens implicated, infections are still reported. The discovery of new respiratory pathogens for which vaccines are not currently available highlights the fact that even well vaccinated dogs can still develop CIRDC. Due to the contagious nature of the organisms involved, animal shelters, dog day-care centers, rescue organizations, and veterinary hospitals continue to be recognized as high-risk environments for development of CIRDC. ■

CAV-2 = canine adenovirus-2; CDV = canine distemper virus; CIRDC = canine infectious respiratory disease; CIRDC = canine infectious respiratory disease complex; CIV = canine influenza virus; CnPnV = canine pneumovirus; CPIV = canine parainfluenza virus; CPV = canine parvovirus; CRCoV = canine respiratory coronavirus; ITB = infectious tracheobronchitis

References

1. Ford RB. Canine infectious respiratory disease. In Greene CE (ed): *Infectious Diseases of the Dog and Cat*, 4th ed. St. Louis: Elsevier Saunders, 2012, pp 55-65.
2. Pecoraro HL, Bennett S, Huyvaert KP, et al. Epidemiology and ecology of H3N8 canine influenza viruses in US shelter dogs. *J Vet Intern Med* 2014; 28(2):311-318.
3. Priestnall S, Erles K. *Streptococcus zooepidemicus*: An emerging canine pathogen. *Vet J* 2011; 188(2):142-148.
4. Renshaw RW, Zylch NC, Laverack MA, et al. Pneumovirus in dogs with acute respiratory disease. *Emerg Infect Dis* 2010; 16(6):993-995.
5. Decaro N, Martella V, Buonavoglia C. Canine adenoviruses and herpesvirus. *Vet Clin North Am Small Anim Pract* 2008; 38(4):799-814.
6. Erles K, Brownlie J. Canine respiratory coronavirus: An emerging pathogen in the canine infectious respiratory disease complex. *Vet Clin North Am Small Anim Pract* 2008; 38(4):815-825.
7. Buonavoglia C, Martella V. Canine respiratory viruses. *Vet Res* 2007; 38(2):355-373.
8. Ford RB. *Bordetella bronchiseptica*: Beyond kennel cough. In Bonagura JD, Twedt DC (eds): *Kirk’s Current Veterinary Therapy XIV*, 14th ed. St. Louis: Elsevier Saunders, 2009, pp 646-649.
9. Mattoo S, Cherry JD. Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to *Bordetella pertussis* and other *Bordetella* subspecies. *Clin Microbiol Rev* 2005; 18(2):326-382.
10. Welborn LV (chair), DeVries JG, Ford RB, et al. 2011 AAHA canine vaccination guidelines. *JAAHA* 2011; 47(5):1-42. Available at aahanet.org.
11. Gore T, Headley M, Laris R, et al. Intranasal kennel cough vaccine protecting dogs from experimental *Bordetella bronchiseptica* challenge within 72 hours. *Vet Rec* 2005; 156(15):482-483.
12. Bey RF, Shade FJ, Goodnow RA, Johnson RC. Intranasal vaccination of dogs with live avirulent *Bordetella bronchiseptica*: Correlation of serum agglutination titer and the formation of secretory IgA with protection against experimentally induced infectious tracheobronchitis. *Am J Vet Res* 1981; 42(7):1130-1132.
13. Hess TJ, Parker DS, Hassall AJ, Chiang Y. Evaluation of efficacy of oral administration of *Bordetella bronchiseptica* intranasal vaccine when used to protect puppies from tracheobronchitis due to *B bronchiseptica* infection. *Intern J Appl Res Vet Med* 2009; 9(3):300-305.
14. Larson LJ, Thiel BE, Sharp P, Schultz RD. A comparative study of protective immunity provided by oral, intranasal and parenteral canine *Bordetella bronchiseptica* vaccines. *Intern J Appl Res Vet Med* 2013; 11(3):153-160.
15. Ellis JA, Krakowka GS, Dayton AD, Konoby C. Comparative efficacy of an injectable vaccine and an intranasal vaccine in stimulating *Bordetella bronchiseptica*-reactive antibody responses in seropositive dogs. *JAVMA* 2002; 220(1):43-48.
16. Davis R, Jayappa H, Abdelmagid OY, et al. Comparison of the mucosal immune response in dogs vaccinated with either an intranasal avirulent live culture or a subcutaneous antigen extract vaccine of *Bordetella bronchiseptica*. *Vet Ther* 2007; 8(1):32-40.
17. Toshach K, Jackson MW, Dubielzig RR. Hepatocellular necrosis associated with the subcutaneous injection of an intranasal *Bordetella bronchiseptica*-canine parainfluenza vaccine. *JAAHA* 1997; 33(2):126-128.
18. Hemsworth S, Pizer B. Pet ownership in immunocompromised children—a review of the literature and survey of existing guidelines. *Eur J Oncol Nurs* 2006; 10(2):117-127.
19. Woolfrey BF, Moody JA. Human infections associated with *Bordetella bronchiseptica*. *Clin Microbiol Rev* 1991; 4(3):243-255.
20. Berkelman RL. Human illness associated with use of veterinary vaccines. *Clin Infect Dis* 2003; 37(3):407-414.



Richard B. Ford, DVM, MS, Diplomate ACVIM & ACVPM (Hon), is Emeritus Professor of Medicine at North Carolina State University’s College of Veterinary Medicine. He is a past president of the NAVC Conference and is a member of the scientific program committee. He serves on the AAHA Canine Vaccination Task Force and AAFF Feline Vaccination Advisory Panel. He received his DVM from Ohio State University and completed an internal medicine residency at Michigan State University.