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Reference: 1. Summary of studies supporting USDA product licensure for Nobivac Intra-Trac Oral Bb. USDA website. Available at: www.aphis.usda.gov/aphis/ourfocus/animalhealth/veterinary-biologics/product-summaries/vet-label-data/83c6706d-ffd8-4e32-ba7a-706e1bcb9333. Accessed October 28, 2020.

MERCK Animal Health

SNOWBALL EFFECT
Canine parainfluenza virus can have a significant impact on young or vulnerable dogs when it interacts with other pathogens.

VACCINATION STATION

Canine Parainfluenza Virus Vaccination

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Canine parainfluenza virus (CPIV) is a highly contagious ribonucleic acid virus that causes respiratory disease in dogs worldwide. It is an important agent in the canine infectious respiratory disease (CIRD) complex (also known as kennel cough), which is spread by dogs in group housing, social situations, and, sometimes, veterinary hospitals. Although considered a noncore vaccine, CPIV can play a role in exacerbating other respiratory infections, and vaccination of at-risk dogs may help promote herd immunity.

CANINE PARAINFLUENZA VIRUS OVERVIEW

Dogs with CPIV may exhibit no clinical signs or mild clinical signs of a dry, harsh cough for up to 7 days, with or without fever and nasal discharge.[1] These clinical signs may become much more severe in dogs with viral or bacterial coinfections (**FIGURE 1**).[2] Additionally, because CPIV suppresses the innate branch of the immune system and causes the loss of cilia and ciliated epithelium, it makes conditions more favorable for coinfections.[3] In puppies or immunosuppressed adult dogs, the presence of CPIV in coinfections can lead to a more severe pneumonia and can be fatal.[3,4]

Transmission of CPIV is mostly through aerosols and fomites.[5] The incubation period for CPIV is 3 to 10 days after infection, and viral shedding typically occurs 6 to 8 days after infection.[5] Because dogs with CPIV can be asymptomatic, they may shed virus without showing clinical signs. Before the development of CPIV vaccines, CPIV could be isolated from up to

FIGURE 1. Dog with complicated canine infectious respiratory disease and mucoid nasal discharge.

CIRD outbreaks can be prevented with a multifaceted approach that involves population control, priority handling, surface disinfection, and vaccination.

50% of dogs with respiratory disease in group housing situations.[6]

Coinfection with multiple pathogens is common in CIRD. The agents of CIRD can act successively or synergistically to cause respiratory illness. In the past, the common agents associated with CIRD were CPIV, canine adenovirus type 2, and *Bordetella bronchiseptica*. Later, canine herpesvirus-1 and canine influenza virus (H3N8 and H3N2) were added to the list of reported agents. More recent advances in identification methods have discovered other pathogens that may play a role in CIRD, and the list continues to grow (**TABLE 1**).[7] The prevalence of these pathogens and the roles that they play in the coinfection process have not yet been well studied.[8]

Outbreaks of CIRD involving CPIV have been reported around the world. When large numbers of dogs are housed together or commingle (e.g., rescue settings, boarding facilities, shelters, daycare facilities), they are more likely to develop clinical signs of CIRD. Clinical signs of CIRD also become more likely the longer dogs stay in these situations.[9] CPIV survives on nonporous surfaces for 4 to 12 days; however, it is susceptible to a range of disinfectants.[4] CIRD outbreaks can be prevented with a multifaceted approach that involves population control, priority handling, surface disinfection, and vaccination.

IMPORTANCE OF VACCINATION

One goal of vaccination against any pathogen is to achieve or maintain herd immunity. If all animals in a population are susceptible to a highly contagious agent, such as CPIV, there is nothing to stop the spread of that agent. Vaccinating individual animals is intended to minimize clinical disease in those individuals and reduce agent shedding. The collective impact of immunizing many or most individuals is the deceleration or even halt of disease spread within the population (i.e., herd immunity).[10] This strategy protects the naïve or still-susceptible animals within the group.

Given the role that CPIV plays in many instances of CIRD, including exacerbating clinical disease in coinfections, preventing its spread is important in controlling respiratory disease in dogs. By vaccinating

TABLE 1 Pathogens Associated With Canine Infectious Respiratory Disease Complex[2,7,8]

PATHOGEN	VACCINE COMMERCIALLY AVAILABLE?
Adenovirus-1	Yes
Distemper virus	Yes
Parainfluenza virus	Yes
Respiratory coronavirus	No
Influenza A virus (H3N8 + H3N2)	Yes
Herpesvirus-1	No
Pneumovirus	No
Hepacivirus	No
Reoviruses	No
Bordetella bronchiseptica	Yes
Mycoplasma canis	No
Mycoplasma cynos	No
Streptococcus equi subsp. *zooepidemicus*	No
Chlamydophila psittaci	No

as often as possible against CPIV (using multivalent vaccines), veterinarians can maximize herd immunity when dogs are housed together or commingle. Based on the ever-growing number of dog parks and daycare facilities, such interactions are increasing.[11]

Previously, the ratio of available vaccines to the agents responsible for CIRD was thought to be much higher. With the discovery of more pathogens that may be involved in causing CIRD, the proportion of ones with developed vaccines decreases (**TABLE 1**). Thus, it is critical that veterinarians vaccinate at-risk animals against the pathogens for which vaccinations exist to help control or prevent infection.

AVAILABLE CANINE PARAINFLUENZA VIRUS VACCINES

Several vaccines against CPIV exist (**TABLE 2**). Most are incorporated in multivalent vaccines with other antigens. CPIV vaccines do not produce sterilizing immunity (i.e., complete prevention of viral replication); rather, they decrease the severity of clinical signs, the amount of virus, and the degree of viral shedding. These vaccines are relatively efficacious and safe. Their duration of immunity is unclear and is likely less than 3 years.[12] More research is needed on the efficacy and immune response to CPIV vaccination to further determine duration of immunity.[3]

How the Vaccines Work

All the CPIV vaccines are attenuated live virus vaccines. They are designed to be administered either parenterally or intranasally.[7] CPIV is not stable in the oral environment; therefore, no oral vaccines against CPIV exist. The parts of the immune response that they stimulate and the possible postvaccinal adverse events depend on the vaccine administration route.

Parenteral vaccination provokes a primarily adaptive, systemic IgG response. These responses are good at defending the body once an agent has invaded it. Mucosal (intranasal) vaccine administration stimulates the innate immune response—a local IgA response designed to prevent adherence and invasion of pathogens—as well as a low-level systemic IgG response.[13,14] When CPIV enters the body, it triggers both the mucosal and the systemic responses of the adaptive immune system. Therefore, it is reasonable to expect that both routes of vaccination would be effective.

Given that CPIV primarily enters the canine system through the mucosa, the World Small Animal Veterinary Association and American Animal Hospital Association vaccination guidelines suggest using the intranasal vaccine, as it may provide superior protection.[15,16] Mucosal vaccination also has the added advantages of not being subject to interference from maternally derived antibodies in younger animals and being able to provide a fairly rapid onset of immunity from stimulation of the innate immune response.[10,16] In one of the few studies comparing intranasal and parenteral CPIV vaccines, dogs vaccinated with the intranasal product had fewer postchallenge clinical signs. Moreover, viral shedding, which was 70% in control animals, was reduced to 50% in the parenteral vaccinates and to 1% in the intranasal vaccinates.[17]

Drawbacks to intranasal delivery include loss of vaccine when it is sneezed or snorted back out—a common occurrence—and potential danger to the person

TABLE 2 Available Canine Parainfluenza Virus Vaccines[a]

ORGANISMS IN VACCINE[b]	ROUTE OF ADMINISTRATION
Parainfluenza only	Parenteral
Leptospira	Parenteral
Leptospira, enteric coronavirus[c]	Parenteral
Distemper virus, adenovirus-2, parvovirus	Parenteral
Distemper virus, adenovirus-2, parvovirus, *Leptospira*	Parenteral
Distemper virus, adenovirus-2, parvovirus, *Leptospira*, enteric coronavirus[c]	Parenteral
Bordetella bronchiseptica	Intranasal
Bordetella bronchiseptica, adenovirus-2	Intranasal

[a]*Only vaccines available in the United States and United Kingdom are listed.*
[b]*In addition to canine parainfluenza virus.*
[c]*Vaccination against enteric coronavirus is not recommended in the AAHA or WSAVA vaccination guidelines.*

Core or Noncore?

CPIV's effect on increasing the severity of illness caused by other respiratory pathogens may make it prudent to consider the parainfluenza vaccine "core" for dogs that are going to be social in any way. Before the use of available modified live vaccines, CPIV was isolated from up to 50% of dogs with respiratory symptoms in a group housing environment.[6] There is increasing evidence that intranasal vaccines are more effective at immunizing dogs and that dual-route vaccination (parenteral and intranasal) may provide even greater protection.[9] Annual vaccination in some form for CPIV may be something to consider as the role of coinfections in CIRD becomes more clear.

administering the vaccine to a fractious patient. The intranasal vaccines may cause transient side effects such as mild sneezing, coughing, or nasal discharge in a small percentage of dogs. These are signs that the innate immune response has been triggered by the vaccine.[13,16]

Schedule of Vaccination

CPIV vaccination is considered noncore (only advised in animals at risk) and is advised to be started in puppies between 6 and 8 weeks of age.[15,16] If a parenteral vaccine is used, it should be given every 2 to 4 weeks until the puppy is 16 weeks old.[14,15] In adult dogs (older than 16 weeks), 1 dose or 2 doses given 2 to 4 weeks apart is advised. The parenteral CPIV vaccine is included in combination products that also contain the core vaccines against canine parvovirus, canine distemper virus, and/or canine adenovirus type 2 and provides immunization against all included pathogens for at least 1 year.

When CPIV enters the body, it triggers both the mucosal and the systemic responses of the adaptive immune system.

Intranasal products can be started in puppies as young as 4 weeks old. This may be useful in group housing situations or other high-risk environments. A single intranasal dose is indicated for puppies and for adult dogs to provide immunization for 1 year.[14,15]

Dogs can safely receive both parenteral and intranasal vaccines against CPIV in the same vaccination visit. In theory, dogs vaccinated at the same time by 2 different routes may be better protected than those vaccinated with either route alone. Additionally, human evidence suggests that vaccination with both a parenteral and a mucosal vaccine may create the most robust immune response.[9] The response to natural CPIV infection and vaccination is nonsterilizing, so titers cannot be used to determine the need for revaccination.[16,18]

COMMUNICATION WITH CLIENTS

It is important that veterinarians educate clients about the significance of CIRD and the need to vaccinate against the causative agents with available vaccines. In at-risk animals, the dangers of coinfection and increased severity of disease are important reasons to vaccinate against pathogens that alone may not seem very significant. Many dogs resent intranasal vaccination, so it is also important for veterinarians to be complete and clear about the benefits of intranasal CPIV vaccination to ensure owner compliance. Additionally, it must be stressed that vaccination is a major part of a multifactorial disease prevention strategy.

CONCLUSION

A growing number of pathogens contribute to the CIRD complex. While CPIV is historically considered a primary pathogen in this disease, its singular impact and clinical signs are not severe. However, when CPIV interacts with other pathogens, particularly in young or immunocompromised dogs, its impact becomes significant. Routine use of available vaccines helps reduce the role that CPIV plays in coinfection with a growing number of pathogens, thereby keeping at-risk dogs and populations heathier. TVP

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