Canine Infectious Respiratory Disease Complex

Editorial review

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About Canine Infectious Respiratory Disease Complex (CIRDC)

CIRDC refers to a contagious cough caused by one or more viral or bacterial pathogens. Laymen often refer to CIRDC as "kennel cough" because of its frequent association with dogs that have been recently housed in kennels or shelters. These settings allow for physical proximity of animals (which facilitates contagion spread) and contribute to disease susceptibility and morbidity in other ways, too. Difficulties associated with sanitation in large groups of dogs, poor air quality, the continual exposure to new animals with additional new pathogens, and the stress associated with kenneling cannot be overestimated as a proximate factor in CIRDC. In fact, potentially pathogenic microbes that often cause subclinical infection or very mild illness in well-acclimated, laboratory-raised dogs can cause severe disease in dogs exposed in less favorable settings.

Pathogens behind CIRDC

Even so, viral and bacterial pathogens are the underlying cause of CIRDC (Table 1). Understanding the prevalence of each pathogen not only can impact treatment of diseased dogs, but also disease prevention. Principles of prevention related to facility design, sanitation, and a variety of other measures are outlined in resources such as Guidelines for Standards of Care in Animal Shelters[1] or the Koret Shelter Medicine Program (http://www.sheltermedicine.com). Vaccination programs can have a tremendous impact on minimizing CIRDC morbidity and mortality, and such vaccination programs are informed by knowledge of disease prevalence.

For a variety of reasons, the true prevalence of pathogens involved with CIRDC is incompletely understood. CIRDC is not a reportable infection, and thus there is no central database recording disease causation. Additionally, many pathogens implicated in CIRDC have only been recognized in the last decade. It is entirely likely that with more sophisticated testing methods and more frequent diagnostic testing, additional new pathogens will be identified in the coming decade. Geographic and lifestyle factors are expected to influence prevalence of each pathogen as a cause of CIRDC; the most important pathogens may vary by geography (eg, continent, country, state, or even county), environment (eg, urban vs. rural), or exposure (eg, shelter animals vs. pets). And finally, there is no single ideal diagnostic test to detect all pathogens involved in CIRDC. Opportunistic or commensal organisms may be identified when their roles in disease causation are minimal, and real pathogens might be missed due to issues of sampling timing, sample collection and processing, or testing methodology (Table 2).

Table 1

Pathogens involved in CIRDC

Viruses
Bocavirus[2*]
Canine adenovirus type 2[3]
Canine coronaviruses[4,5]
Canine distemper virus
Canine herpesvirus[3]
Canine influenza virus (H3N8)
Other influenza A virus types[6,7*]
Parainfluenza virus
Pneumovirus[8*]
Reoviruses[9*]
Bacteria
Bordetella bronchiseptica
Streptococcus equi subsp. *zooepidemicus*
Mycoplasma spp.* (especially *M. cynos*[10,11])
Secondary bacterial pathogens

*Importance as a naturally occurring cause of CIRDC somewhat speculative.

Table 2

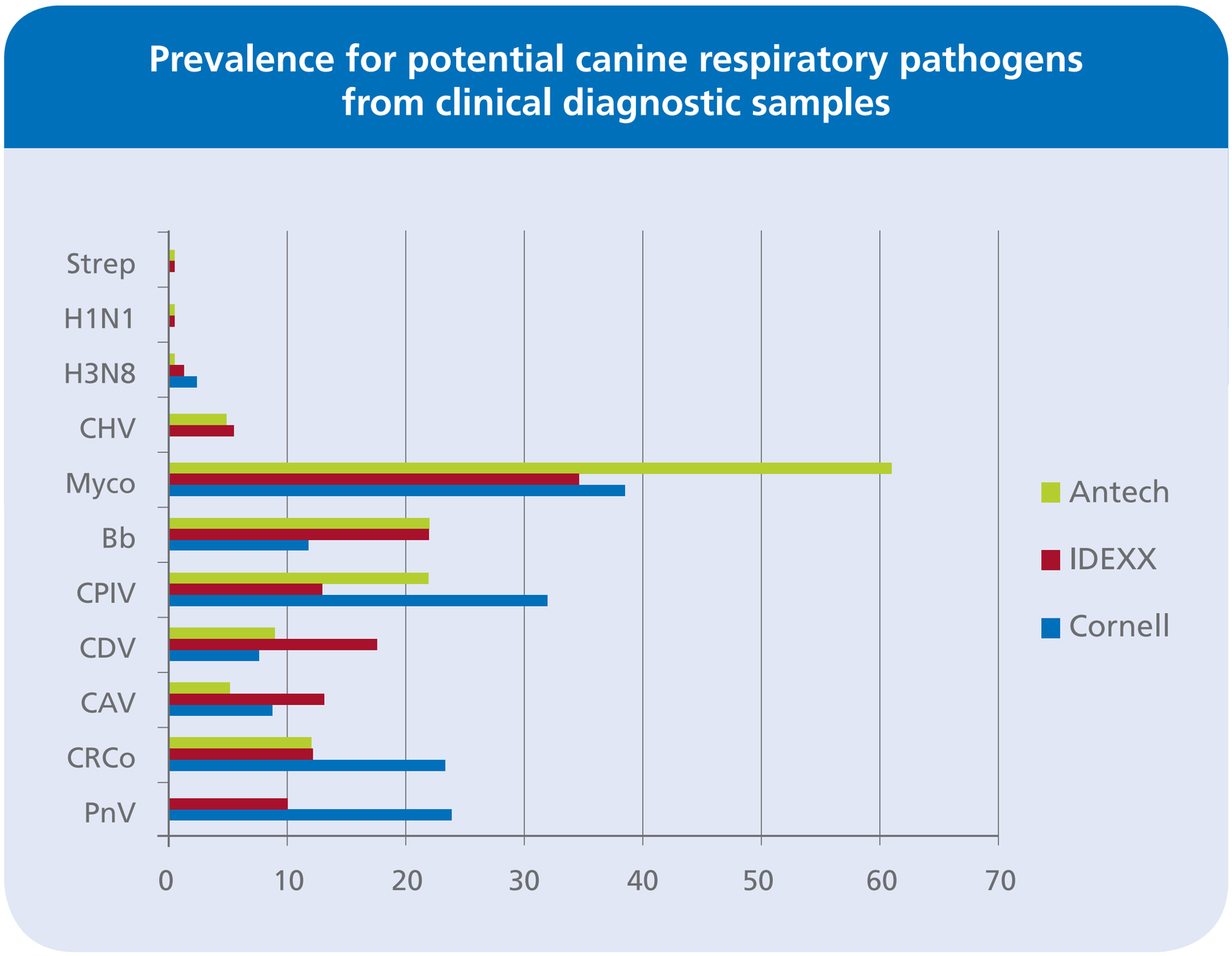
Limitations of commonly used CIRDC diagnostic testing methods

Bacterial or viral culture
Pathogen may not be present at sampling site (false negative)
Recovered bacteria may be present incidentally (false positive)
Commensal or opportunistic bacteria may overgrow pathogen
Pathogen may be difficult to transport or cultivate (false negative)
Antimicrobial therapy may hinder bacterial recovery (false negative)
Bacterial culture will not identify viral pathogens and vice versa
Antibody-based serologic assays
Acute illness may precede antibody production (false negative)
Vaccination may result in positive titers without infection (false positive)
Previous exposure doesn't prove disease causation
Polymerase chain reaction (PCR) assays
Pathogen may not be present at sampling site (false negative)
Potential pathogen may be present incidentally (false positive)
Only detects pathogens included on testing panel
Modified live vaccines may cause positive test results (false positive)
Viral shedding may end before sample collection (false negative)

CIRDC pathogen prevalence

Suspected prevalence of agents that may cause CIRDC in dogs in North America have been published, but methodologies, test populations, and other variables make it difficult to merge the resulting data. Unpublished data from 3 large veterinary diagnostic testing facilities are compiled in Figure 1. It is very likely that most of the diagnostic samples included in this data compilation were obtained from dogs with clinical signs of cough or respiratory disease, but information on individual sample origin or reason for sampling are not available. In all likelihood, these data underestimate the importance of viral pathogens with short periods of shedding, such as canine influenza virus (CIV). To underscore this point, in a recently published study using serologic assay in dogs with suspected CIRDC, 618 of 1,268 samples (49%) were positive for CIV, a number far in excess of that suggested by PCR assays from any of the 3 participating diagnostic laboratories.[12] Although the study with the very high seroprevalence included mostly group-housed dogs from states with enzootic influenza, it illustrates the difference in results that can be obtained depending on testing population, timing, and type. In many cases, more than a single pathogen is recognized simultaneously in the same dog. These coinfections further complicate an understanding of the importance of each individual pathogen in disease causation.

Figure 1



Prevalence is defined as positive percentage of all samples tested. Data include samples submitted to Cornell Diagnostic Laboratory from October 1, 2011 to October 1, 2012 (blue), IDEXX Laboratories Inc., IDEXX Canine Respiratory Disease (CRD) RealPCR™ Panel during 2012 (red), and Antech Diagnostics from January 2011 through March 2013 (green).

The number of samples tested for each pathogen is as follows, where NST means not specifically tested: canine pneumovirus (PnV; Cornell n=499; IDEXX n=200, and Antech n=NST); canine respiratory coronavirus (CRCo; Cornell n=503, IDEXX n=4062, Antech n=2229); canine adenovirus (CAV; Cornell n=497, IDEXX n=4062, Antech n=4820); canine distemper virus (CDV; Cornell n=500, IDEXX n=4062, Antech n=4816); canine parainfluenza virus (CPIV; Cornell n=359, IDEXX n=4062, Antech n=4821); Bordetella bronchiseptica (Bb; Cornell n=205 via PCR and n=401 cultures, IDEXX n=4062, Antech n=4780); Mycoplasma (Myco; Cornell n=299, IDEXX n=4062, Antech n=4760); canine herpesvirus (CHV; Cornell =NST, IDEXX n=4062, Antech n=4795); canine influenza virus H3N8 (H3N8; Cornell n=471, IDEXX n=4062, Antech n=2506); H1N1 influenza virus (H1N1; Cornell n=NST, IDEXX n=4062, Antech n=4715); *Streptococcus equi* subsp. *zooepidemicus* (Strep; Cornell n=NST, IDEXX n=4062, Antech n=4828). Although the large majority of results are based on PCR assays, Cornell Diagnostic Laboratory routinely performed viral isolation, and both Cornell and Antech commonly performed bacterial culture on submitted materials.

Vaccinating against CIRDC pathogens

Vaccinations can provide individual and group protection from disease by priming the immune response of the vaccinated animal to potential pathogens before exposure occurs. Guidelines such as the American Animal Hospital Association Canine Vaccine Guidelines[13] can be extremely useful to practicing veterinarians. However, the choice of which vaccines to administer must be made after consideration of the dog as a unique animal, considering factors such as the dog's health, risk of pathogen exposure and subsequent illness, risk from vaccination, as well as the owner's wishes in light of both financial costs and perceptions of benefit from vaccination.

Vaccinations are commercially available for some, but not all, of the pathogens associated with CIRDC (Table 3). Respiratory infections with a single pathogen may damage the protective defense mechanism, thereby allowing an opportunity for additional pathogens to cause infection. Coinfections are very likely to increase disease morbidity and mortality compared with infections with a single pathogen. In the data from diagnostic laboratories compiled here, coinfections were recognized in 43% of samples from IDEXX Laboratories and 38% of samples from Cornell Diagnostic Laboratory. It is possible that vaccine-induced protection from one CIRDC pathogen may offer indirect protection from disease due to an unrelated pathogen by reducing the opportunity for coinfection. This may even provide some degree of protection from CIRDC pathogens for which there is currently no commercially available vaccine. As an example, clinical illness scores of dogs vaccinated against CIV were markedly reduced as compared to non-vaccinated dogs after exposure to a combination of CIV and *S. equi* subsp. *zooepidemicus*, even though dogs were not vaccinated against *S. equi*.[14]

Table 3

Commercially available vaccine types for CIRDC

Pathogen	Antigen Type	Formulation	Route of Administration	AAHA Guideline Recommendation	
				Pet dogs	Shelter populations
B. bronchiseptica	Live avirulent bacteria	Mono, Multi	IN, Or	Non-core	Core*
	Cellular antigen extract	Mono	SC		
Parainfluenza virus	MLV	Multi	SC‡, IN	Non-core	Core*
Canine adenovirus	MLV	Multi	SC, IN	Core†	Core†
Canine influenza virus	Killed virus	Mono	SC	Non-core	Non-core
Canine distemper virus	MLV, recombinant, (measles—not recommended)	Multi	SC	Core	Core

IN=intranasal; MLV=modified live virus; Mono=monovalent vaccine; Multi=multivalent vaccine; Or=oral; SC=subcutaneous.

*In a shelter setting, mucosal vaccine is preferred due to rapid onset of protection.
†Canine adenovirus type 2 as a parenteral injection is considered a core vaccine for pet dogs due to protection against CAV-1, the pathogen responsible for infectious canine hepatitis.
‡Canine parainfluenza virus can result in either CIRDC or neurologic manifestations; the mucosal vaccine provides improved protection against manifestations of CIRDC as compared with the parenteral vaccine.

Many of the vaccines that offer protection from CIRDC are available as either mucosal or parenteral formulations. While technically difficult to develop, mucosal vaccines offer a number of potential advantages over parenteral vaccines. The immunologic responses elicited by mucosal vaccination, including a key IgA response, are especially advantageous against the pathogens that cause CIRDC. The natural route of exposure for the pathogens of CIRDC is mucosal, and much of the disease pathology relates to mucosal surfaces. Mucosal vaccines can be given to very young puppies because maternal antibody interference does not occur, while maternal immunity does interfere with early parenteral vaccination. Additionally, mucosal vaccines offer a very rapid onset of protection after administration and do not require an initial booster vaccination. Although a minor consideration, the use of attenuated live mucosal vaccines may offer some degree of "herd" protection in settings such as shelters where recently vaccinated dogs are housed in close proximity to other dogs.

Conclusions

Although complete data are lacking, a number of conclusions can be drawn regarding the pathogens involved in CIRDC:

- Both morbidity and mortality depend on a number of factors in addition to simple pathogen exposure
- A single ideal testing method for all the pathogens with a potential role in CIRDC has yet to be identified
- The importance of certain commonly encountered potential pathogens, including canine respiratory coronavirus and *M. cynos*, has yet to be fully elucidated
- A number of potential CIRDC pathogens have been recognized only in the last several years, and it is very likely that additional pathogens will be identified
- Despite the recognition of new pathogens, *B. bronchiseptica* continues to have an important role in CIRDC
- Vaccinations can reduce the likelihood and severity of disease associated with several of the important pathogens responsible for CIRDC

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