Canine Infectious Respiratory Disease Complex (CIRDC) - Diagnosis and Treatment; Prevention and Management

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BACKGROUND

Canine infectious respiratory disease complex (CIRDC) is a highly contagious, multifactorial condition that continues to be a challenge for shelters. Management of CIRDC requires a multifaceted approach due to its multifactorial etiology. In addition to the pathogens associated with CIRDC, environmental factors and host immune system response play equally important roles in the development of CIRDC. In reality, many of the associated pathogens are insufficient in themselves to cause disease without the additional stress, high contact rates, and crowding often associated with sheltering.

ETIOLOGIC AGENTS

Multiple bacterial and viral pathogens, acting both sequentially and synergistically, are associated with CIRDC. Bacterial pathogens implicated in CIRDC include *Bordetella bronchiseptica*, *Mycoplasma* spp., and *Streptococcus equi* subsp. *zooepidemicus*. Viral pathogens include distemper (CDV), parainfluenza (CPIV), adenovirus type 2 (CAV-2), influenza (CIV H3N8), respiratory coronavirus (CRCoV), and pneumovirus (CnPnV).

New findings regarding known CIRDC pathogens, as well as current research on emerging pathogens are adding to the already complex pathogenesis of CIRDC. High-density environments, such as shelters, where exposure, susceptibility, and transmission of infectious diseases are amplified can contribute to outbreaks of known CIRDC pathogens, as well as the emergence of novel pathogens. Several emerging agents that potentially contribute to CIRDC were first detected in dogs housed in high-density environments. Respiratory coronavirus was first recognized in 2003 during a CIRDC outbreak at a shelter in London. Histopathological findings in experimental CRCoV infections are consistent with those seen in early stages of CIRDC, supporting the theory that CRCoV predisposes dogs to secondary infections. Pneumovirus was first recognized in 2010 through a retrospective study of CIRDC from 2 shelters in the U.S. Since then it has been detected in the United Kingdom and 8 U.S. states. Although its role as a causative agent in CIRDC remains unclear, it is also thought to predispose dogs to secondary infections. Continuing to define the role of these emerging pathogens is critical to CIRDC management.

DISEASE COURSE

The incubation period for CIRDC is typically 2–3 days but can range from 2 days (CIV) to 4–5 weeks (CDV). All CIRDC pathogens have a preclinical shedding period, complicating disease management. Clinical signs and shedding typically last for 5–10 days; however, some pathogens can shed for prolonged periods (*Bordetella, Mycoplasma,* and CDV). Clinical signs are typically mild, self-limiting, and resolve with supportive care. Signs can include coughing, sneezing, nasal and ocular discharge. Severe infection can sometimes be seen, more commonly in younger and immunocompromised animals.

DIAGNOSIS

All of the pathogens associated with CIRDC cause overlapping, nonspecific clinical signs. Accordingly, the cause of CIRDC cannot be diagnosed based on clinical signs alone in a single dog. Patterns in the affected population and severity of signs may provide some clues as to the likely etiologic pathogen(s). For example, in a naïve population, CIV infection will result in a high incidence of clinical signs in all dogs regardless of age or vaccine status. If some animals show distinctive clinical signs, such as neurological signs characteristic of distemper, it is possible that other dogs showing milder disease are also infected with the same pathogen. Conversely, a CDV outbreak is unlikely if many dogs are affected, particularly dogs over 5 months of age, and none show characteristic neurological signs.

Diagnostic testing is indicated if an outbreak has occurred, if affected dogs are not responding to supportive care, or if affected dogs are showing systemic signs of disease. A diagnosis can help guide effective treatment plans and control measures. Acutely affected dogs should be sampled, ideally prior to treatment, in sufficient numbers to provide data representative of the larger population (at least 10% of the population). Collection of specimens from multiple dogs (at least 5–10) may increase the chance of positive test results.

Several diagnostic tests are available but sensitivity and specificity will vary depending on the pathogens involved, the location of sample collection, and the timing of collection. For example, CIV shedding peaks early in the course of disease and may be missed by the time clinical signs are noticed, resulting in false negatives. Current diagnostic options include culture and sensitivity, serology, virus isolation, polymerase chain reaction (PCR), and histopathology.

Culture and sensitivity is useful for bacterial pathogens that demonstrate antimicrobial resistance (e.g., recent isolates of *Strep. zoo* can carry doxycycline resistance genes). Serology's use is limited due to vaccine interference; however, it is useful for CIV diagnosis in non-endemic communities. Virus isolation is uncommonly used now due to its relatively slow turnaround time. Polymerase chain reaction testing is the most practical option for viral detection and respiratory PCR panels are available from most commercial laboratories. To minimize the chance of false negative results, contact the laboratory regarding optimal sample collection, transport, and to ensure that the pathogens of interest are included in their panels (e.g., respiratory coronavirus as opposed to enteric coronavirus). Keep in mind that false positives can result from recent vaccination with a modified live virus. Some laboratories now offer quantitative real-time PCR results that can help differentiate vaccination from field strain infection.

Of course, merely documenting the presence of a pathogen does not necessarily indicate causation. Most of the pathogens associated with CIRDC can be isolated with some frequency even from clinically normal dogs, especially in a densely housed canine population. If the same pathogen is found in several dogs, this raises the index of suspicion that a causative relationship exists, but always keep in mind that necropsy is the most powerful diagnostic tool available. Necropsy can help clarify both the presence and the role of the involved pathogens. If you are uncertain whether a single death represents an isolated incident or the beginning of an outbreak, it is prudent (and virtually free) to obtain lung specimens and oropharyngeal swabs and hold them for future analysis if indicated. Formalin fixed, frozen and refrigerated specimens should be obtained, for histopathology, viral isolation, and bacterial culture respectively.

PREVENTION

In light of the multifactorial etiology of CIRDC, implementing effective preventative measures can reduce the prevalence of CIRDC within a shelter setting. The two cornerstones of prevention include decreasing exposure to CIRDC pathogens by using appropriate biosecurity measures and increasing the resistance to CIRDC pathogens by supporting each animal's health and well-being with appropriate vaccinations, prevention of airway irritation, and providing a low stress environment.

Reduction of Crowding and Decreasing Time in the Shelter

Crowding and the stress associated with crowding is the greatest risk factor for disease outbreaks in shelter populations. High population densities lead to greater risk of disease introduction, higher contact rates, increased stress, reduced air quality, and compromised husbandry and biosecurity practices. Housing dogs in each side of a double-sided cage intended for a single dog; housing multiple unrelated dogs per cage (particularly if not done in "all in/all out" fashion"); failure to isolate symptomatic animals; and delays in moving animals through the facility are frequent precursors of serious outbreaks in overcrowded shelters. Even in a boarding facility or vet clinic, it is important to anticipate times of peak population, recognize that these will be periods of increased risk for respiratory disease outbreaks, and plan for sufficient additional staff such that husbandry is not compromised.

Accordingly, a simple, yet underappreciated strategy for CIRDC prevention is to reduce the amount of time each dog spends in the shelter. Edinboro *et al*'s 2004 shelter-based CIRDC study found that each day in a shelter increased the risk of CIRDC by 3%. Management practices that increase length of stay for

shelter dogs should be carefully assessed to ensure the benefit of these practices outweighs the risk of disease they may create. This could include routine quarantine of apparently healthy animals, delays while dogs await behavior assessment or surgery, or failure to move dogs to public-viewing areas of the shelter as soon as they are available for adoption. Increased time for each dog in the shelter also contributes to increased crowding with all the associated risks. Reducing the average length of stay for sheltered animals starts with proactive population management.

Environmental Decontamination/Removal of Infected Animals

Shortened lengths of stay, along with reduced crowding, will facilitate implementation of appropriate biosecurity measures, including adequate sanitation practices and prompt recognition and isolation of affected animals, which are critical in managing CIRDC, as well. Most CIRDC pathogens survive in the environment no more than a few hours (CDV) to a few weeks (*Bordetella*) and are inactivated by virtually all routinely used disinfectants. Adenovirus is an exception; like other un-enveloped viruses, it is reliably inactivated by a limited number of disinfectants, including household bleach (5% sodium hypochlorite) diluted at 1:32 (1/2 cup per gallon), calcium hypochlorite (e.g., Wysiwash®) and sodium dichloroisocyanurate (e.g., Bruclean®), potassium peroxymonosulfate (e.g., Trifectant®) and accelerated hydrogen peroxide (e.g., Virox®, Accel®). Survival of primary and secondary pathogens may be greatly enhanced by persistent moisture in the environment; therefore surfaces should be in good repair to prevent pooling of water, and cleaning should be followed by thorough drying on a daily basis.

The cleaning process itself may serve to spread, rather than prevent, disease if not carefully thought out. Ideally, dogs should be held in doubled sided runs separated by a guillotine door, such that the dog can be held on one side while the other side is cleaned. For facilities with a good dog walking program such that runs are not soiled with urine or feces, complete cleaning and disinfection need only occur at the conclusion of a dogs' stay, with daily spot cleaning sufficient to keep the run tidy. If dogs must be removed from their run for cleaning, they should not be left in a common holding kennel nor tied in aisle ways while contaminated water and disinfectant is sprayed nearby. Disinfectant should be applied via a low pressure sprayer or other application system rather than a mop and bucket which will quickly become contaminated.

Remember that mildly infected dogs may play a substantial role in maintaining CIRDC in a given population, especially for the less environmentally durable pathogens such as distemper. A common - and dangerous - misapprehension is that a mildly infected dog is shedding only a mild pathogen. In fact, the severity of clinical signs is dictated as much by the dog's immune system as by the inherent virulence of the pathogen. A perky dog with a mildly snotty nose may very well be shedding a pathogen such as distemper or influenza, which could be fatal for another animal. Prompt removal of all symptomatic animals, no matter how mild the signs, has been critical in resolving many outbreaks. Staff should be trained to carefully scan for sneeze marks on kennel walls, as well as observing dogs for clinical signs before walking, cleaning or otherwise interacting. Because airborne transmission of CIRDC is a possibility, ideally isolation areas should have separate air flow; however, if this can not be achieved, do not despair. Facilities have managed to maintain effective isolation by providing at least 20 feet of physical distance between sick and healthy dogs and paying careful attention to fomite control.

Vaccination

Although CIRDC is not a vaccine preventable condition, appropriate vaccination plays an important role in controlling CIRDC. In some cases, such as with canine distemper, appropriate vaccination can prevent disease entirely, while in other cases vaccination will only help limit the incidence and severity of disease.

For a shelter setting, the recommended vaccination protocol is for all dogs over 4 weeks of age to receive a multivalent, parenteral, modified live virus (MLV) vaccine against distemper, adenovirus-2, and parvovirus immediately upon admission or, ideally, 3–5 days before admission. Puppies should be revaccinated every 2 weeks until 18–20 weeks of age due to possible interference by maternal antibody.

A recombinant parenteral vaccine is also available against distemper. While the recombinant vaccine may provide better protection in the face of maternal antibody and does provide rapid immunity, the modified live vaccine likely provides even more rapid immunity and is the better choice for high risk shelters in dogs and puppies for whom maternal antibody is not likely to be present. Many dogs and

puppies entering shelters have no evidence of either prior exposure, vaccination or maternal antibody to canine distemper, suggesting that even for puppies in most shelters the modified live vaccine could be the better choice.

In addition, all dogs over 2 weeks of age should receive a bivalent or trivalent, mucosal MLV vaccine against *Bordetella* and parainfluenza immediately upon admission, or, ideally, at least 3 days before admission. Mucosal vaccines are available for either oral or intranasal administration. The only available oral vaccine is a monovalent *Bordetella* product, while the intranasal vaccine is available in bivalent or trivalent formulations containing parainfluenza and/or adenovirus-2, providing potentially broader protection. Puppies less than 6 weeks old should be revaccinated with the mucosal vaccine once after the age of 6 weeks old. Mucosal *Bordetella* vaccines are designed to stimulate both local mucosal immunity and systemic immunity, thereby providing rapid onset of protection within 3 days after a single dose. In comparison, parenteral *Bordetella* vaccines do not produce protection until 2 to 3 weeks after a booster vaccination. The rapid protection offered by mucosal vaccination is important in a shelter setting where there is continuous introduction of susceptible animals. Not only is protection provided quickly but two challenge studies have shown that a single dose mucosal *Bordetella* vaccine can provide immunity for at least 12 to 13 months. In addition, mucosal vaccines are not affected by maternal antibody and are therefore preferred for use in puppies.

If canine influenza is endemic in the community, a monovalent, parenteral, inactivated virus vaccine against influenza should be given to all dogs over 6 weeks of age on admission and boostered in 2–4 weeks. Ideally, this series should be completed prior to admission, as well. The requirement for a booster limits the usefulness of this vaccine in some shelters, but it should be considered for pet dogs that stay in boarding kennels, attend doggy day care centers, frequent dog parks, or otherwise congregate with other dogs, especially in areas known to be endemic for canine influenza. This vaccine may also be useful for shelters in endemic areas if dogs frequently stay for a prolonged period, or for shelters transferring dogs from non-endemic to endemic areas.

TREATMENT

Treatment is typically symptomatic and supportive. There is no single "drug of choice" that will be appropriate for all CIRDC cases within shelters. For dogs in a home with mild illness, antibiotic treatment may be unnecessary. For dogs in the more challenging environment of a shelter, however, antibiotic treatment is often indicated to treat and prevent bacterial infections. Oral doxycycline at 10 mg/kg once daily is a relatively good empirical choice when *Bordetella* or *Mycoplasma* infection is suspected but may be less effective if *Strep. zoo* is present. For secondary infections subsequent to viral infections, cephalosporins, fluroquinolones, or other broad spectrum antibiotics are likely to be more effective than doxycycline. The use of steroids, antitussives, and expectorants is generally contraindicated in the shelter setting. Additional supportive care includes maintaining appropriate nutrition and hydration, minimizing excitement by modifying the environment (e.g., reducing barking triggers), and preventing tracheal irritation by walking on harness or gentle leader.

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