Canine Infectious Respiratory Disease Complex in Shelter Dogs

Stephanie Janeczko, DVM, MS, DABVP (shelter medicine & canine/feline), CAWA
Canine Infectious Respiratory Disease Complex

• Highly contagious upper respiratory disease – amongst the most common causes of acute respiratory disease in dogs

• Multiple pathogens may be involved:
  - Canine parainfluenza virus
  - Canine adenovirus 2
  - Canine distemper virus
  - Canine influenza virus
  - Canine herpesvirus
  - Canine (respiratory) coronavirus
  - Canine reovirus
  - *Bordetella bronchiseptica*
  - *Streptococcus equi* subsp *zooepidemicus*
  - *Mycoplasma* spp.
  - Secondary bacterial pathogens
Canine Infectious Respiratory Disease Complex

• Clinical signs – not suitable to distinguish various causes of CIRDC

• Typically upper airway
  • Ocular, nasal discharge
  • Coughing +/- terminal retch
  • Fever
  • Otherwise BAR
• May have pulmonary involvement
  • Fever
  • Labored breathing
  • Lethargy
  • Anorexia
Canine Infectious Respiratory Disease Complex

- Clinical signs, severity, prevalence of individual etiologic agents can vary: pet dog vs. shelter dog
  - Pet dogs: Bb, CPiV most common, rarely CDV, never CIV in one study
  - Shelter dogs: CIV, Streptococcus spp., Bb in 2009

<table>
<thead>
<tr>
<th>Table 1. Prevalence rates (%)</th>
<th>Myco</th>
<th>Bb</th>
<th>A-2</th>
<th>CDV</th>
<th>CHV</th>
<th>Para</th>
<th>RCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Sick (n = 23)</td>
<td>43.5</td>
<td>13</td>
<td>4.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.3</td>
</tr>
<tr>
<td>Shelter Sick (n = 24)</td>
<td>87.5</td>
<td>25</td>
<td>25</td>
<td>8.3</td>
<td>4.2</td>
<td>4.2</td>
<td>25</td>
</tr>
<tr>
<td>Shelter Healthy (n = 10)</td>
<td>60</td>
<td>10</td>
<td>30</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

(No CIV of Strep zoo found in any dogs)

Canine Infectious Respiratory Disease Complex
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Highly variable incubation periods – typically 3-10 days but range from 2 days to 5+ weeks
Canine Infectious Respiratory Disease Complex

<table>
<thead>
<tr>
<th>Organism</th>
<th>Incubation Period (days)*</th>
<th>Shedding Period*</th>
<th>Environmental Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canine adenovirus-1</td>
<td>4 to 9</td>
<td>6 to 9 months</td>
<td>Weeks to months</td>
</tr>
<tr>
<td>Canine adenovirus-2</td>
<td>3 to 6</td>
<td>1 to 2 weeks</td>
<td>Weeks to months</td>
</tr>
<tr>
<td>Canine distemper virus</td>
<td>3 to 6, longer for neurological signs</td>
<td>Weeks to months</td>
<td>Hours</td>
</tr>
<tr>
<td>Canine herpesvirus-1</td>
<td>6 to 10; may be longer with stress-induced reactivation</td>
<td>Unknown</td>
<td>Hours</td>
</tr>
<tr>
<td>Canine influenza virus</td>
<td>2 to 4</td>
<td>7 to 10 days</td>
<td>Hours</td>
</tr>
<tr>
<td>Canine parainfluenza virus</td>
<td>3 to 10</td>
<td>8 to 10 days</td>
<td>Hours</td>
</tr>
<tr>
<td>Canine respiratory coronavirus</td>
<td>Probably days</td>
<td>6 to 8 days</td>
<td>Hours</td>
</tr>
<tr>
<td><em>Bordetella bronchiseptica</em></td>
<td>2 to 6</td>
<td>Months</td>
<td>Has the potential survive and grow in environmental water for several weeks</td>
</tr>
<tr>
<td>Mycoplasma cynos</td>
<td>3 to 10</td>
<td>Months</td>
<td>Hours</td>
</tr>
<tr>
<td><em>Streptococcus equisubspecies zooepidemicus</em></td>
<td>Probably days</td>
<td>At least 2 weeks</td>
<td>Unknown; other streptococci can survive weeks</td>
</tr>
</tbody>
</table>

*Incubation and shedding periods are approximate and may differ when co-infections or immunosuppression operate.

CIRDC in shelters

• Community acquired vs. shelter exposure

• Morbidity depends on population and pathogens
  • Ranges from low to high rates of endemic disease
  • Puppies, immunologically naïve dogs at greater risk

• Mortality generally low, with some exceptions

• Introduction of new agents always possible
A few caveats for CIRDC in shelter dogs

• Various causative agents cause clinically indistinguishable signs requiring laboratory confirmation of diagnosis

• Severity of symptoms does not determine the pathogen(s) involved

• Many causative agents cause either mild and/or subclinical signs, but may also cause severe symptoms
CIRDC Transmission

• Particular shelter practices may enhance transmission through a variety of routes:
  • Overcrowding
  • Co-housing and co-mingling, including play groups
  • Housing design
  • Inadequate isolation
  • Cleaning procedures
  • Common areas and surfaces
Shelters and re-emerging diseases

- The risk of CIRDC increases as the list of potential pathogens grows

- Shelter populations are at particular risk for CIRDC
  - High density housing
  - Random sourced animals
  - Little to no preventive care prior to intake

- Role in emergence of new infections?
  - Endemic disease
  - Potential for mutations
  - Antibiotic resistance
  - Co-infections
The role of emerging diseases

• “Most emerging infections are caused by pathogens already present in the environment, brought out of obscurity or given a selective advantage by changing conditions and afforded an opportunity to infect new host populations.”

• New pathogens associated with acute respiratory disease in dogs within the last 10 years
  • 2003: type II respiratory coronavirus*
  • 2005, 2015: canine influenza viruses*
  • 2007: Strep zoo*
  • 2010: canine pneumovirus*

• Those diseases that were previously considered eradicated or controlled but are rapidly increasing in incidence or range
  • Canine distemper virus
Canine Infectious Respiratory Dz Complex

Bacteria:  
- *Bordetella*  
- *Streptococcus*  
- *Mycoplasma*  
- Secondary invaders

Viruses:  
- Distemper  
- Influenza  
- Parainfluenza  
- Adeno  
- Respiratory Corona  
- Pneumovirus  
- Herpes

Synergy

Husbandry:  
- Crowding  
- Stress  
- Incomplete disinfection  
- Failure to isolate  
- Poor air quality, airway irritation
Canine respiratory coronavirus

• Group 2 coronavirus, CRCoV
  • Different from GI tract coronavirus in dogs

• 2003: UK shelter dogs, circulating since at least 1996

• Typically associated with mild upper respiratory symptoms
  • Questioned as to ability to cause clinical disease as a primary pathogen
  • Less frequent reports of more severe disease
Canine respiratory coronavirus

• >50% U.S. dogs tested have evidence of prior exposure based on seroprevalence

• High rates of seroconversion over relatively short (e.g. 21 days) periods of time → easily transmitted

• Some evidence that CRCoV is not limited to infection of respiratory tissues
  • Often co-infections were also present
  • Theoretical possibility of fecal-oral transmission
Pneumovirus (CnPnV) infection

- Recently identified pathogen associated with CIRDC
- Family: Paramyxoviridae
- Most closely related to a murine pneumovirus and respiratory syncytial viruses

http://www.bumc.bu.edu/microbiology/people/faculty/paul-duprex-ph-d/
Pneumovirus infection

- Canine pneumovirus (CnPnV) – isolated from shelter dogs with acute upper respiratory symptoms
- Role as a primary pathogen remains unclear
  - Most dogs were co-infected, CIV or CPiV typically
  - Potential for virulence – MPV causes clinical, subclinical disease
  - Epidemiology remains unknown
- Ongoing research - prevalence and genetic diversity of CnPnV, role in respiratory disease in dogs

Image: Cornell University Animal Health Diagnostic Center
Canine Influenza

• H3N8 originally found in greyhounds at Florida racetracks (2004), circulating since at least 1999

• Subsequently reported in most states, not associated with racetracks - problematic for any dogs in high density housing
Canine Influenza

New canine influenza strain affecting Chicago outbreak | Dr. Justine Lee

Posted by justinelee in Animal Safety, Blog, Pet Health

Canine Influenza Virus (CIV) outbreak in MidWest caused by new strain of virus: H3N2 not H3N8

According to scientists at Cornell University and University of Wisconsin, the recent canine influenza outbreak affecting more than 1,000 dogs in Chicago, IL and other parts of the Midwest is been identified to be caused by a different strain of Canine Influenza Virus (CIV) than was earlier assumed. Initially, this CIV outbreak was thought to be due to H3N8 (which was originally identified in at a Greyhound track in Florida back in 2004).
Canine Influenza Virus Surveillance Network
Recent H3N2 Testing Summary
12/19/2015 - 2/2/2016 (last 45 days)

The influenza data displayed is a compilation of several different sources. Multiple laboratories (below) are contributing testing information to enable a more complete picture of H3N2 activity nationally.

This map represents testing efforts of the participating veterinary diagnostic labs and does not capture all testing performed nationally. The data should not be used as the sole information source for the distribution of H3N2 in dogs in the United States.

CIV Surveillance Partnership Contributors

Cornell University Animal Health Diagnostic Center
Idexx Reference Laboratories (national)
Antech Diagnostics (national)
Iowa State University Veterinary Diagnostic Laboratory
Michigan State Univ. Diagnostic Center for Pop. and Animal Health
Ohio State Animal Disease Diagnostic Lab
Pennsylvania Animal Diagnostic Laboratory System
South Dakota Animal Disease Research and Diagnostic Laboratory
Texas A&M Veterinary Medical Diagnostic Laboratory
University of Georgia Athens Veterinary Diagnostic Laboratory
University of Minnesota Veterinary Diagnostic Laboratory
Wisconsin Veterinary Diagnostic Laboratory
Canine Influenza

• High morbidity seen in non-endemic populations - ?

• Clinical signs: indistinguishable from those caused by other pathogens in the CIRDC
  • Cough (may persist for several weeks)
  • Nasal discharge
  • Mostly mild disease
  • Severe disease, lower respiratory involvement possible
    • +/- high fever and pneumonia
    • +/- Hemorrhagic pneumonia

~20% of infected dogs show no outward signs of disease
End peak shedding

Clinically ill dogs shed highest levels of virus early.
Strep zoo

- *Streptococcus equi* subsp. *zooepidemicus*
  - Beta-hemolytic Strep sp., Lancefield group C
  - More commonly associated with horses as the causative agent in strangles
  - Rarely isolated from healthy dogs – emerging cause of severe respiratory disease

- Strep canis
  - Normal commensal, Lancefield group G
Strep zoo

• Clinical signs:
  • Cough and nasal discharge
  • Fever
  • Peracute death
    • Found “dead in a pool of blood”
    • With or without antemortem signs
  • All ages affected
  • Most cases apparently within 7-14 days of exposure, as soon as 48 hours

Strep zoo

- Epidemiology largely unknown:
  - Incubation period?
  - Shedding and carrier states?
  - Risk factors?

- Unknown risk to other pets in homes or rescues
  - One case of transmission to exposed pet at kennel
  - No transmission from shelter to home documented
  - One clinical case report of transmission from a dog to his attendant
  - Rhinitis & meningitis, outbreak reported in cats
Canine Distemper Virus

- Enveloped RNA virus (Paramyxoviridae, *Morbillivirus*) with wide host range

- Clinical signs 1-4+ weeks following exposure; severity depends on:
  - Strain virulence
  - Dose, environmental conditions
  - Age
  - Host immune status

- Shedding 7d following infection to up to 90d PI
Canine Distemper Virus

• Variable signs in dogs – subclinical to severe fatal disease

• Severe generalized distemper – often associated with loss of MDA
  • Conjunctivitis
  • Progressively worsening cough, bronchopneumonia
  • Anorexia, vomiting, diarrhea
  • +/- neuro or other signs

• Mild dz in up to 50% of cases helps maintain virus circulating in the population

Warning - this is still CDV! A mildly affected dog can shed virus that will result in severe fatal disease in a pup.
Friendly reminder 😊

• Various causative agents cause clinically indistinguishable signs requiring laboratory confirmation of diagnosis

• Severity of symptoms does not determine the pathogen(s)

→ Many causative agents cause either mild and/or subclinical signs, but may also cause severe symptoms
Diagnostic testing

• Caution: positive test results for one or more organisms does not necessarily prove causation of clinical signs... many of these pathogens have been identified in clinically healthy animals
  • PCR panels vs. necropsy

• Testing of multiple animals helps elucidate pathogen mix in the population
  • Approx 10-30% or 3-5 animals
  • Typically acutely affected, pre-tx
  • Recently exposed may be appropriate
Diagnostic testing

• When to consider testing –
  • Increasing morbidity
  • Increasing mortality
  • Poor response to treatment
  • Unusual clinical signs
  • Zoonotic or multi-species involvement
  • Transmission to community
Diagnostic testing – what samples?

• Upper respiratory signs → deep nasal or pharyngeal swabs
  • PCR
  • Bacterial C&S
  • Virus isolation

• Lower respiratory signs → tracheal wash
  • PCR
  • Bacterial C&S
  • Virus isolation
  • Cytology

• ID pathogen(s) vs. guide individual animal treatment
Diagnosis: Necropsy

- Identify pathogens and their role in disease
- Often the most efficient way to get an accurate diagnosis
- Document initial findings

- Non-fixed samples for bacterial/viral isolation
  - Obtain first
  - Refrigerated for bacteria, frozen for viruses
  - Upper respiratory tract and lung

- Tissue samples for histopathology
  - Preserve samples (9:1 ratio formalin : tissue)
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Treatment Considerations

• Definitive diagnosis really needed to determine more specific treatment and management strategies

• Careful consideration regarding treatment:
  • Ability to provide humane level of care
    • Supplies
    • Space/housing
    • Staffing
  • Ability to protect the rest of the population
  • Retain focus on prevention
Treatment Considerations
Treatment

• Treatment remains largely supportive:
  • Stress reduction
  • Control coughing, break the cycle
  • Fluid therapy
  • Nutritional support
  • Antibiotics if indicated
  • Other treatments – antiemetics for CDV
  • Nebulization and coupage
  • Oxygen support
Antimicrobial therapy

• Antibiotics when indicated – in the face of primary or secondary bacterial pathogens, Mycoplasma spp.
• Variety of factors to consider in selection:
  • Time dependent vs. concentration dependent
  • Ability to penetrate respiratory tissues
  • Efficacy against pathogens likely to be of concern
  • Severity and progression of symptoms
  • Host factors
  • Implications for use in a large population

• Will not help with primary viral infection
Antimicrobial therapy

• Culture & sensi always ideal but not always feasible

• Upper respiratory signs, first line treatment:
  • Doxycycline considered drug of choice for shelters:
    10 mg/kg po SID
  • Cost effective, SID dosing, effective, resistance uncommon
  • Minocycline - very similar to doxy – also 10 mg/kg SID

• Other bacterial components, bronchopneumonia require different antibiotic selection
  • Broad spectrum coverage – e.g. penicillin with fluoroquinolone
Strep zoo

• Treatment:
  • Early recognition and antibiotic therapy very effective (if sensitive)
    • Penicillins – injectable pen G followed by oral meds one common protocol
    • Convenia shown to be efficacious in at least one outbreak
    • Fluoroquinolones?

• Aggressive therapy necessary for more severe, later stage cases; may still be fatal
Antivirals for CIV?

• **Tamiflu** - Oseltamivir phosphate – neuraminidase inhibitor
• Not recommended for treatment of CIV infected dogs:
  • Most recover without needing antivirals
  • Pharmacokinetic studies lacking
  • Must be administered early in the course of infection
  • Public health concerns, legal restrictions coming?

• Limited data on other treatment options:
  • Nitazoxanide, tizoxanide inhibited viral replication of CIV in vitro

Laura V. Ashton LV et al. *In Vitro Susceptibility of Canine Influenza A (H3N8) Virus to Nitazoxanide and Tizoxanide.* Veterinary Medicine International Volume 2010 (2010).
Preventive Strategies

• Plan A: Prevent exposure
  • If exposure can’t be zero, limit the dose to as little as possible:
    • Avoid overcrowding
    • Excellent sanitation
    • Fomite control
    • Adequate isolation +/- quarantine
    • Ventilation
    • Reduce length of stay
Preventive Strategies

• Plan B: Strengthen host defense
  • Good husbandry, nutrition
  • Treat concurrent infections
  • Vaccination
  • Reduce stress
Preventing exposure

• Avoid overcrowding – stay within your capacity for care

• Crowding = major stressor
  • Exacerbates challenges shelters already struggle to manage
  • Significant risk factor for disease
  • Not inevitable
Capacity for Care

• Housing capacity:
  • Not just an open cage, but an appropriate enclosure for that particular animal
  • Ideally below your max capacity

• Staffing capacity
  • Staff and/or volunteers to meet the physical and behavioral needs of that animal

• Additional sufficient resources as needed for that animal
  • Medications, vet care, training, etc
Preventing Exposure

• Limit LOS: dogs in high-density populations at greatest risk
  • The strongest prognostic factor for coughing (regardless of vaccine group) was the number of days spent at the shelter, with each additional day increasing the risk of coughing by 3%\(^1\)

• Number of days in the shelter was the only factor significantly associated with positive serologic test results. For every 3 days in the the odds of a positive result increased


• What can we do TODAY to move that animal closer to their final outcome?
  • Written SOP and criteria for behavior, medical to determine adoption, transfer, etc
  • Eliminate holds and bottle necks – extra staffing, resources, fast track/slow track program, etc.
Preventing exposure

- Excellent sanitation procedures and fomite control
  - Appropriate use of housing
  - Labeled, dedicated equipment
  - Dedicated staff
  - Appropriate order of cleaning
  - Diligent hand sanitation
Preventing exposure

• Adequate isolation +/- quarantine

• Intermixed in general population is not an option – prompt removal is critical
  • Separate biosecure location, ventilation ideal
  • If not – try to separate by at least 25’ apart
  • Limit foot traffic, dedicated staff
  • Appropriate PPE
Preventing exposure

• Address ventilation
  • Know your HVAC system
  • Fresh air and outdoor access
Preventing exposure

• Address ventilation
  • Address local contaminants
    • Aerosolization with power washers
    • Improperly mixed disinfectants
    • Manage humidity – dry surfaces
  • Reduce barking
  • Alleviate overcrowding
Don’t forget about the cats…

• CPiV, *Bordetella*, CIV, Strep zoo all reported in cats

• Isolation areas must be separate

• Limit fomite control, cross contamination via staff
...or the people

- *Bordetella* known to cause infections in immunocompromised individuals
- Case report of zoonotic transmission from dog to animal handler of Strep zoo
- Appropriate training and education for staff, adopters, owners, visitors
- Proper use of PPE
Preventing exposure

- Protect high risk populations as much as possible:
  - Naïve animals
  - Incoming animals in the face of an outbreak
  - Puppies < 5 months old

- Appropriate segregation and housing
- Dedicated staff and appropriate sanitation procedures
- “Clean break” in population, consider halting intake
Strengthen host defenses

• Good husbandry, nutrition
• Reduce stress
• Treat concurrent infections
• Vaccination
The role of vaccination

• Vaccines available to protect against some CIRDC pathogens:
  • *Bordetella bronchiseptica*
  • Parainfluenza virus
  • Adenovirus
  • Canine distemper virus
  • Canine influenza virus

• Vaccines not available to protect against others:
  • Respiratory coronavirus
  • Strep zoo
  • Mycoplasma

• Not vaccine preventable disease, but still an important tool
Core vaccinations

- DA2PP given at intake for dogs 4-6+ weeks old
  - Repeat q 14 days while in the shelter, stop at 18-20 weeks old

- Vaccination highly effective for CDV:
  - Clinically relevant protection within hours
  - Longer time frame to prevent mild signs, actual infection, viral shedding

- Reasonable protection against CAV

- Don’t rely on it for CPiV
Distemper vaccination

- This is a core vaccine - don’t assume they are protected!

Core vaccinations

- Intranasal *Bordetella* AND Parainfluenza at intake for dogs as young as 3-4 weeks of age
  - Dogs < 6 weeks old: repeat once in 14 days
  - Dogs > 6 months old: not necessary

- Caution not to give via parenteral route: severe reactions, including acute hepatic necrosis and death may occur

- Oral *Bordetella* vaccine → effective, but lacks CPiV component

The Canadian Veterinary Journal
La Revue vétérinaire canadienne

Respiratory disease outbreak in a veterinary hospital associated with canine parainfluenza virus infection

J. Scott Weese and Jason Stull
Canine Influenza Vaccination

• H3N8 approved vaccine & H3N2 conditionally approved products for CIV protection

• Parenteral killed product, 2 doses 2-4 weeks apart
  • Immunity should not be expected until approximately one week following the second dose
  • Limited benefit unless exposure can be prevented
CIV Vaccination

• Vaccine limits the severity and duration of clinical signs, viral shedding but does not prevent infection

• Included in AAHA’s 2011 Canine Vaccination Guidelines as a non-core vaccine
  • Recommended for use in certain populations of shelter-housed dogs.
  • Transfers to/from, sometimes within endemic shelters or communities
  • Certain higher risk pet dogs

Other vaccine considerations

- Remember: vaccination with available products helps limit severity of clinical signs in co-infections
- Histopath lung scores <<< in co-challenged dogs when vaccinated

Canine distemper titers

- Simultaneous with diagnostics, helps to clarify susceptibility and risk
  - Guidance, not absolutes

- Must limit use for dogs without current or historical clinical signs – distinguish protection vs. infection
CDV Titer, no clinical signs

Positive*

- Adult: Adopt or transfer without special precautions
- Puppy: Adopt or transfer ASAP with waiver

Negative

Assess exposure, risk (age, vx hx etc), adoptability

High risk: consider 4-6 week quarantine if possible

* Remember that titers may rise faster than development of clinical signs. Low risk ≠ no risk!