Canine Influenza Virus

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Kennel Cough

- A low level of upper respiratory infection is common at any shelter or kennel
- “Upper Respiratory”
  - nasal sinuses, trachea, large airways
- “Lower Respiratory”
  - lungs (bronchopneumonia, pneumonia)
- Any shelter manager manages “kennel cough” syndrome in a few dogs at any point in time
- A large outbreak or repeated outbreaks can have long term effects on a shelter and impact the entire community

The many causes of kennel cough

**Bacteria**
- *Bordetella bronchiseptica*
- *Mycoplasma spp.*
  - Arthritis
  - Many other infections

**Viruses**
- Canine parainfluenza
- Canine distemper virus (CDV)
  - Seizures, twitching, paralysis
  - Hard pad
- Canine herpesvirus (CHV)
  - Abortions and fading puppies
- Canine adenovirus 2 (CAV2)
  - Hepatitis
- Canine influenza (CIV)

Things that can look like kennel cough

- Allergic Bronchitis
- Congestive Heart Failure
  - Listen for a heart murmur
  - Can resemble pneumonia
    - Coughing up pink foamy fluid
    - Breathing hard
    - Blue gums
  - Chest x-rays and other tests can tell the difference
- Heartworm Disease

Canine Flu

- Influenza A virus (orthomyxovirus)
- Related to (Hemagglutinin 16 Neuraminidase 9)
  - Human flu – H3N2
  - Equine flu – H3N8
  - Swine flu – H1N1
  - Avian flu – H5N1
  - Canine flu – H3N8
- First isolated from racing greyhound that died from pneumonia at tracks in Florida in 2003-2004
- Canine flu has since marched its way across the US
  - Not uncommon in shelters, rare in veterinary practice

Who can get it?

- Because the virus is new, most dogs are susceptible
  - Few have been vaccinated
  - Few have been exposed and infected
- Horses can be infected, but show mild symptoms
- No evidence that cats can be infected
  - Cats housed with infected dogs have been tested
- No evidence that people can be infected
Canine Flu

Epidemiology

- Study of risk factors and patterns of disease

  • Contagiousness
    - Likelihood that exposure will result in infection
    - CIV is highly contagious – nearly 100%

  • Morbidity
    - Likelihood that infection will cause disease
    - CIV has high morbidity – 80-90%

  • Mortality
    - Likelihood that illness will result in death
    - CIV has low mortality – 5-8% (lower with prompt treatment)
    - Most recover within 30 days, often within 7-10 days

Transmission

Modes of Transmission

  • Aerosols and Droplets
    - Tiny droplets produced when an animal coughs or sneezes
    - Droplets travel up to 4 feet through the air
    - Human flu aerosols can travel up to 50 feet
    - Aerosols cause many to get sick quickly in shelters

  • Direct Contact with respiratory secretions

  • Fomites
    - Objects contaminated by respiratory secretions
    - HANDS ARE THE PREDOMINANT Fomite IN SHELTERS
    - Shelter workers have taken CIV home to infect pets

Common Shelter Fomites

- Staff hands
- Visitor hands
- Bowls
- Litter boxes
- Toys
- Bedding

- Clothing
- Hair

Fomites You Might Not Think Of

- Door knobs
- Keyboards
- Telephones
- Cell phones
- Light switches
- Leashes
- Cage cards

Transmission

Incubation Period

- The time between exposure and apparent symptoms

  - 2-4 days for CIV

  - Much shorter than other causes of kennel cough
    - 1-14 days for other causes

  - Respiratory Pathogen Chart

Virus Shedding Period

- Time after infection that the dog is shedding infectious organisms in respiratory secretions

  - Begins at 2 days post infection
  - Continues for 7-10 days
  - Peak shedding is 2-4 days post-infection
    - This overlaps with the incubation period
    - Dogs can shed virus prior to showing clinical signs
    - 10-20% of dogs will be infected and shed, but never become ill
Transmission

Virus Shedding Period
• Comparison to other respiratory Pathogens
  • CHV – 2-3 weeks (asymptomatic carriers)
  • CDV – up to 90 days
  • Parainfluenza – 6-8 days
  • Bordetella bronchiseptica – 90 days or more (asymptomatic carriers)
  • CAV2 – 10 days
  • Mycoplasma spp. – 90 days or more (asymptomatic carriers)

Carrier State
• Long term shedding after recovery
• No carrier state with CIV
• There are carrier states for other respiratory pathogens
  – Bordetella bronchiseptica
  – Mycoplasma spp.
  – CHV
  – Dogs who have recovered from the respiratory phase of CDV
    can shed virus for up to 90 days
  • They seem clinically normal, but later develop neurologic
    signs which reveal their CDV infection.

Clinical Signs

Symptoms – Clinical Signs
• Distinguishing CIV from other causes of URI/LRI can be
difficult
• Most dogs in the shelter are infected within 2 weeks
  – This may be less apparent with a second round
  – Dogs of all ages are affected
• Sudden increase in the prevalence of kennel cough
  – Prevalence – percentage of animals in a given population who
    have a disease at a point in time
• Suddenly increase in severity of kennel cough
• Prolonged to complete lack of response to antibiotic
  therapy

Animals fall into 3 categories
• Asymptomatic infection – 10-20%
• Mild Infection - 60-85%
• Severe Infection – 5-20%
• Most dogs look like garden variety kennel cough
• A few get severely ill

Mild Infection
• Productive cough for several weeks
  – Gag or swallow at the end
  – Like dog has something caught in their throat
  – Sometimes cough up foamy fluid or mucus
• Little response to antibiotics
• Mild fever or lethargy
• Purulent nasal discharge
  – Purulent – having the quality of pus
  – Due to secondary bacterial infection

Severe Infection
• High fever – 105-106°F
• Tachypnea
  – Rapid breathing
  – > 40 breaths per minute while resting
• Pneumonia - Need chest x-rays to confirm
• Prolonged recovery
• Fatality rate is 5-8%
  – Peracute hemorrhagic fatal pneumonia reported only in the
greyhound
  – Peracute – less than 24 hours from first symptoms
  – Hemorrhagic – coughing up blood (hemoptysis)
Other Causes of Pneumonia

Allergies
- COPD
  - Chronic obstructive Pulmonary Disease

Protazoons
- Toxoplasma
- Neospora

Bacteria
- many

Viruses
- CDV

Fungus
- Histoplasma
- Blastomyces
- Cryptococcus

Parasites
- Lung flukes
- Migrating hooks/rounds
- Heartworms

Diagnosis

- CIV can’t be distinguished from other respiratory pathogens based on clinical signs
- Coinfections may occur, confusing matters
  - Coinfection – infection with more than one organism simultaneously
- Diagnostic tests
  - Bacterial culture of trans-tracheal wash
  - Virus isolation (culture) from nasal and throat swabs
  - Blood titers
  - PCR from nasal and throat swabs

Nasal and Throat Swabs
- Must be taken in first week of infection to be positive
- As soon as symptoms begin is best
  - Peak shedding 2-4 days post-infection
- Submit samples from multiple animals for
  - Antigen detection
  - Virus isolation
  - PCR
    - Polymerase chain reaction
    - Detects presence of viral DNA
  - Contact the lab in advance for handling instructions

Antigen Detection (immunoassay kits) – Swabs
- Directigen Flu-A
  - By BD – Becton-Dickinson
- QuickVue Influenza Test
  - By Quidel

Swab Collection Technique
- Wear exam gloves to prevent contamination of the sample with your own DNA
- New gloves for each dog
- Touch the swab tip only to the area sampled
  - Avoid contamination with your own DNA and DNA in the environment
Diagnosis

Transtracheal Wash
- Performed by a veterinarian
- Dog is lightly sedated, so they can still cough
- Catheter passed into the trachea (wind pipe)
- Fluid rinse collected in a sterile manner (aseptically)
- Submitted for:
  - Cytology – look at the cells present and possible bacteria
  - Bacterial culture – check for coinfections, and to test for antibiotic sensitivity
    - Ask for culture and sensitivity, not just culture
  - CIV PCR

Diagnosis

Virus isolation
- Takes a long time – a week or more
- Probably won’t help animals that are sick at the time
- But can help identify the cause of a severe outbreak
- Remember to contact your lab in advance for instructions on sample handling and shipping
  - Use polyester rather than cotton tipped swabs
  - Placed in sterile dry tubes or tubes with transport medium
  - Shipped on ice to arrive within 2 days
- Can help decide whether you need to vaccinate for CIV
- Many false negatives

Diagnosis

Blood titers
- Most reliable test for identifying CIV infection in a particular dog
- Antibodies detected as soon as 7-10 days after infection
- Take 2 blood samples
  - 7-10 days after first signs
  - Then 2 weeks after the above sample
- Collect in a red top tube and let clot
- Spin down, harvest serum and put in freezer
- Send all samples to the lab at the same time (LABEL THEM!!)
- Four-fold increase in titer is diagnostic for CIV

Diagnosis

CIV Labs
- Cornell University (PCR, titers, virus isolation)
  – New York State Animal Health Diagnostic Center
- Colorado State University (H1, PCR, ELISA)
  – CSU Veterinary Diagnostic Laboratory
  – [http://www.dlab.colostate.edu](http://www.dlab.colostate.edu)
- UC-Davis (PCR)
  – Lucy Whittier Molecular & Core Diagnostic Center

Diagnosis

Ancillary Diagnostics
- CBC
  - Complete blood count
  - High white may indicate pneumonia or infection
  - Low white count might indicate overwhelming infection, or concurrent parvovirus
- Profile & urinalysis
  - tests liver, kidney, blood sugar, proteins, minerals, etc.
- Chest x-rays – to detect pneumonia
- Necropsy – ask the lab to look for CIV

Outbreak Control
- Entire shelter must be quarantined/isolated, unless there are truly separate kennels which are not cross-contaminated
  - Quarantine – separate exposed from unexposed animals to see if the former become sick
  - Isolation – separating infected animals with symptoms, to limit infection of others
  - Ideally, these should be 2 separate groups
  - But because CIV spreads so quickly, most dogs have already been exposed before quarantine is possible
  - 14 days is sufficient for quarantine/isolation if there are no breaches
Outbreak Control

- **Deep cleaning and disinfection**
  - CIV is killed by most disinfectants, including **quats**, peroxysgens and bleach
    - **Quats** - Quaternary ammonium compounds
  - CIV can live for 24-48 hours on nonporous surfaces
  - 8-12 hours on porous surfaces
  - Only minutes on hands

Outbreak Control

- **Deep cleaning and disinfection**
  - Review cleaning and disinfection protocols to make sure we are doing things as we know we should
    - Clean with detergent to remove organic debris
    - Then disinfect – soak for 10 minutes
    - Rinse and dry before returning the animal
    - Remove and disinfect/discard all possible fomites
  - If you can’t soak every cage/run every day, then rotate and do each at least once or more weekly

Outbreak Control

- **Increase air exchanges**
  - **Air exchange** – number of times per hour air in a room is moved out and replaced
    - 10-12 acceptable
    - Increase to 15 during an outbreak
    - Set fans by open windows - fresh air in
    - Close vents to stop air-sharing with rest of the shelter

Outbreak Control

- **Wear PPE**
  - **Personal Protective Equipment**
  - Isolation gowns – less than $2 each
  - Gloves and booties
  - Staff assigned to either quarantine/isolation or naïve population for the day
  - Change out of your street clothes when you clock in, and into you street clothes when you clock out (scrubs work well)

Outbreak Control

- **Inform the public - 30 day period**
  - Give each adoptive family written information on CIV
    - What to look for
    - What to do in case symptoms occur
    - Advise of risk to other dogs in the adoptive home
    - Remind that CIV is a community problem, came form the community, and the shelter makes every effort to eradicate the pathogens that come in the door every day
    - Also that CIV is not prevented by kennel cough vaccine

Outbreak Control

- **Inform the public – 30 day period**
  - Consider releasing adopted dogs only after the 14 day quarantine
    - They may still have symptoms, but are no longer shedding
    - Single dog homes are the best situation
    - Or vaccinate dogs in the adoptive home
    - Provide a complete medical record for transfer to the new veterinarian
      - Exam findings, test results, treatments, progress notes
Outbreak Control

• Inform the surrounding shelter community
  – Issue a “CIV Advisory” to inform neighboring
    • shelters
    • Veterinary clinics
    • rescue groups
    • foster homes
    • boarding kennels
    • Groomers
    • trainers
  – Inform the general public – newspaper, PSA radio
  – Be a considerate member of the animal welfare community

Outbreak Control

• Review intake Quarantine Procedure
  – Intake quarantine of at least 2 weeks is required to keep respiratory outbreaks down to a dull roar
  – If your intake quarantine is shorter, you will have frequent problems with kennel cough
  – If you can’t do a 2 week intake quarantine, consider “cohort admissions”
    • Add dogs to one room or area, until it is full
    • Add no more until the room is empty
    • Scrub from top to bottom before the new groups comes in
    • Multiple small rooms make this easier

Outbreak Control

• When to consider depopulation**
  – Short incubation and shedding makes CIV more manageable than CDV, Bordetella and Mycoplasma.
  – Quarantine/isolation need only be for 14 days
  – High contagiousness makes it harder to manage
    • exposure of just one naïve dog puts the entire naïve population at risk
  – **When new intakes cannot be separated from the rest of the isolated/quarantined population (separate air)
  – Consider reducing population density for 30 days as an alternative to complete depopulation

Depopulation

Arguments For

• Highly contagious
• Prolonged shedding
• Resistant to disinfection
• Prolonged survival in the environment
• High morbidity
• High mortality
• Many at risk

Arguments Against

• Zoonotic
• Resource intensive to treat (severe form)
• Unable to effectively isolate/quarantine
• Unable to disinfect

**CIV

Treatment

• Antibiotics for secondary infection indicated by:
  – Fever
  – Productive cough
  – purulent nasal discharge
  – pneumonia
  – Tetracyclines for mild form
    • doxycycline 5-10 mg/kg PO BID x 2-3 weeks
    • PO – per os – by mouth
    • BID – Latin “bis in die” – two times daily
  – Plus IV antibiotics for severe form

Treatment

• IN Bordetella vaccine booster for all
  – IN - intranasal
  – Will decrease severity of secondary bacterial infection with Bordetella

• Antitusives
  – Cough suppressants
  – Contraindicated in dogs with productive cough
  – Contraindicated – “against indicated” – cause more harm than good
**Treatment**

- **IV fluids** for severe form
  - Prevents/treats dehydration
  - Loosens and thins respiratory secretions so that they can be coughed up and eliminated

- **Coupage**
  - Clapping hands on the chest to loosen secretions and promote coughing

**Treatment**

- **Oxygen therapy**
  - For severe pneumonia
  - Cage or nasal cannula

- **Nebulization**
  - Treatment with steam to loosen secretions
  - Some put antibiotics in the nebulizer or other drugs to thin the respiratory secretions

**Treatment**

- **Tamiflu**
  - Generic - oseltamivir
  - For best results in people, it must be given with 48 hours of being infected with flu
  - Have no idea whether it helps dogs with flu
  - But it does make more sense to use it for canine flu than for parvovirus
    - N in flu virus = neuraminidase
    - Neuraminidase is an enzyme that breaks down mucus on the surface of the respiratory and GI tracts to the virus can attach
    - Flu viruses have it, but parvovirus does not
  - There are no studies to tell us the dose or frequency to use, or whether it helps to treat CIV

**Treatment**

- **Euthanasia**
  - Some shelters may need to euthanize dogs with severe form of CIV
  - It can be resource intensive to treat
  - But remember that euthanasia will not change the outcome of the outbreak, unless all were euthanized within 2-4 days of exposure
  - Depopulation might be considered of quarantine/isolation of all dogs for 14 days is not possible in your facility

**Immunity**

- Antibodies persist for at least 5-6 years after infection
- But we don’t know if these antibodies protect from disease
  - Studies have not yet been done
- In people, flu viruses mutate often, so that new flu vaccines must be produced each year to keep up with the changes in the virus

**Immunity**

- **Vaccine**
  - Not useful once an outbreak has begun
    - Does not prevent infection
    - Lessens severity of symptoms
    - Lessens but does not prevent shedding
    - Killed vaccine requires at least 2 doses, 2 weeks apart to take effect
    - Immunity is best 1-2 weeks after the second dose (a month after the first vaccine)
    - Outbreak is over by the time the vaccine takes effect
Immunity

Vaccine

- May be useful to lessen severity of outbreaks
  - only if dogs are in the shelter for longer than 3-4 weeks
- Will help minimize community impact of an outbreak in shelters with short turnover time
  - Turnover time – average number of days between admission and leaving the shelter
  - Those adopted out infected with CIV will be less likely to have clinical signs, and if they do, they will be less severe
- Vaccine is only conditionally licensed at this time
- Shelter workers should consider vaccinating their pets