Canine infectious respiratory disease (CIRD) occurs most frequently among dog populations in shelters and in training and boarding kennels. It is also referred to as infectious tracheobronchitis or kennel cough when it occurs under these circumstances. Characteristic clinical signs associated with the most common clinical presentation are low-grade fever, a dry hacking cough, retching, and recovery within 1–3 weeks. Severe bronchopneumonia, which may be fatal, can be seen in complicated cases.

Viruses currently recognized as being associated with CIRD fall into two categories. Canine parainfluenza-2 virus, canine adenovirus-2 and canine distemper virus have long been recognized, whereas canine herpesvirus, canine respiratory coronavirus and canine influenza virus are considered newly emerging. Detection of a canine pneumovirus in dogs with acute respiratory disease has been reported recently. Viruses may either act alone or in synergy with Bordetella bronchiseptica or Mycoplasma spp. in inducing CIRD.

Despite widespread vaccination of dogs, canine parainfluenza-2 virus is the most commonly detected viral pathogen in nasal, pharyngeal or tracheal swabs. By itself, it can cause laryngeal infection, coughing and serous nasal discharge. Clinical signs are limited to the upper respiratory tract. Damage to the tracheal epithelium predisposes to secondary infections. Canine adenovirus-2 replicates in the nasal mucosa, pharynx, tonsillar crypts, trachea and bronchi, and causes a mild, self-limiting, acute respiratory disease.

The clinical picture resulting from canine distemper virus infection depends on viral virulence, together with onset and level of the immune response, and ranges from very mild respiratory signs to severe respiratory involvement as a component of multisystemic disease (Figures 1 and 2).

A canine influenza virus (CIV) was discovered in 2004 following a series of respiratory outbreaks among racing greyhounds in Florida. Molecular characterization of this virus showed it to be closely related to, but genetically distinct from, equine influenza virus H3N8. However, the canine virus mutated sufficiently from the equine virus to enable horizontal transmission across the canine population and to no longer infect horses. Most CIV infections are clinically mild and self-limiting, but fatal hemorrhagic pneumonia also can occur. The Animal Health Diagnostic Center (AHDC) at Cornell University began a national CIV surveillance program in August 2005. CIV has now been identified in 30 states and is considered endemic in parts of Colorado, Florida, New York and Pennsylvania. Sera from Michigan dogs tested at ADHC have all been negative for antibodies to CIV. At DCPAH, we are currently conducting a larger scale serological survey for CIV antibodies in Michigan animal shelters.

A novel coronavirus, designated canine respiratory coronavirus (CRCoV), was initially detected in respiratory samples collected from dogs in a shelter with high incidence of CIRD. Molecular analyses showed that CRCoV was distinct from canine enteric coronavirus, and serological studies have shown CRCoV to be present worldwide. The virus has been isolated, but experimental infections have not yet been reported. In a limited survey at DCPAH, we detected CRCoV RNA in 8/50 nasal swab extracts collected from Michigan dogs.

Canine herpesvirus (CHV) has occasionally been associated with CIRD.
Following experimental inoculation, CHV has been reported to result in mild tracheitis or pharyngitis.

Our laboratory offers comprehensive testing for viral agents that can either cause or complicate canine respiratory disease. For ante-mortem testing, PCR-based testing of nasal swab extracts is the default method. It is very important—especially for CIV testing—to collect specimens very early during the clinical course and even from in-contact dogs. Refrigerated overnight sample submission is preferred. Serological testing is available for CDV and CIV. Additionally, immunohistochemistry (Figure 2) and in situ hybridization are available for postmortem laboratory diagnosis of such cases.

For additional information on these and other viral diseases, please contact the laboratory at 517.353.1683.

**Suggested background reading:**

AVMA Backgrounder: Canine Influenza, September 7, 2009.

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**Pet Food Linked to Illness in Dogs Results in a National Recall**

By: Kent Refsal, DVM, PhD and Patricia Schenck, DVM, PhD

Beginning in July 2010, the team of endocrinologists at DCPAH began seeing an unusual type of case. Dogs from various parts of the US were being examined by veterinarians and found to have elevated concentrations of serum calcium. The majority of the dogs displayed PU/PD, and some were identified as having loss of weight, loss of appetite, or azotemia. The veterinarians sent blood samples to DCPAH for specialized testing to explore the cause of the clinical condition.

When presented with an elevation of calcium on a chemistry profile result, the veterinarian must consider whether this is likely to be the cause of clinical signs, and, if so, the possible differential diagnoses. In dogs, the list of possibilities includes hypercalcemia of malignancy, primary hyperparathyroidism, renal disease, hypervitaminosis D, and granulomatous disease. The DCPAH Endocrine Section offers a variety of tests that can be used to help determine the cause of hypercalcemia. These tests include assays for parathyroid hormone, ionized calcium, parathyroid hormone-related protein (a factor produced by some tumors), and 25-hydroxyvitamin D (the prominent metabolite in the circulation that is an indicator of dietary intake of vitamin D).

To date at DCPAH, 19 dogs have been found to have elevated serum concentrations of 25-hydroxyvitamin D. When requested in 16 of the dogs, accompanying results showed an elevation of ionized calcium and low to low-normal concentrations of parathyroid hormone. Test evidence for vitamin D excess is an infrequent finding, and further investigation ensued. The affected dogs ranged in age from 8 months to 8 years. There were 3 mixed breed dogs and individuals from 14 different purebred breeds. The samples from these dogs originated from 9 states: Michigan, Texas, Colorado, Wisconsin, California, Illinois, North Dakota, New Jersey, and Utah. In the dogs tested at DCPAH, there was either a brief written history and/or communication by telephone with the referring veterinarian. In telephone conversations with veterinarians, the discussion included possible sources of excess vitamin D.

Hypervitaminosis D is generally viewed as an uncommon occurrence. Reasons for hypervitaminosis D include excessive dietary intake of vitamin D or ingestion of rodenticide containing vitamin D3 (cholecalciferol) as the principal ingredient. Another related cause is ingestion of the topical cream used as an adjunct for treatment of psoriasis in humans, where the principal ingredient is an analog of calcitriol (1,25-dihydroxyvitamin D). From the histories of the affected dogs, a common factor was identified in each of these 16 dogs: all were being fed a commercial diet from the Blue Buffalo Co., specifically the Blue Buffalo Wilderness Chicken Recipe. There have since been reports from veterinarians around the country about dogs with hypercalcemia that have been fed this diet. Dogs seem to recover when the diet is changed, and we are not aware of any deaths related to this problem.

The problem of hypercalcemia and hypervitaminosis D related to the consumption of this food is ongoing, with new cases identified as a result of the publicity and national recall of the dog food. A dietary history should be included in evaluation of any hypercalcemic patient. A press release from Blue Buffalo Co. (http://www.bluebuffalo.com/news/blue-news.shtml?gclid=CJzu9rg_6QCFYMy55wodH57TBQ) provides information about the specific products and lot numbers involved. Please call DCPAH to speak with our endocrinologists if you have questions or have a dog that is hypercalcemic and requires follow-up testing.
Tips about Bugs and Drugs

By: Carole Bolin, DVM, PhD

1. Some bacteria commonly isolated from companion animals have patterns of intrinsic resistance for certain antimicrobials. Intrinsic resistance implies that all isolates of that bacterium are resistant to that particular drug or class of drugs. Understanding the patterns of intrinsic resistance can aid in the choice of empiric therapy, prior to the results of culture and sensitivity.

2. Linezolid is never useful for gram-negative organisms.

3. Staphylococcus aureus, S. intermedius, and S. pseudintermedius are usually resistant to ampicillin.

4. In dogs with acute UTI, urine pH can be helpful in ‘guessing’ the organisms likely involved and therefore guiding empiric therapy. Alkaline urine is often associated with staphylococcal or Proteus infection, whereas acidic urine is more likely to be associated with E. coli or enterococcal infection.1

5. Bacteriology Susceptibility Profiles (Antibiograms) are tables that provide cumulative antimicrobial susceptibility testing data from a particular population (or institution) for a defined period of time. These summaries provide guidance in the selection of empirical antimicrobial therapy for infection. Data are reported as the percentage of isolates that are susceptible to a particular drug. Summaries for bacteria isolated from dogs and cat specimens submitted for culture at the DCPAH in 2009 are now available on our website (see “Diagnostic Sections/Bacteriology/Antimicrobial Susceptibility Testing/Bacteriology Susceptibility Profiles”). Equine and bovine pathogen profiles will be available in the near future.

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Organism | Intrinsic Resistance
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Pseudomonas aeruginosa | Ampicillin Amox/Clav Trimethoprim/sulfa Tetracyclines Cefazolin Cefotaxime
Enterococcus sp. | All Cephaolsporins Clindamycin Trimethoprim/sulfa Low-level resistance to all aminoglycosides
Proteus vulgaris | Ampicillin Cephalothin Cefazolin Tetracyclines Polymixin B Nitrofurantoïn
Klebsiella sp. | Ampicillin Ticarcillin

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Toxic Differentials of Central Nervous System Depression in Small Animals

By: Wilson K Rumbeiha BVM, PhD, DABT, DABVT

Toxin-induced central nervous system (CNS) depression in pets is characterized by acute onset of lethargy, ataxia, sleepiness, depressed respiration, and, in severe cases, coma. Death is due to respiratory arrest. A number of compounds cause CNS depression (household chemicals, pesticides, recreational drugs, and human and animal medications). Examples of such compounds are given in Table 1.

Dogs or cats are exposed to these compounds accidentally or maliciously. Accidental exposure to human medications, household chemicals and recreational drugs is a common cause of pet poisoning.

Intentional poisoning is commonly seen with ethylene glycol but will also occur with alcohol. Teenagers will give alcohol to dogs to “see how they will act.” Accidental exposure to euthanized carcases that have been improperly disposed of in dumpsters has poisoned pets as well.

When a pet is presented acting lethargic, ataxic, sleepy or comatose, intoxication should be included in the differential diagnosis. Exposure to some of these compounds may initially present as CNS depression but progress to CNS excitation. Smaller doses may be associated with depression, while larger doses may present as CNS excitation. Other clinical signs may include hypothermia and cardiovascular involvement resulting in hypotension. Accurate diagnosis demands a thorough history accompanied by appropriate selection of analytical samples. From live animals, urine and whole blood in EDTA are the samples of choice. Vomit and baits/environmental samples should also be submitted. From deceased animals, collect stomach contents, fat, and liver in addition to urine. At DCPAH, testing for these compounds or their metabolites is by GC/MS or LC-MS/MS, with the exception of lead, which is tested by ICP/MS as part of our heavy metal panel.

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TABLE 1: Compounds which cause CNS depression in small animals

<table>
<thead>
<tr>
<th>Classification</th>
<th>Examples of Compounds in this Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Environmental/Household</td>
<td>ethylene glycol, propylene glycol, lead, petroleum hydrocarbon solvents (e.g., benzene, toluene, methyl bromide), ethanol, methanol, isopropyl alcohol and other alcohols</td>
</tr>
<tr>
<td>Anticonvulsant medications</td>
<td>phenytoin, metharbital, carbamazepine, primodone, succinamides, paraldehyde</td>
</tr>
<tr>
<td>Sedatives, anesthetics</td>
<td>barbiturates, benzodiazepines (e.g., diazepam), glutethamide, propofol, ketamine, acepromazine</td>
</tr>
<tr>
<td>Medications</td>
<td>antihistamines, barbiturates, bromides, opioids, Ivermectin, piperazine, amitriptyline</td>
</tr>
<tr>
<td>Pesticides</td>
<td>amitraz</td>
</tr>
<tr>
<td>Recreational drugs</td>
<td>cannabinoids (marijuana), opiates and opioid agonists, e.g., heroin, morphine, codeine</td>
</tr>
</tbody>
</table>
**DCPAH on the Road**

DCPAH will be on the road again this winter at the conferences listed below. We will have an updated CD with all the latest tests, fees, and forms on hand, as well as knowledgeable folks to answer all your diagnostic questions. Mention that you read this in the newsletter and receive a free token of our appreciation!

**North American Veterinary Conference**
Orlando, Florida – January 15-19
Booth 321

**Michigan Veterinary Conference**
Lansing, Michigan – January 28-30
Booth 41

**Midwest Veterinary Conference**
Columbus, Ohio – February 24-27
Booth 515

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**Arbovirus Testing at DCPAH in 2010**

By: Steve Bolin, DVM, PhD

Arboviruses are viruses that are spread by ticks, mosquitoes, and other biting insects. Every year, the DCPAH tests Michigan mammals and birds for these viruses. The arboviruses of concern for infection of both animals and humans include Eastern equine encephalitis (EEE) virus and West Nile virus (WNV). Michigan also experiences sporadic outbreaks of epizootic hemorrhagic disease (EHD) virus—an arbovirus that can cause die-offs in deer.

As of November 5, 2010, Michigan has confirmed 58 EEE cases in animals, and 75 additional suspect cases, based on clinical signs of disease. Only Florida has had more confirmed animal EEE cases this year. For comparison, in previous years, Michigan had zero confirmed cases (2006), 6 cases (2007), and 1 case (2008)—all in horses. In 2009, 1 horse and 2 emus were diagnosed. To date, we have tested 40 brain samples from horses, alpacas, llamas, deer, turkeys, and dogs for EEE by polymerase chain reaction (PCR) assay and found 16 brains to be positive for EEE virus. Of those, 14 were from horses and 2 were from deer.

Most of the 40 brain samples were also tested for WNV using a PCR assay. So far this year, WNV has not been detected in brain or other tissue samples from Michigan mammals or birds. However, by testing blood samples for antibody against WNV, we identified 3 live horses infected with the virus—one in Michigan, one in Oklahoma, and one in Ontario, Canada.

Working closely with wildlife biologists from Michigan’s Department of Natural Resources and Environment, the DCPAH helped detect several cases of EHD in deer that were found dead in southwest Michigan during September and October of 2010.