Treating Respiratory Infections in Dogs
From the nose to the alveoli

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Significant respiratory disease can be caused by primary bacterial pathogens in dogs. Even more common are bacterial infections that complicate an underlying disease. Frustrating nasal discharge, incessant or chronic cough, hypoxemia, or even death can result. Management strategies to address the challenges of chronic rhinitis, canine infectious respiratory disease complex (CIRDC, kennel cough), chronic airway disease, and acute and recurrent pneumonias are considered here.

CANINE CHRONIC RHINITIS

One of the most frustrating diseases for clients and veterinarians is idiopathic chronic rhinitis, and the role of bacteria in this disease is perplexing. A wide variety of bacterial species can be isolated from the nasal cavity of healthy dogs, including *Bordetella bronchiseptica*, *Pseudomonas aeruginosa*, and *Mycoplasma* spp. Yet the nasal cavity does not normally overtly react to the presence of these organisms. Primary bacterial infections of the nasal cavity are thought to be quite rare, particularly in chronic disease. More likely, normal inhabitants of the nasal cavity are able to take advantage of interference with normal drainage or changes in the nasal mucosa or secretions that result from other nasal diseases, to grow in sufficient numbers to contribute to clinical signs.

A predominantly secondary nature of bacterial infections of the nasal cavity explains why the common treatment approach with antibiotics usually fails. A classic clinical course can be described as follows: (1) dogs are presented with chronic nasal discharge; (2) antibiotics are prescribed for 2 to 3 weeks; and (3) a week or more after discontinuing the antibiotics, the nasal discharge returns. A far more effective way to achieve control of canine chronic rhinitis is to eliminate the underlying disease.

Differential diagnoses for nasal disease that can be complicated by bacterial rhinitis include nearly all nasal diseases, including foreign body, neoplasia, aspergillosis, polyps, tooth root disease, prior trauma, irritant exposure, oronasal fistula, palate defects, and, potentially, allergic disease and gastroesophageal reflux. Computed tomography, rhinoscopy and oral examination, dental radiographs, and nasal biopsy are often needed to thoroughly investigate for these diseases. Unfortunately, results of bacterial culture of the nasal cavity are not known to be of clinical benefit.

Despite the best diagnostic efforts, no underlying disease will be identified in a subset of dogs with chronic nasal discharge. These dogs often have lymphoplasmacytic or neutrophilic and lymphoplasmacytic infiltrates on nasal biopsy. As such, idiopathic rhinitis in dogs is sometimes known as *lymphoplasmacytic rhinitis*. A number of treatments are recommended to control clinical signs in these dogs, including antibiotics, antihistamines, nonsteroidal antinflammatory drugs (NSAIDS), corticosteroids (not to be used in conjunction with NSAIDS), intranasal saline drops, improved indoor air quality, omega-3 fatty acids, and itraconazole. Itraconazole for these cases has been suggested to be of potential benefit because of a hypothetical reaction to non-

invasive fungal organisms, although even anecdotal reports of success have been in dogs receiving treatment for several months.

In my experience, in the absence of a specific disease to address directly, antibiotics are the most likely treatment to be successful in controlling nasal discharge. This statement appears to be in contradiction to the scenario described above as usually failing. The difference is in the intention of treatment and the selection and dosing of antibiotics. I can imagine 3 potential rationales for the use of antibiotics in these patients. First, the overgrowth of normal inhabitants has led to invasion into the deeper tissues of the nasal cavity. In this instance, antibiotics should be administered as for other deep-seated infections such as discospondylitis or pyelonephritis. Antibiotics that are effective in relieving signs should be continued for a minimum of 4 to 6 weeks. If signs recur, the same antibiotic should be restarted and continued for 3 months or longer. In many cases, it may be necessary to continue to administer the antibiotic indefinitely. Second, there are fastidious pathogens that we have yet to characterize well, such as certain species of *Mycoplasma* or *Bartonella*. For these types of pathogens, elimination of organisms may not be possible or may require many months of treatment. Thirdly, some antibiotics appear to decrease inflammation, presumably due to alterations in bacterial populations, alterations in a specific bacterial species' ability to stimulate the inflammatory response, or direct anti-inflammatory actions. Such effects would be expected only while treatment is being administered. The common conclusion of these rationales is that a cure may not be possible and that extended antibiotic treatment is needed.

Specific antibiotics that can be effective and have few negative long-term consequences include amoxicillin, doxycycline, and azithromycin. The chosen drug should be administered as a trial for 1 to 2 weeks. If significant improvement is seen, it should be continued long-term as described above. If signs recur on discontinuation of the antibiotic, the same drug should be prescribed again and administered for an even longer period of time. If improvement is not seen with the initially chosen drug, this drug can be discontinued and a different antibiotic tried. Fluoroquinolones are broad-spectrum antibiotics with few adverse effects and good tissue penetration that can be administered long term. However, I reserve their use for dogs in which I have ruled out a primary disease process to the best of my ability and that have failed to respond to one or more of the other, more narrow-spectrum, drugs. If no improvement is seen after trials with 2 or 3 antibiotics, the dog is not likely to respond to antibiotics, and this therapy should be discontinued. Consideration should again be given to an underlying disease, or another of the previously mentioned treatment options should be tried.

CANINE INFECTIOUS RESPIRATORY DISEASE COMPLEX (CIRDC, KENNEL COUGH)

In most dogs with CIRDC, more than one pathogen contributes to the clinical signs. While bacteria can certainly play a role, viruses are frequently present as the sole cause of signs, or as a coinfection. Much as with colds and flu in people, antibiotics rarely make a big difference in severity or duration of clinical signs. In addition, the bacteria most frequently identified in clinical cases, *B. bronchiseptica* and *Mycoplasma cynos*, have not been shown to be eliminated from dogs after routine antibiotic treatment. Regardless of whether antibiotic treatment is elected, rest and the judicious use of cough suppressants are recommended in order to minimize the continual irritation of the airways caused by excessive coughing. Clients should be counseled to avoid exercise and excitement for these patients as long as the cough persists. Narcotic cough

suppressants (hydrocodone, butorphenol) can help decrease the frequency and severity of cough and may allow for restful sleep.

In practice, antibiotics are often prescribed for CIRDC, and their use is justified because of the potential presence of *Bordetella* or *Mycoplasma*. Doxycycline (5 to 10 mg/kg PO q12h, followed by a bolus of water) is effective against *Mycoplasma* and many *Bordetella* isolates. Although the ability of doxycycline to reach therapeutic concentration within the airways has been questioned because it is highly protein bound in dogs,[1] the presence of inflammatory cells may increase locally available concentrations of the drug and account for its anecdotal success. Amoxicillin with clavulanate (20 to 25 mg/kg PO q8h) is also effective in vitro against many *Bordetella* isolates. Antibiotics should be administered for 5 days beyond the time the clinical signs resolve or for at least 14 days.

Nebulization of gentamicin has been used to treat refractory cases or in outbreaks of infection involving dogs housed together, although no controlled studies have been published. An early study by Bemis et al showed that bacterial populations of *Bordetella* in the trachea and bronchi were reduced for up to 3 days after treatment with nebulized gentamicin but not orally administered antibiotics, and clinical signs were reduced.[2] Note that the numbers of organisms returned to pretreatment values within 7 days. Some clinicians have since reported success in managing difficult cases and outbreaks with this treatment. The protocol used by Bemis et al is 50 mg of gentamicin sulfate in 3 mL of sterile water, delivered by nebulizer and face mask for 10 minutes every 12 hours for 3 days.[2] Sterile technique must be maintained to keep from delivering additional bacteria to the airways. Nebulization of drugs has the potential to induce bronchospasms, so dogs should be carefully observed during the procedure. Pretreatment with bronchodilators should be considered, and additional bronchodilators (metered dose inhaler and/or injectable) should be at hand for use as needed.

B. bronchiseptica can primarily cause bronchopneumonia in some dogs (see discussion below). Further, some dogs with an initial presentation of CIRDC progress to develop pneumonia. In these cases, treatment should follow recommendations for pneumonia rather than CIRDC.

CHRONIC AIRWAY DISEASE (CHRONIC BRONCHITIS AND TRACHEOBRONCHOMALACIA)

Common chronic airway diseases of dogs include idiopathic chronic bronchitis and tracheal and/or bronchial collapse (tracheobronchomalacia). In some dogs, the chronic airway inflammation is initiated by infection; in other dogs, it might increase the chance of developing infection. Normal airway clearance is likely impaired in dogs with chronic airway disease due to changes in respiratory epithelium and mucus quantity and quality and to early airway closure. It is presumed that these changes increase the likelihood of significant bacterial infections. Further, dogs with chronic airway disease often require treatment with corticosteroids to manage cough, adding to a predisposition to infection.

The true prevalence of bacterial infection in dogs with chronic airway disease is not known. An early published study found an association between chronic bronchitis and infection with *B. bronchiseptica*.[3] More recent published studies have not found bacterial infection to be common.[4,5] However, most recent study populations are from hospitals that see a large number of referred cases. These patients are more likely to have failed antibiotic trials before referral or to be receiving antibiotics at the time of specimen collection, which would result in underrepresentation of the prevalence of bacterial infection. On the other hand, it is common for

people with chronic bronchitis to have signs that wax and wane over time, independent of treatment with antibiotics, and a similar phenomenon appears to occur in dogs. An apparent clinical response to antibiotics could simply be coincidental with a natural waning of signs.

Bacterial infection aside, other disease processes can contribute to cough in dogs with chronic airway disease. Parasitic disease (lungworms and heartworm disease), allergic bronchitis, left atrial enlargement or heart failure, upper airway obstruction such as from laryngeal paralysis or brachycephalic airway syndrome, and esophageal disease or gastroesophageal reflux are examples of diseases that can concurrently affect these dogs. Therefore, the best approach for treating dogs with chronic airway disease is to do a thorough diagnostic evaluation to identify as many contributing problems as possible so that each can be addressed specifically. A minimal evaluation should include chest and neck radiographs, including chest radiographs taken during inspiration and expiration as a way of screening for obvious tracheobronchomalacia; heartworm testing; and a CBC. Unfortunately, inflammation associated with bronchial disease is rarely reflected in a CBC. It is much better to evaluate the type of inflammation occurring in the airways with a direct airway specimen. In most cases, a tracheal wash provides an adequate and representative specimen with minimal stress to the patient. If there is localized disease on thoracic radiographs or other concerning findings from the history, physical examination, or other tests, then bronchoscopy may be useful. Airway specimen cytology is also the best way to identify active bacterial infection, and subsequent culture results can assist in antibiotic selection. Cultures are always performed for aerobic bacteria. Although the role of *Mycoplasma* infections in patients such as these is not well established, if the client is highly motivated, culture or polymerase chain reaction (PCR) testing for *Mycoplasma* should also be considered. PCR is likely a more sensitive test for *Mycoplasma* than culture, which also requires special media and handling. The microbiology laboratory should provide quantitative or semiquantitative results for any bacterial organisms grown, as a small amount of growth does not necessarily equal disease.[6] Similarly, culture results should be considered in light of the cytologic response present.

Dogs with chronic airway disease do not remain static with respect to their degree of compromise. Chronic bronchitis is a progressive disease. In addition, concurrent diseases may progress and new problems may develop. As such, repeat evaluation is indicated in these patients if they have a sudden worsening in signs that does not spontaneously improve within 1 or 2 weeks or if they develop difficulty breathing.

A common clinical dilemma arises with respect to the timing of collection of airway specimens. Typically, the expense and slight risk of a tracheal wash results in a delay of the procedure until the patient is tried on an antibiotic. While this approach can be successful, there is a consequence. If the patient fails to respond to the antibiotic, the presence of the antibiotic can be sufficient to interfere with the growth of organisms from airway specimens under laboratory conditions, even when it did not do so in the patient. If a dog has been receiving antibiotics, it is ideal to delay airway specimen collection for at least a week after discontinuing short-acting drugs, such as amoxicillin, or for 2 weeks after discontinuing antibiotics with high tissue concentrations, such as fluoroquinolones.

Regardless of whether antibiotics are prescribed as a clinical trial or based on airway specimens, it is ideal to initiate treatment at a time separate from other changes to overall management to better assess clinical response. For instance, if steroids and antibiotics are begun at the same time it can be hard to determine the effectiveness of either.

Organisms involved in bronchial infections generally originate from the oropharynx. They are frequently gram-negative with unpredictable antibiotic sensitivity patterns. The role of *Mycoplasma* organisms in canine chronic bronchitis is not well understood. These organisms may be an incidental finding or pathogenic. Antibiotics that are generally effective against *Mycoplasma* spp include doxycycline, azithromycin, and fluoroquinolones. Of these, fluoroquinolones are the most effective against a wide range of gram-negative organisms.

In addition to the susceptibility of identified organisms, the ability of an antibiotic to penetrate the airway secretions to reach the site of infection should be considered in selection. Antibiotics that are likely to reach concentrations effective against susceptible organisms include fluoroquinolones,[7] azithromycin, and possibly amoxicillin-clavulanate. Beta-lactam antibiotics do not generally reach therapeutic concentrations in airway secretions of healthy (not inflamed) subjects. If used for bronchial infections, the high end of the dosage range should be used.

Doxycycline is often recommended as a first choice because *Mycoplasma* and many *Bordetella* isolates are susceptible to this drug. It may have an additional benefit of mild antiinflammatory properties. The ability of doxycycline to reach therapeutic concentration within the airways is questionable because it is highly protein bound in dogs,[1] but the presence of inflammatory cells may increase locally available concentrations of the drug.

If an antibiotic is effective, a positive response is generally seen within 1 week. Treatment is then continued for at least 1 week beyond the time when the clinical signs stabilize. Antibiotic treatment usually is necessary for at least 3 to 4 weeks. Even longer durations may be necessary in some cases, particularly if bronchiectasis is present. If clinical signs worsen after antibiotics are discontinued, the same antibiotic should be prescribed again for a longer duration.

ACUTE AND RECURRENT BACTERIAL PNEUMONIA

The bacteria that cause pneumonia in dogs often originate in the oral cavity and pharynx and enter the lungs via the airways. This results in “classic” bronchopneumonia, which primarily affects the gravity-dependent cranial and ventral lung lobes and can often be diagnosed by thoracic radiography. Bacteria can also enter the lungs through the hematogenous route, resulting in an interstitial pattern that may involve the caudal lobes most severely. Bacterial pneumonia of hematogenous origin was documented in more than half of cats with bacterial pneumonia based on postmortem examination.[8] I am not aware of a similar study in dogs. A wide variety of organisms have been isolated from dogs with bacterial pneumonia, including gram-positive and gram-negative aerobes. Anaerobes may be present, usually in combination with aerobes, particularly in dogs with aspiration pneumonia or lung lobe consolidation. *Mycoplasma* spp have been isolated from dogs and cats with pneumonia, but their exact role in the disease is not known. *M. cynos*, as mentioned above, may be pathogenic in dogs. Community-acquired infectious pneumonia has been described in puppies and is most often caused by *B. bronchiseptica* (49% of cases).[9]

As with bacterial infections of other parts of the respiratory tract, the possibility of underlying diseases or predisposing factors should be considered during history taking, physical examination, and selection of diagnostic tests. Factors to be considered include exposure to viruses or bacteria from dogs with CIRDC or distemper; aspiration of ingested material or gastric contents because of cleft palate, megaesophagus, or other causes of overt aspiration; decreased clearance from the lungs of normally inhaled debris, particularly in animals with chronic bronchitis, ciliary dyskinesia, or bronchiectasis; immunosuppression resulting from drugs,

malnutrition, stress, or endocrinopathies; and the inhalation or migration of foreign bodies. Neoplasia or parasitic or fungal infections may rarely be complicated by bacterial infections.

Predisposing factors are of particular concern for dogs with recurrent bacterial pneumonia. Recurrence of signs within 1 or 2 weeks of discontinuing treatment is often indicative of an insufficient duration of therapy. Delayed recurrence of signs strongly suggests an underlying predisposition. Such a conclusion can be supported by the identification of different organisms on culture of airway specimens. In dogs with recurrent pneumonia, advanced diagnostic procedures such as esophageal swallowing studies with fluoroscopy, bronchoscopy, computed tomography, and/or tests of ciliary function or structure are considered.

The mainstay of treatment for bacterial pneumonia is antibiotics. Other supportive measures are also important, particularly in patients with increased breathing efforts. Lastly, good follow-up evaluation is important for early detection of relapse.

The selection of antibiotics ideally is based on the results of airway culture. For dogs with bacterial pneumonia, tracheal wash is often very rewarding. However, financial limitations or condition of the patient may preclude specimen collection. Also, antibiotic therapy should be initiated promptly, which will precede results of fluid culture. Therefore, empirical selection of antibiotics is required for at least initial management.

The antibiotic sensitivity of the involved organisms is difficult to predict because of the wide spectrum of possible organisms. Further, gram-negative organisms are commonly involved, and their sensitivity to specific antibiotics is difficult to predict. Airway penetration by antibiotics need not be a major consideration in patients with bacterial pneumonia. Antibiotics generally achieve concentrations within the pulmonary parenchyma equal to those in plasma.

Antibiotics are initially selected on the basis of clinical signs and, if available, morphology and gram-staining characteristics of organisms from airway specimens as examined cytologically. Modification of antibiotic selection is then based on clinical progression and results of any cultures. For animals with mild or moderate clinical signs, reasonable choices include amoxicillin-clavulanate, cephalexin, or trimethoprim-sulfonamide.

Animals with severe clinical signs or possible sepsis should be treated initially with intravenous antibiotics. In my practice, we commonly use the combination of a fluoroquinolone and ampicillin with sulbactam. Sulbactam is a beta-lactamase inhibitor, as is clavulanate, and the combination of ampicillin with sulbactam provides a drug with similar activity as amoxicillin-clavulanate in an intravenous formulation. If this combination results in a positive clinical response, the patient is easily transitioned to an oral fluoroquinolone and amoxicillin-clavulanate for the continuation of treatment at home. Alternatively, meropenem can be administered intravenously or subcutaneously. At the time of discharge, the client can be instructed on subcutaneous administration, or the dog can be changed to the oral combination of a fluoroquinolone and amoxicillin-clavulanate. The latter is more convenient but may not be sufficient in some resistant infections.

Antibiotic treatment should be continued for at least 1 week after the clinical signs resolve. For most dogs with bacterial pneumonia, total duration of treatment is usually 4 to 8 weeks. Recommendations for monitoring patients are described later in this section.

Dogs with bronchiectasis can be particularly challenging to manage, due to recurrent infections and the common colonization of the airways with *Pseudomonas*. Nebulization of antibiotics is rarely indicated as an adjunctive treatment for bacterial pneumonia because systemic delivery of antibiotics should be adequate and nebulized antibiotics cannot reach all infected regions. However, some dogs with severe bronchiectasis have frequent recurrences of

life-threatening pneumonia. These episodes of pneumonia are treated as in other dogs. However, in between episodes, it may be necessary to provide continuous, or near continuous, antibiotic coverage. These patients, in particular, should be managed based on tracheal wash cultures. If they have become chronically infected with *Pseudomonas*, long-term daily treatment with a fluoroquinolone may be necessary. In people, some success in decreasing the frequency of pneumonia has been seen with the daily nebulization of antibiotics. I have successfully employed nebulization in the management of patients with severe bronchiectasis but have found the use of saline alone to be successful, presumably through hydration of secretions and mucolytic effects.

Airway hydration is an important component of the management of dogs with pneumonia. Drying of airways causes increased viscosity of secretions and decreased ciliary function, interfering with normal airway clearance. Systemic dehydration is the biggest contributor to airway drying. Animals with any evidence of dehydration should receive fluid therapy. Diuretics are relatively contraindicated in such animals. Additional moisture for the airways can be provided through saline nebulization in patients needing additional support.

Physiotherapy is also important for the management of bacterial pneumonia in dogs with greatly decreased activity levels, consolidated regions of lung, or significant bronchiectasis. Physiotherapy also is indicated after nebulization. Lying in one position impairs airway clearance, and lung consolidation can occur if one side remains dependent for prolonged periods. Recumbent dogs should be turned at least every 2 hours. Dogs that have sufficient lung function and are able should be mildly exercised to cause them to take deeper breaths and to cough, promoting airway clearance. If mild exercise is not possible, coupage can be performed. In coupage, the clinician strikes the animal's chest over the lung fields with cupped hands. The action should be forceful but not painful and should be continued for 5 - 10 minutes, if tolerated.

Bronchospasm can occur secondary to inflammation from bacterial pneumonia, but this consequence is much more common in cats than dogs. Bronchodilators are considered for dogs showing increased respiratory efforts, particularly if expiratory wheezes are auscultated. There is limited evidence that bronchodilators may improve mucociliary clearance. Patient status should be monitored closely because bronchodilators may worsen ventilation:perfusion mismatching, worsening hypoxemia. Bronchodilators are discontinued if clinical signs do not improve or if they worsen.

Expectorants are of questionable value in dogs and cats. Acetylcysteine is a mucolytic agent that some clinicians believe is beneficial for the treatment of dogs with severe bronchopneumonia when administered intravenously. It is possible that the antioxidant effects of this drug, rather than its mucolytic property, account for any benefit that may be seen. Acetylcysteine should not be administered by nebulization due to its irritant effects on the respiratory mucosa.

Dogs with bacterial pneumonia should be closely monitored for signs of deteriorating pulmonary function. Respiratory rate and effort and mucous membrane color are monitored at least twice daily. Thoracic radiographs and the CBC should be evaluated every 24 to 72 hours. If the animal's condition does not improve within 72 hours, it may be necessary to alter treatment or perform additional tests.

After demonstration of improvement, thoracic radiography and a CBC should be performed every 1 to 2 weeks to ensure continued resolution and to determine when to discontinue antibiotics. Thoracic radiographs should ideally also be evaluated 1 to 2 weeks after discontinuation of antibiotics for the early detection of recurrence. As previously stated, dogs typically require treatment for 4 to 8 weeks.

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