INTRODUCTION

Chronic bronchitis (CB) is the most common chronic respiratory impairment in dogs. The condition is defined as a chronic cough occurring for two consecutive months during the preceding year that is not attributable to another cause (e.g. neoplasia, congestive heart failure). This definition is based loosely on the definition of chronic bronchitis in humans, which is characterized by a well-defined cascade of clinical and histologic changes. The early changes are typically triggered by an inciting irritant stimulus (usually cigarette smoking), and include increases in airway mucus production, impairment of mucociliary clearance, and alterations in the local immune response. The cascade of events in dogs is similar to that seen in humans, and, if left untreated, results in a cycle of chronic inflammation, chronic cough, copious mucoid airway secretions, and decreased mucociliary clearance. This session will focus on the diagnostic approach and therapeutic management of the patient with chronic bronchitis.

EPIDEMIOLOGY

The average age at the time of diagnosis of chronic bronchitis is eight years of age or older, and many clients will report a several year history of intermittent cough. All breeds of dog can be affected. Higher incidence has been reported in West Highland White Terriers, Poodles, Cocker Spaniels, Pomeranians, and German Shorthair Pointers. Many dogs afflicted with CB are obese, but are typically otherwise healthy.

DIAGNOSTIC EVALUATION

Because chronic bronchitis is a diagnosis of exclusion, it is important to complete a full diagnostic evaluation for any dog presented with a chronic cough. Common differentials for chronic cough in dogs should include congestive heart failure, heartworm disease, pneumonia, neoplasia, infectious tracheobronchitis, and tracheal collapse. Less common conditions include foreign bodies, parasitic bronchitis, and primary ciliary dyskinesia. The initial laboratory evaluation of the chronic bronchitis dog is an important means of characterizing the overall health of the dog, and serves as a screen for other potential aggravating or inciting conditions. Evaluation for all animals should include CBC, serum biochemical profile, urinalysis, fecal flotation, Baermann analysis, and heartworm antigen test. Additional screening tests may include serologic testing for infectious diseases (fungal, viral, Rickettsial) and echocardiography, where indicated. Arterial blood gas analysis in the early stages of disease can be normal or may reveal mild hypoxemia due to ventilation/perfusion mismatch. Severely affected dogs may become hypercapnic due to ventilatory failure.
DIAGNOSTIC IMAGING

Thoracic radiographs typically show bronchial or peribronchial patterns, and can also reveal secondary conditions including pneumonia, bronchiectasis, and right-sided cardiac enlargement secondary to pulmonary hypertension (cor pulmonale).

ENDOSCOPIC ASSESSMENT

Bronchoscopic examination in cases of chronic bronchitis usually reveals non-specific mucosal erythema with a roughened, cobblestone, or granular appearance, and copious amounts of mucus. Large airways may appear relatively normal in dogs with significant small airway collapse and mucus trapping. The airways of severely affected dogs may have a pale appearance as a result of fibrosis. Bronchoscopy is also a valuable tool for evaluation of tracheal and bronchial collapse secondary to chondromalacia, mainstem bronchus collapse secondary to cardiomegaly, and other large airway abnormalities (e.g. bronchoesophageal fistula, foreign bodies, lumenal tumors). Bronchomalacia is a particularly important co-morbidity, as the presence of distal airway collapse may be an indication for cough suppression, a treatment modality not typically utilized in chronic bronchitic patients.

DIAGNOSTIC SAMPLING

Bronchopulmonary cytology is typically characterized by non-degenerate neutrophilic inflammation. A smaller yet significant population of dogs will have cytology characterized by eosinophilic inflammation. Eosinophilic airway inflammation has historically been associated with hypersensitivity reactions, and has been erroneously used to make the distinction between “allergic” bronchitis and idiopathic chronic bronchitis. While eosinophils can certainly be recruited in allergic reactions, eosinophils can also be associated with neoplastic disease (e.g. lymphosarcoma), fungal infections, and systemic parasitism. Additionally, studies in humans suggest that acute exacerbations of chronic bronchitis can be associated with a transient inflammatory shift from neutrophils to eosinophils.

Most dogs with chronic bronchitis do not have active infection at the time of diagnosis. However, culture and sensitivity should always be performed on airway samples in the newly diagnosed bronchitic, in acute exacerbations of previously stable disease, or with radiographic evidence of bronchiectasis. Airway samples should be cultured for general aerobic and Mycoplasma culture. Anaerobic culture should also be considered in patients with bronchopneumonia.

THERAPY

CB is a slowly progressive condition for which there is no definitive cure. In the absence of intervention, the cycle of cough-induced inflammation and inflammation-induced cough will self-perpetuate. The three goals of therapeutic intervention in chronic bronchitis are, 1) do no further harm; 2) slow the progression of the histologic changes, and; 3) control the clinical signs. Because the inciting cause in dogs is rarely identified, the primary treatment of CB is based on controlling airway inflammation. Therapeutic tools commonly used in the control of CB include
modulators of the inflammatory cascade, bronchodilators, anti-tussives, antimicrobials, environmental manipulation, and weight management. Surgical intervention may be indicated in management of severe secondary changes or exacerbating conditions (e.g. tracheal collapse, bronchiectasis).

Control of airway inflammation is the single most effective means of ameliorating the clinical signs of CB in humans. Most of the clinical signs of CB in humans and dogs (coughing, expiratory dysfunction, mucus hypersecretion) can be primarily or secondarily attributed to airway inflammation.

Oral corticosteroids are successful as a sole therapy in resolving the clinical signs in the majority of canine CB patients, and have historically been considered the mainstay of therapy in veterinary medicine. The short-acting oral corticosteroids (prednisone, prednisolone) should be started at anti-inflammatory doses (1-2mg/kg/day divided BID), and tapered to the lowest effective dose. The dose reductions should initially be every 1-2 weeks until physiologic doses (0.25-0.5mg/kg/day) are attained, at which point the dose should be maintained for 2-4 weeks. In the event of a relapse during the steroid taper, the previous dose at which signs were controlled should be reinstituted, and the duration at that dose should be doubled prior to tapering.

Side effects of oral corticosteroids are many and known, and can be prohibitive in some cases. These include polydipsia, polyuria, inappropriate urination, lethargy, aggression, polyphagia, weight gain, and corticosteroid withdrawal syndrome (iatrogenic hypoadrenocorticism). In cases where control is achieved but adverse effects are intolerable, combination therapy with bronchodilators or anti-tussives (when appropriate) may provide control at lower steroid doses.

Inhaled corticosteroids are the standard of care in humans with CB. Advantages of inhaled steroids in humans include increased drug delivery to the affected site, significant reduction in systemic absorption, and reduction in prednisone-associated adverse effects. Anecdotal use of inhaled corticosteroids in dogs has been associated with improvement in clinical signs and reduction in prohibitive side effects. Fluticasone propionate (Flovent, GlaxoSmithKline) at 200, 225, or 250g dose can be administered to dogs using tidal breathing with a spacer device and facemask. At a dose of 2 puffs q12h, a single vial lasts approximately 30 days. Limitations to the usage of inhaled corticosteroids in veterinary medicine are many, and include a lack of controlled studies demonstrating efficacy, delivery, and reduced systemic absorption, drug delivery problems, patient compliance, and cost.

Other inflammation modulators that have been historically utilized in CB include antihistamines, mast cell stabilizers, anti-oxidants, Omega-3 fatty acids, NK-1 receptor antagonists, and mucolytics. With limited experimental data available and minimal anecdotal success reported, the regular use of the therapeutics cannot be fully advocated. In addition, some therapies may do more harm than good (e.g. anticholinergic effect of antihistamines).

The role of bronchoconstriction in canine CB remains unclear. Studies supporting the use of bronchodilators in CB have demonstrated improvements in objective data (pulmonary function tests) and subjective assessments (reduction in coughing, improvement in thoracic auscultation
findings, owner perception of exercise tolerance). In addition, bronchodilators appear to have a steroid-sparing effect in some cases. Bronchodilators commonly used in canine CB are the methylxanthines and inhaled beta agonists (usually combined with inhaled corticosteroids).

The mechanism of methylxanthine bronchodilation was initially attributed to phosphodiesterase inhibition. It is now believed that both the mechanism of activity and mechanism of adverse effects of this class of drugs are mediated by adenosine inhibition. In addition, the methylxanthines possess additional effects, including anti-inflammatory effects (sPL-A2 inhibition) and stimulation of respiratory musculature (cAMP-mediated). Metabolism of the methylxanthines is variable, and, when combined with limited formulations, can make dosing quite difficult, particularly in small dogs. Because of patient-to-patient variability in therapeutic and toxic dosages, administration should start at the low end of recommended doses, and increase to effect. Theophylline should be administered in slow-release formulations, and should start at 5-10mg/kg PO BID. Frequency and duration can be increased to as high as 20mg/kg BID should clinical signs warrant and adverse effects allow. Because of an increased risk of methylxanthine toxicity, co-administration of theophylline with fluoroquinololones should be avoided when possible.

Studies both in people and in dogs suggest that the long-term use of beta-agonists may worsen airway inflammation, and has been associated with an increased risk of asthma-related death in human asthmatics. For that reason, beta-agonists are rarely used as mono-therapy. However, as mentioned above, some canine chronic bronchitics exhibit better symptom control when combining anti-inflammatory therapy with long-acting bronchodilation. In dogs who exhibit symptom improvement following a short trial of oral bronchodilators, a transition to long-acting inhaled bronchodilators may offer an option for better long-term control. This can be accomplished by using combination inhaled products such as combination fluticasone propionate + salmeterol (Advair®). Combination products can be administered using the same spacer device and facemask as stand-alone inhaled corticosteroids.

This author typically reserves trials of bronchodilators once anti-inflammatory therapy has been stabilized. My experience is that canine patients exhibiting partial improvements with anti-inflammatory therapy, but still exhibiting cough or wheeze at higher tidal flows (e.g., post-exercise), may experience improvements with additive bronchodilator therapy.

As mentioned earlier, most dogs do not have active airway infections at the time of diagnosis. For this reason, antimicrobial therapy is rarely indicated in cases of CB. If indicated, therapeutic decisions should be based on culture and sensitivity results whenever possible. Empirical therapy selections (while awaiting C/S) should have coverage of common airway pathogens (Mycoplasma, Staphylococcus, Streptococcus, Pasteurella, Bordetella), and may include azalides, tetracyclines, fluoroquinololones, and macrolides. If radiographic evidence of pneumonia or bronchiectasis is present, spectrum of activity should be expanded to cover Gram-negative bacteria, anaerobes, and Mycoplasma.

The cough reflex in cases of CB is usually a protective and therapeutic mechanism. Coughing aids in the clearance of excess viscid secretions, and can minimize aspiration of irritants and organisms in the face of an impaired mucociliary transport system (secondary ciliary dyskinesis). For these reasons, most coughs associated with chronic bronchitis should not be directly suppressed, but
should be alleviated by suppression of the inflammatory cascade. Some coughs may require direct suppression, and include dry, hacking paroxysmal coughs (which may also be associated with concurrent tracheal collapse), coughs associated with cough-induced syncope, and night coughing. The most effective anti-tussives for use in canine CB are the narcotic cough suppressants, including hydrocodone (0.25-1.0mg/kg PO q6-12h), codeine (1-2 mg/kg PO q6-12h), and butorphanol (0.25-1.0 mg/kg PO q6-12h). The most common side effect is sedation, which can be beneficial in some cases for alleviation of night coughing. Other side effects are rare at the anti-tussive doses, and include constipation and respiratory depression.

Well-controlled bronchitic patients who experience either acute or progressive worsening should be screened for late-stage complications of chronic bronchitis. Two common complications of chronic bronchitis include bronchiectasis and pulmonary hypertension. Bronchiectasis is a progressive, irreversible destruction of bronchial wall cartilage, leading to persistent dilatation of the large airways. Airway wall destruction is caused by persistent inflammation. Leukocyte proteases can initiate airway wall destruction. Bacterial infection, a recurrent consequence of bronchiectasis, can worsen airway wall destruction through the generation of bacterial toxins. Bronchiectasis results in impaired mucociliary clearance, mucus stasis and accumulation, and subsequent airway obstruction. Ultimately, if left untreated, bronchiectasis will lead to ineffective cough and an increase in dead space ventilation. Because bronchiectasis is frequently complicated with bacterial infection, radiographic detection of ectatic airways in a poorly controlled bronchitic likely warrants antibiotic therapy. If possible, antimicrobial therapy should be based on airway culture and susceptibility. If this is not possible, empirical therapy should include spectrum for gram negative enterics, Staphylococcus spp., and Streptococcus spp. Because of the high likelihood of recurrent infections, some patients may require pulse or prophylactic antibiotic therapy, particularly in late stage disease.

Pulmonary hypertension is a multifactorial complication of chronic airway disease. The best understood component of pulmonary hypertension secondary to chronic airway disease is chronic alveolar hypoxia. Airway wall remodeling and airway collapse decrease ventilation in severely affected segments of lung. The resulting alveolar hypoxia causes local pulmonary arteriolar vasoconstriction (hypoxic pulmonary vasoconstriction). If this occurs locally, the result of this vasoconstriction is an improvement in matching of ventilation and blood flow and correction of hypoxemia. However, in severe, global airway disease, the vasoconstriction is extensive, resulting in an increase in pulmonary vascular resistance, and eventually, pulmonary hypertension. Symptoms of pulmonary hypertension are similar to those exhibited by bronchitics, including non-productive cough, lethargy, cyanosis, and exercise intolerance. The diagnosis of pulmonary hypertension can be difficult, as the gold standard diagnostic test is right heart catheterization. However, thoracic radiographs reveal right sided cardiomegaly (cor pulmonale) and pulmonary arterial enlargement. Estimates of elevated right sided pressures can occasionally be made using echocardiography. Severe cases may exhibit syncope or post-tussive collapse. Early pulmonary hypertension may be primarily a smooth muscular response, and as a result, may respond to pulmonary vasodilator therapy. Pharmacologic therapy is largely limited to sildenafil (2-5 mg/kg q8-12 hours), although the most effective pulmonary vasodilator is oxygen therapy.

Obesity is a major complicating factor in the management of canine CB cases. Obesity causes decreases in thoracic wall compliance, increased abdominal pressure on the diaphragm, and
increases the work of breathing. Common locations for geriatric fat deposition in dogs include pericardium, mediastinum, and the cervical and thoracic subcutaneous space, all of which have the effect of decreasing ventilatory volume. Weight management alone can improve exercise tolerance and oxygenation. The most important factors in creating a successful weigh management plan are client education and reasonable goals from the start. A weight-loss plan should try to target 1-3% weight loss per week, with the expectation that this rate will decrease as the dog approaches goal weight.

Environmental modifications can also help to decrease irritant, antigenic, or traumatic stimulation of the airways. Steps to decrease airborne pollutants can include elimination of cigarette smoking in the dog’s environment, elimination of aerosol and powder cleaners or deodorants, and using room or whole-house air filtration systems. Saline nebulization/airway humidification (bathroom “spa” therapy) can help to mobilize airway secretions. Use of harnesses instead of collars can also reduce direct stimulation of the large airways.

The overall prognosis for canine CB is poor. It is important to emphasize to clients that the goal of management of CB is reduction of clinical signs and slowing the progression of this condition. It is also important to emphasize to clients that no chronic cough is benign, and that earlier intervention can prevent or delay the onset of potentially life-threatening sequelae (e.g. syncope, hypoxemia, pulmonary hypertension) and irreversible structural changes (e.g. bronchiectasis, fibrosis).

REFERENCES:


