Feline lower respiratory diseases

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Bronchial diseases. Bronchial obstruction can develop due to inflammatory infiltrates (eosinophils, neutrophils, or macrophages) or hypertrophy of bronchial tissues. The result is obstructive airway disease. Obstructive airway disease is characterized by increased airway resistance with resultant expiratory dyspnea. There is no clear terminology for the bronchial obstructive diseases in the cat. Bronchitis is inflammation of the airways. Asthma generally implies a reversible bronchoconstriction related to hypertrophy of smooth muscle in airways, hypertrophy of mucous glands, and infiltrates of eosinophils. Asthma in cats is primarily due to Type I hypersensitivity reactions; the etiology is generally undetermined. Cats with bronchitis not due to asthma generally have infiltrates of neutrophils or macrophages as well as hypertrophy of mucous glands, hyperplasia of goblet cells, excessive mucous, and ultimately fibrosis secondary to chronic inflammation. Calicivirus is the most common viral disease of cats leading to acute bronchial disease. *Bordetella bronchiseptica*, *Mycoplasma* spp., and possibly, *Chlamydia felis* are the bacteria capable of inducing bronchial disease. If disease occurs due to *Chlamydia* occurs, it is mild. Heartworm associated respiratory disease can result in bronchitis. Bronchitis may also result from *Aelurostrongylus abstrusus*, *Eucoleus aerophila*, or *Toxocara cati* infestation.

Cats with bronchitis can be of any age; chronic bronchitis usually develops in middle-aged to older cats. There is no obvious breed or gender predilection. Primary presenting complaints include cough, dyspnea, and wheezing. Some cats will have a terminal retch following cough. Physical examination abnormalities include cough, dyspnea, and crackles, and wheezes in the pulmonary tissues. Increased bronchovesicular sounds may be the only abnormality noted on auscultation. If dyspnea occurs, it commonly has a pronounced expiratory component. Open mouth breathing or panting commonly occur during periods of stress.

CBC is generally normal with the exception of eosinophilia in some cats with allergic bronchitis. Thoracic radiographs reveal primarily a bronchial pattern. Overinflation and air trapping is seen in some dyspneic cats with chronic disease. Air bronchograms are commonly seen in cats with bronchitis due to bacterial infection. Cytology of transtracheal wash samples generally reveal increased mucous with the primary cell types being eosinophils, neutrophils, or macrophages. Bacteria may or may not be visualized. Aerobic and *Mycoplasma* culture as well as antibiotic susceptibility testing should be performed regardless of the type of inflammatory cell and whether or not bacteria are seen.

Cats with eosinophilic TTW cytology should be assessed for dirofilariasis using adult antigen detection tests and antibody tests if from endemic areas. Fecal flotation (*Toxocara*), Baermann examination of feces (*Aelurostrongylus*), and fecal sedimentation (*Paragonimus*) should be performed in cats with eosinophilic TTW cytology particularly if indoor-outdoor and from parasite endemic areas.

Non-dyspneic cats are generally treated with broad spectrum antibiotics while awaitng diagnostic test results (Table 1). I generally use doxycycline initially due to efficacy for the primary bacterial respiratory pathogens and anti-inflammatory effects. I generally do not use oral theophylline (phosphodiesterase inhibitor) or terbutaline (beta 2 agonist) unless necessary. Feline terbutaline pharmacokinetics varies from people; serum levels are extremely high in cats. This drug should be avoided in cats with cardiac disease or disease resulting in hypertension like renal failure and hyperthyroidism. Phosphodiesterase inhibitors often cause anorexia and behavior change in cats. Inhalational albuteral given via inhaler may work more quickly and oral or injectable bronchodilators in cats with dyspnea. Cats with neutrophilic TTW cytologic results and positive bacterial cultures are treated with appropriate antibiotics for 4- 8 weeks depending on radiographic severity of disease and response to therapy. Some cats with acute bronchitis will have the disease resolve and not recur. Most cats with chronic bronchitis will require life-long anti-inflammatory therapy and perhaps, bronchodilator therapy.

If an eosinophilic component is present on TTW cytology, glucocorticoids will likely be required. Oral, repositol, or inhalational glucocorticoids can be administered. I generally attempt oral prednisolone therapy initially. Administration of methylprednisolone acetate every 2-3 weeks adequately controls some cats with asthma or allergic bronchitis. Titrate the dosage of glucocorticoid to the lowest dose required to control clinical signs of disease. Use of inhalational steroids can be very effective and if fluticasone are used, minimal systemic side-effects occur. In dyspneic cats, delivery of glucocorticoids by inhalation may work more quickly than those delivered orally or by injection. Chambers for the delivery of inhalational drugs can be purchased at www.aerokat.com. Use of omega 3 fatty acid supplementation may lessen requirements for glucocorticoids. Since allergic bronchitis can be related to dietary hypersensitivity, a hypoallergenic diet trial should be tried in cats with recurrent or persistent disease. Cats that become refractory to prednisolone will often respond to methylprednisolone, dexamethasone, or triamcinolone. Some cats with allergic bronchitis asthma will have seasonal exacerbations. Removal of potential irritants in the environment including clay litter, cigarette smoke, hairspray, and carpet cleaners should be considered in all cases of bronchial inflammation.

Parasitic diseases. Parasites leading to cough or dyspnea in cats include *Toxocara cati*, *Toxoplasma gondii*, *Aelurostrongylus abstrusus*, *Eucoleus aerophila*, and *Paragonimus kellicotti*. *Aelurostrongylus abstrusus* has an indirect life cycle with rodents as intermediate hosts; the organism occurs in Colorado. It is difficult to prove respiratory cough due to roundworms; demonstration eggs in the feces of coughing kittens supports a presumptive diagnosis. There is no effective primary treatment for the migrating phase of the parasites.

Diagnosis of the primary respiratory parasites is based on demonstration of the organism in transtracheal aspiration samples, bronchoalveolar lavage samples, or in feces. Most of the agents are intermittent shedders and so fecal examination techniques may have to be repeated multiple times. The Baermann funnel technique will increase the odds of finding larva.

Fecal sedimentation techniques are superior to flotation techniques for demonstration of *Paragonimus kellicotti*. Serologic tests are available to help support a diagnosis of toxoplasmosis. Lungworms generally respond to ivermectin at 0.4 mg/kg, SQ, once. Since

eosinophilic pneumonitis occurs with these agents, prednisolone is generally administered at 1.0-2.0 mg/kg, daily, PO concurrently with ivermectin. Fenbendazole is an alternate therapy; 25 mg/kg, PO, daily for 5 days, repeated again in 5 days is often used. Praziquantel can be used for the treatment of *Paragonimus kellicotti*. Clindamycin administered at 10-12 mg/kg, BID, PO for 4 weeks can be effective for the treatment of toxoplasmosis.

Dirofilariasis. In general, it can be assumed that the incidence of heartworm disease in cats in a given area to be approximately 10% of the incidence in dogs. Worm burdens are usually low (1-2 worms) but morbidity and mortality tends to be greater than in dogs. Cough is common and bronchial disease can occur prior to development of adult heartworms (heartworm associated respiratory disease). Many cats have aberrant signs including sudden death, vomiting and central nervous system abnormalities. Cats are usually microfilaria negative and commonly antigen negative due to low worm burdens or single sex infections. Multiple different antibody tests are currently available; these assays are thought to be more sensitive than antigen testing and do not cross react with other parasites. However, positive results only document exposure not current infection or clinical illness. In one study of cats in Florida, the sensitivity and specificity for the Synbiotics antibody test were 68% and 93%. The sensitivity and specificity for the HESKA antibody test were 89% and 77%. In contrast, the sensitivity and specificity of antigen testing were approximately 75% and 98%. Thus, it is important to test cats with both antibody and antigen tests. Demonstration of pulmonary arterial distension, tortuosity and blunting by thoracic radiography is an important diagnostic procedure. Occasionally, worms can be detected by echocardiography.

Heartworm infection in cats is generally self-limiting in 2 years and so most cats should be managed symptomatically with glucocorticoids. Infected cats should be placed on preventative to avoid new infections. To date, melarsamine is not recommended for treatment of cats. Microfilaricides are not required in cats. Ivermectin, selamectin, milbemycin, and moxidectin are approved for use as preventives. Selamectin, milbemycin, and the product containing moxidectin have the advantage of controlling roundworms and hookworms; selamectin and the moxidectin containing product also controls ear mites and fleas.

Pneumonia. Pneumonia is inflammation of the lung parenchyma; bronchopneumonia is pneumonia that has begun in the terminal bronchioles. Bacterial pneumonia is rarely a primary disease. Occasionally, *Bordetella bronchiseptica* or *Mycoplasma* spp. will induce pneumonia directly due to their adverse effects on mucociliary apparatus function. *Yersinia pestis* can cause pneumonia in infected cats and is directly zoonotic. Febrile cats with cough in the Southwestern states should be handled carefully. *Toxoplasma gondii* causes interstitial pneumonia.

Most cases of bacterial bronchopneumonia are secondary to immunosuppressive diseases or previous inflammatory insults including viral infection, aspiration, and irritant inhalation. Owners should be carefully questioned concerning potential exposure to other animals and clinical signs associated with immunosuppressive diseases or aspiration.

Most cats with bacterial pneumonia will be clinically ill. Common complaints include depression, anorexia, dyspnea, productive, moist cough with a terminal retch, and exercise intolerance. Some cats with bacterial pneumonia will present only with cough. Physical

examination findings commonly include fever, crackles and wheezes, and muffled lung sounds in cases with consolidated or abscessed lung lobes. Many cats will have increased tracheal sounds, a tracheal cough, and pharyngeal inflammation due to transport of inflammatory cells up the mucociliary apparatus to the mouth.

The initial diagnostic plan for cats with suspected bacterial pneumonia should include a CBC, biochemical panel, urinalysis, thoracic radiographs, FeLV antigen test, and FIV antibody test. Neutrophilic leukocytosis with or without a left-shift is common but not present in all cases. Monocytosis is common in chronic pneumonia. Assessment of the biochemical panel and urinalysis will often detect underlying immunosuppressive diseases. Thoracic radiographs usually reveal a mixed alveolar, bronchial, and interstitial pattern. Aspiration pneumonia generally has radiographic lesions that are most pronounced in the right middle lung lobe. If interstitial pneumonia is noted, *T. gondii* IgM and IgG serology should be considered. Particularly if the cat has a history of hunting or eating raw meat.

Esophageal diseases are commonly evident on evaluation of thoracic radiographs. Laryngeal paralysis commonly predisposes to aspiration pneumonia and is characterized by inspiratory stridor; this disease is rare in cats. Further diagnostic testing for cats with inspiratory stridor includes laryngeal function assessment by visualization under sedation. Intravenous administration of low-doses of ultra-short acting thiobarbiturates will enable examination of laryngeal function. Following documentation of pulmonary disease on thoracic radiographs, a TTW for cytology, aerobic bacterial and *Mycoplasma* culture, and antibiotic susceptibility testing should be performed. PCR assay for *T. gondii* DNA can be performed on the washings or BAL as well. Transthoracic aspiration of consolidated lung lobes should be considered for anaerobic culture and antibiotic susceptibility testing. Bronchoscopy for bronchoalveolar lavage and biopsy is superior to TTW and is sometimes required.

The combination of increased numbers of neutrophils and macrophages on cytologic assessment of secretions obtained by TTW and positive bacterial culture confirms the diagnosis of bacterial pneumonia. Bacterial culture is commonly positive in healthy cats and so the presence of bacteria without inflammatory cells does not document pneumonia. Treatment consists of airway hydration, antibiotic therapy, physical therapy, expectorants, and bronchodilators.

Following correction of underlying conditions, the most important treatment of bacterial pneumonia is hydration. The mucociliary apparatus functions best in a well-hydrated animal and is essential for the clearance of infection. Affected cats should receive parenteral fluid therapy until able to maintain hydration orally. Airway hydration can be accentuated by nebulization or by placing the animal in a closed bathroom while running hot water through the shower.

Antibiotic therapy should be based on culture and antibiotic susceptibility testing. Septic cats should be treated initially with parenteral antibiotics. Oral antibiotics should be administered for 6-8 weeks or for at least 2 weeks following resolution of radiographic evidence of disease.

Antibiotics can be administered by nebulization. Aminoglycosides are commonly used. Renal toxicity is not a concern since serum levels of aminoglycosides remain low following nebulization. If nebulization is used, 25 mg of gentamycin is generally mixed in 3-4 ml saline.

Saline has some mucolytic effects and will aid mucociliary apparatus function. Nebulization is generally administered 3-4 times daily. Mucolytic agents such as acetylcysteine are generally not used during nebulization of cats due to severe bronchoconstriction. If acetylcysteine is used, a topical beta-2 agonist like isoetharine should also be nebulized. Nebulization can be administered through most oxygen cages. Electric air pumps and hand-held nebulizers that give a particle size of 5 microns can be rented from many human home respiratory care companies. There are also veterinary products now available. Nebulization can be performed by attaching the nebulizer to a closed box with holes placed on the opposite side to allow escape of CO_2.

Oxygen therapy is indicated due to acute dyspnea in some cats with bronchopneumonia. If a oxygen cage is not available, oxygen can be administered via nasal tube. Positive end expiratory pressure aids in the treatment of some pulmonary conditions but is not practical in most clinical settings.

Passive physical therapy is indicated for the treatment of bacterial pneumonia. Gentle percussion using a cupped hand is the technique most commonly used but is not tolerated by many cats. Playing with the cat to encourage mild exercise may be beneficial.

Bronchodilator treatment may be of benefit in the treatment of bacterial pneumonia (Table 1). I generally use this therapy if above treatments are not rapidly resolving the disease. Phosphodiesterase inhibitors improve mucociliary apparatus function and may strengthen muscles of respiration. Bronchodilators can be indirect anti-tussives.

Cats with consolidated lung lobes should be receive antibiotics that penetrate tissue well and have a spectrum against anaerobes. Clindamycin hydrochloride or azithromycin are appropriate choices and also have a *T. gondii* spectrum. I generally combine enrofloxacin with clindamycin for the treatment of consolidated lung lobes. Thoracic radiographs should be reassessed in all cases within 3-4 days post-treatment and then every 2-3 weeks until radiographic evidence of disease has resolved. If the consolidated lung lobes that are not starting to inflate within 7-10 days post-treatment, surgical exploration should be considered, particularly if systemic signs like fever persist.

Feline plague. Feline plague is caused by *Yersinia pestis*, a gram-negative coccobacillus found most commonly in mid- and far-western states, particularly New Mexico and Colorado. Rodents are the natural hosts for this bacterium; cats are most commonly infected by ingesting bacteremic rodents or lagomorphs or by being bitten by *Yersinia* infected rodent fleas. Humans are most commonly infected by rodent flea bites, but there have been many documented cases of transmission by exposure to wild animals and infected domestic cats. Infection can be induced by inhalation of respiratory secretions of cats with pneumonic plague, bite wounds, or by contaminating mucous membranes or abraded skin with secretions or exudates. Bubonic, septicemic, and pneumonic plague can develop in cats and humans; each form has accompanying fever, headache, weakness, and malaise. Since cats are most commonly infected by ingestion of bacteremic rodents, suppurative lymphadenitis (buboes) of the cervical and submandibular lymph nodes is the most common clinical manifestation. Exudates from cats with lymphadenopathy should be examined cytologically for the presence of large numbers of the characteristic bipolar rods. The diagnosis is confirmed by fluorescent antibody staining of

exudates (available at Centers for Disease Control, Fort Collins, CO); culture of exudates, tonsillar area, and saliva; as well as by documenting increasing antibody titers.

Tetracycline derivatives (doxycycline, 5 mg/kg, PO, BID, for 21 days), enrofloxacin (5 mg/kg, PO, IM, or IV, BID for 21 days), chloramphenicol, and aminoglycosides can be used successfully for the treatment of plague. Parenteral antibiotics should be used during the bacteremic phase. Drainage of lymph nodes may be required. Cats with suppurative lymphadenitis should be considered plague suspects, and extreme caution should be exercised when handling exudates or treating draining wounds. Suspect animals should be treated for fleas and housed in isolation. All exposed humans should be directed to their physician for prophylactic antibiotic administration. Cats are not infectious to humans after 3-4 days of antibiotic treatment.

Pyothorax. Pyothorax is the most common infectious disease leading to dyspnea in the cat. Any bacteria can be involved, but anaerobes including *Nocardia* and *Actinomyces* are common. Unless there is an obvious foreign body, I manage pyothorax medically initially with appropriate antibiotic therapy and pleural space lavage. Unilateral or bilateral tube placement is dependent on the individual case.

The pleural space is lavaged twice daily with approximately 20 ml/kg of warmed 0.9% saline or Ringer's solution. The lavage fluid should be instilled slowly; the injection should be discontinued if respiratory distress occurs. The lavage fluid remains in the pleural space for 1 hour unless respiratory distress occurs. Approximately 25% of the initial lavage volume will be absorbed by the patient. Lavage efficacy is monitored by clinical findings, thoracic radiographs and cytology of the pleural effusion. Most animals with successful pleural lavage will have a decrease in fever and improvement in general attitude within the first 48 hours. I generally perform recheck radiographs 48 hours after tube placement. Radiographs are made following complete removal of all lavage fluid. The radiographs are assessed for pleural space fluid volume, atelectasis, and areas of encapsulated fluid. Cytology of pleural fluid is generally performed prior to lavage. Numbers of neutrophils, macrophages and bacteria as well as the percentage of degenerate neutrophils are estimated. Most cases with pyothorax will have a gradual decrease in inflammatory cells numbers over 3-5 days.

Systemic antibiotic therapy should ultimately be based on culture and sensitivity results. Success in culture of anaerobic bacteria is dependent on sample handling and the laboratory. Anaerobic bacterial culture must be requested specifically and samples must be submitted in a capped syringe within 1 hour or in appropriate transport media (Anaerobic culturette, Marion Scientific Corp.; Portacul, Bectin Dickinson) within 24 hours. Due to the high incidence of anaerobic infections, antibiotics with an anaerobic spectrum should be started immediately following diagnosis of pyothorax and continued throughout the course of disease. Many animals with pyothorax will have bacteremia or septicemia and intravenous antibiotics are indicated in the initial treatment period. I commonly use ampicillin (22 mg/kg, IV, q 6-8 hours) or cefoxitin (22 mg/kg, IV, q 6-8 hours). It was recently shown that amoxicillin-clavulanate has a better broad-spectrum anaerobic effect than ampicillin.

Aminoglycosides are only used if there is evidence of septic shock and only after dehydration and hypokalemia have been corrected. Enrofloxacin can be used parenterally to improve gram negative spectrum in septic animals. Oral antibiotic therapy should be continued for at least 4-6 weeks after initial diagnosis. Thoracic radiographs are generally suggested 7 and 28 days following tube removal. The combination of pleural lavage and antibiotic therapy have been reported to successfully resolve pyothorax in 60% of cats.

Feline infectious peritonitis. The effusive form of feline infectious peritonitis can lead to pleural effusion and resultant clinical signs of disease. Some affected cats do not have evidence for peritoneal effusion. This syndrome occurs most commonly in cats from crowded environments that are less than 2 years of age. Concurrent ocular, CNS, hepatic, and renal disease often is detected; most cats have a history of weight loss and fever.

Effusions from cats with FIP are sterile, colorless to straw-colored, may contain fibrin strands, and may clot when exposed to air. Protein concentration on fluid analysis commonly ranges from 3.5 g/dl to 12 g/dl. Mixed inflammatory cell populations of lymphocytes, macrophages, and neutrophils occur most commonly; non-degenerate neutrophils predominate in most cases but in some cats macrophages are the primary cell type seen.

Measurement of protein concentrations in effusions can aid in the diagnosis of effusive FIP. If the albumin-to-globulin ratio of the effusion is > 0.81, FIP is unlikely. If the albumin-to-globulin ratio of the effusion is < 0.81 but > 0.4, the positive predictive value for FIP is approximately 80%. If the albumin-to-globulin ratio of the effusion is < 0.4, the positive predictive value for FIP is 100%.

Serology can be falsely negative in cats with effusive disease and the presence of antibodies in serum does not confirm FIP. A test to detect the 7B protein of coronaviruses has been introduced and purported to correlate to FIP. However, not all cats that are positive develop FIP. Thus, all positive coronavirus tests should be interpreted with other clinical factors including signalment (generally young cats), appropriate clinical signs and physical examination abnormalities, and appropriate laboratory abnormalities like lymphopenia and hyperglobulinemia. Definitive diagnosis of FIP still requires documentation of characteristic histopathologic findings or the organism in inflamed tissues by immunohistochemistry or PCR.

Polymerase chain reaction for the detection of coronavirus has been evaluated for diagnostic accuracy in a limited number of cats. Positive reactions were detected in the pleural or peritoneal effusions from 13/15 cats with effusive FIP. At this time, detection of coronavirus by PCR in whole blood does not appear to correlate to the development of FIP. The new mRNA based assays were initially thought to correlate well with FIP but in further work it was shown that healthy cats can also be positive in these tests. There is no effective treatment. Administration of alpha interferon at 10,000 U/kg, SQ, daily may lessen clinical signs of disease in some. Use of the feline omega interferon with prednisolone was used in some cats with FIP with resolution of disease in 4 cats. However, the study was not controlled and so the results are difficult to interpret.

Chylothorax. Chyle consists predominantly of chylomicrons and is usually white or pinkish in color. The total protein varies but is usually high (3-10 g/dl). The predominant cell type is the lymphocyte, but neutrophils numbers increase as chyle is present in the chest chronically. Chylous effusion can be documented by showing the effusion triglyceride concentration to be greater than serum. The cholesterol concentration of the fluid generally is equal to or less than serum. If stored in the refrigerator, a cream layer will form on the top of a chylous effusion.

Chyle is carried from the intestinal tract from intestinal lymphatics that form the cisterna chyli in the abdomen. The thoracic duct is the continuation of this system in the thoracic cavity. The thoracic duct empties into the venous system of the neck. Known causes of chylothorax include trauma, mediastinal diseases like lymphoma or thymoma, dirofilariasis, fungal disease, and cardiac diseases including pericardial effusions; most cases are idiopathic. Cats with chylothorax are presented for dyspnea and sometimes cough. Sequelae are weight loss, electrolyte disturbances, and clinical syndromes associated with the primary etiology. Thoracic radiographs and thoracocentesis make the diagnosis. The further diagnostic plan generally consists of heartworm serology and ultrasound of the mediastinum or repeated thoracic radiographs following thoracocentesis. If a mass is detected, aspiration is usually performed to differentiate lymphoma from thymoma. Lymphangiography is generally only performed if thoracic duct ligation is to be attempted. The primary disease should be treated if possible. Medical treatment consists of giving a low fat diet to reduce production of chyle. Rutin at 50 mg/kg, PO, q 8 hours may stimulate macrophage removal of chylomicrons. Some advocate low dose glucocorticoid treatment and low dose heparin therapy to decrease inflammation and fibrin production, respectively. Surgical options include thoracic duct ligation, pleuroperitoneal shunt placement, omentalization, pericardectomy, and pleurodesis. At Colorado State University, most cats requiring surgery will receive the combination of thoracic duct ligation, omentalization, and pericardectomy.