Clinicopathologic and radiographic features and etiologic agents in cats with histologically confirmed infectious pneumonia: 39 cases (1991–2000)

Ellen S. Macdonald, DVM, DACVIM; Carol R. Norris, DVM, DACVIM; Roy B. Berghaus, DVM, MS; Stephen M. Griffey, DVM, PhD

Objective—To determine clinicopathologic and radiographic features and etiologic agents in cats that died as a result of infectious pneumonia.

Design—Retrospective study.

Animals—39 cats.

Procedure—Medical records of cats in which infectious pneumonia was confirmed by histologic examination of necropsy specimens were reviewed. Signalment, clinical signs, and results of a CBC, viral serologic tests, and thoracic radiography were evaluated. Infectious agents were classified as bacterial, viral, fungal, protozoal, or parasitic. Histologic features (severity, duration, anatomic location, and distribution) were analyzed.

Results—Clinical signs referable to the respiratory tract were not detected in 14 of 39 (36%) cats, and results of a CBC (4/18 cats) and radiography (3/13) were unremarkable. Sixteen of 39 (41%) cats lacked clinical signs of systemic illness. Etiologic agents identified included bacteria (n = 21), viruses (11), fungi (6), protozoa (2), and parasites (1). Cats with clinical signs related to the respiratory tract (19/24 [79%] cats) were more likely to have severe histologic changes than cats without signs related to the respiratory system (6/14). Twenty-nine of 38 (76%) cats had histologic evidence of systemic disease, whereas the remaining cats had lesions limited to the respiratory tract.

Conclusions and Clinical Relevance—Infectious pneumonia is uncommon in cats. Cats with infectious pneumonia may lack clinical signs and have unremarkable results for a CBC and thoracic radiography, yet frequently have systemic infections. Therefore, clinicians should maintain an index of suspicion for pneumonia and evaluate the respiratory tract when infection is detected in other organ systems. (*J Am Vet Med Assoc* 2003;223:1142–1150)

Pneumonia is defined as inflammation of the pulmonary parenchyma and can be attributable to noninfectious or infectious causes. Noninfectious causes of pneumonia in cats have been sparsely documented[1-4] and include inhaled or circulating toxins or irritants, as well as inflammatory or immune-mediated disorders. Infectious agents associated with pneumonia in small animals include bacteria, viruses, fungi, protozoa, rickettsia, and parasites.[5] Infectious pneumonia is uncommon in cats, and there are few documented reports of this disorder. The objectives of the retrospective study reported here were to evaluate clinicopathologic and radiographic features and etiologic agents of cats with infectious pneumonia in which the diagnosis was confirmed during histologic examination.

From the Veterinary Medical Teaching Hospital (Macdonald), and the Departments of Pathology, Microbiology and Immunology (Norris, Griffey) and Medicine and Epidemiology (Berghaus), School of Veterinary Medicine, University of California, Davis, CA 95616-8734. Dr. Macdonald's present address is the Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Tennessee, Knoxville, TN 37996-4544.
Address correspondence to Dr. Norris.

Criteria for Selection of Cases

Medical records of all cats that underwent necropsy at the Veterinary Medical Teaching Hospital, University of California-Davis, between January 1991 and December 2000 and that had a pathologic diagnosis of pneumonia were reviewed. Inclusion criteria required a histologic diagnosis of pneumonia in the record, identification of an infectious agent, and confirmation of the diagnosis during review of the slides by a pathologist (SMG).

Procedure

For each cat, the following information was recorded when available: breed; sex; age (juvenile cats were defined as cats < 1 year old, and adult cats were ≥ 1 year old); clinical signs; and results of a CBC, viral serologic tests, and thoracic radiography. When serial radiographic examinations had been performed, radiographs obtained closest to the time of necropsy were used for evaluation. The original radiographic report in the medical record, which had been interpreted by a board-certified radiologist, was used for analysis. Concurrent systemic infections were identified on the basis of clinical data and results of postmortem examination.

Infectious agents were classified as bacterial, viral, fungal, protozoal, or parasitic. Identification of bacterial, protozoal, or parasitic organisms was performed on the basis of direct observation of organisms or positive results for culture of lung specimens obtained during necropsy. Sterile instruments were used to collect specimens, and efforts were made to minimize or prevent contamination during collection. Viral infection was determined on the basis of 1 or more of the following criteria: a positive result for antigen titer of FeLV, positive result for antibody titer against FIV or **feline infectious peritonitis (FIP)** virus, positive result for virus

isolation of lung tissue via cell culture or serum-neutralization tests, observation of intranuclear inclusion bodies, or positive results during immunohistochemical analysis. For FIP, characteristic histopathologic lesions of pyogranulomatous inflammation with vasculitis, in conjunction with a clinical assessment consistent with infection (eg, leukocytosis and hyperglobulinemia) with or without seropositive status, were used to determine a final diagnosis. Fungal infection was confirmed by detection of intralesional organisms in conjunction with positive results for fungal culture or a positive result for the antigen titer (ie, *Cryptococcus neoformans*).

Histologic specimens were immersed in neutral-buffered 10% formalin, processed by use of routine methods, and embedded in paraffin. Specimens were sectioned at a thickness of 5 µm and stained with H&E. On the basis of histologic changes identified at the time of original diagnosis, additional stains (eg, Brown and Brenn, Gomori methenamine silver, Giemsa, periodic acid-Schiff, and mucicarmine) and immunohistochemical analysis (antibodies against toxoplasma and coronavirus) were used on some tissues. Histologic specimens were classified by a pathologist (SMG) who was unaware of clinical and radiographic features for each set of tissues. Several classifications were scored, which included severity (mild, < 25% of sample affected; moderate, 25 to 50% of sample affected; or severe, > 50% of sample affected), duration (peracute, evidence of recent hemorrhage with acute inflammation, such as neutrophils, fibrin, or proteinaceous edema; acute, evidence of neutrophilic inflammation without evidence of healing; subacute, evidence of early chronic inflammation with lymphocytes, plasma cells, or, possibly, macrophages with evidence of healing; or chronic, some component of neutrophilic inflammation with chronic inflammation, such as lymphocytes, plasma cells, or macrophages and evidence of fibrosis), and distribution of lesions within the lungs (focal, multifocal, or diffuse) or elsewhere in the body. Lesions were anatomically localized as predominantly affecting the airways (trachea, bronchi, or both), interstitium (anatomic space between the basement membranes of the alveolar epithelial cells and the capillary endothelial cells inclusive of the perivascular, perilymphatic, and peribronchiolar connective tissue),[6] or alveoli (bronchioles, alveolar ducts, alveolar sacs, and alveoli exclusive of the interstitium). The predominant cell type or types (neutrophils, macrophages, lymphocytes, plasma cells, or mixed inflammatory cells) were also reported. Identification of the source of infection (hematogenous, inhalation, or local extension) was evaluated when apparent. Pneumonia was classified as a primary or secondary cause of death or as an incidental finding during necropsy.

Statistical analysis—The Pearson χ^2 test was used to examine relationships between categoric variables by use of contingency tables. When expected cell counts were < 5 in 2-by-2 comparisons, the Fisher exact test was used. All analyses were conducted as 2-sided tests, and values of $P < 0.05$ were considered significant. Tests were performed by use of commercially available statistical software.[a]

Results

A search of the veterinary medical database revealed that necropsy was performed on 31,323 cats at the University of California-Davis during the 10-year period of the study. Of these, 110 cats with pneumonia were identified, but only 39 were confirmed as infectious in origin. Pneumonia in 12 other cats was suspected to have had an infectious origin; however, it was not confirmed by use of the aforementioned inclusion criteria. The 59 cats with noninfectious pneumonia most commonly had sterile inflammation of the lungs secondary to neoplasia, endogenous lipid disorders, or suspected toxins or irritants.

Thirty-nine cats met the criteria for inclusion in the study, comprising 23 domestic shorthair cats, 3 domestic medium-hair cats, 3 domestic longhair cats, 3 Siamese, 1 Persian, 1 Chartreaux, 1 Abyssinian, 1 Balinese, 1 Burmese, and 2 cats of unspecified breed. Sex was recorded for 34 cats (17 males and 17 females). Sex had not been recorded in the medical records of 5 juvenile cats. Cats were separated into adults (≥ 1 year old; range, 1 to 17 years old [n = 21]) and juveniles (< 1 year old; range, 3 days to 8 months [18]).

Clinical signs referable to the respiratory tract, including tachypnea or dyspnea (19 cats), nasal discharge (8), or coughing (3), were recorded in 25 cats, with 5 cats having 2 clinical signs concurrently. Nasal discharge was recorded in 8 cats, and the discharge was characterized as purulent in 3 cats and serous in 3 other cats; character of the nasal discharge of 2 cats was not recorded.

Signs of respiratory tract disease were not significantly ($P = 0.364$) associated with the etiologic agents. Consequently, clinical signs of respiratory tract disease were not helpful in predicting the cause. For 14 cats, signs of respiratory tract disease were not detected. Clinical signs of systemic illness were reported in 23 cats and included lethargy (15 cats), anorexia (14), and fever (body temperature > 39.2°C [> 102.5°F], [6]). In the 6 febrile cats, pneumonia was attributable to viruses in 3, fungi in 2, and bacteria in 1. Four cats did not have signs of respiratory tract disease, nor did they have clinical signs consistent with systemic manifestations of pneumonia.

A CBC was performed in 18 of 39 cats, and abnormalities were detected in 14 cats. This included 4 cats with leukocytosis (range, 18,500 to 45,100 WBCs/µL; reference range, 4,500 to 14,000 WBCs/µL), neutrophilia (range, 16,000 to 46,200 cells/µL; reference range, 2,000 to 9,000 cells/µL), and a left shift (range, 300 to 1,800 immature neutrophils/µL; reference range, < 300 immature neutrophils/µL); 3 cats with leukocytosis and neutrophilia; 2 cats with leukopenia (range, 1,400 to 2,200 WBCs/µL; reference range, 4,500 to 14,000 WBCs/µL), 1 of which also had a left shift; and 1 cat each with a left shift, leukocytosis, or leukocytosis with a left shift. Four cats had leukograms with values within reference ranges.

Four of 14 cats that were tested for FeLV infection had positive results. Of those 4, 2 had pneumonia sec-

ondary to sepsis, 1 had aspiration pneumonia, and 1 had concurrent FIP. Eight cats were tested for FIV, and none had antibodies against the virus. Three cats were tested to detect antibodies against coronavirus, and 2 of the 3 had antibodies (titers of 1:400 and 1:6,400, respectively). Both seropositive cats had FIP, which was confirmed on histologic examination during necropsy. Nine cats had histopathologic lesions classic for infection with coronavirus (**Fig 1**), and immunohistochemical stains were used to identify coronavirus in histologic specimens in 5 of the 9 cats. Of these 5 cats, 3 had positive results for immunohistochemical stains (1 for lung specimens and 2 for other tissues [kidneys, brain, or liver]). Two cats had negative results for immunohistochemical analysis, but both of those cats had clinical signs and histopathologic lesions consistent with FIP.

Lateral and dorsoventral thoracic radiographs were taken in 13 of 39 cats. The predominant radiographic pattern was classified as mixed (n = 5), interstitial (3), alveolar (1), or other (1); the remaining 3 cats were considered within normal limits. Mixed patterns included bronchointerstitial (n = 3) and a combination of bronchointerstitial and bronchoalveolar (2). Other major radiographic features included a nodular pattern in 1 cat and bronchiectasis in another cat.

Etiologic agents responsible for pneumonia were identified as bacterial (n = 19), viral (9), fungal (6), protozoal (2), parasitic (1), and a combination of bacterial and viral (2). Of the 21 cats with pneumonia attributable to bacteria or a combination of bacteria and a virus, 12 were further classified as having pneumonia that originated from hematogenous spread (ie, the same organism was isolated from 1 or more other sites in the body), 8 originated from inhalation, and 1 originated from local extension. In cats with pneumonia that originated from hematogenous spread, source of the bacteria was undetermined (defined as colonization of multiple organs in the body by bacteria but failure to identify the primary source that spread into the bloodstream) in 5 cats. In the remainder of those cats, bacteria originated from the gastrointestinal tract (n = 2), uterus (2), myocardium (1), umbilicus (1), gingiva (1), and bite wounds (1). Pneumonia acquired via inhalation resulted from aspiration of gastric contents in 6 cats and from presumptive acquisition of airborne bacteria in 2 cats (1 cat had impaired mucociliary defenses as a result of chronic bronchitis and bronchiectasis, and the other cat had a *Bordetella* infection). In the remaining cat, pneumonia was attributed to local extension secondary to pyothorax.

Bacterial infections were identified in the 21 cats on the basis of visual observation of bacterial organisms during histologic examination (n = 8; **Fig 2**) and results of aerobic and anaerobic bacterial cultures (13). In 1 of the 8 cats, bacterial organisms were observed during histologic examination, but specific bacteria were not identified during bacterial culture. Of the 13 cats with culture results, 8 had 1 species of bacteria isolated, and 5 had mixed infections of 2 or more bacteria. Seventeen cats had aerobic organisms identified or isolated, including *Streptococcus canis* (n = 5), *Pasteurella multocida* (5), *Escherichia coli* (2), *Pseudomonas* spp (1), *Bacillus* spp (1), *Enterobacter cloacae* (1), *Enterococcus* spp (1), *Staphylococcus* spp (1), β-hemolytic *Streptococcus* spp (1), *Bordetella bronchiseptica* (1; **Fig 3**), and eugonic fermentor 4a (1). Two cats had anaerobic isolates. *Fusobacteri-um* organisms were cultured from 1 of these cats, and *Fusobacterium* spp, *Peptostreptococcus* spp, and *Porphy-romonas* spp were cultured from the other cat.

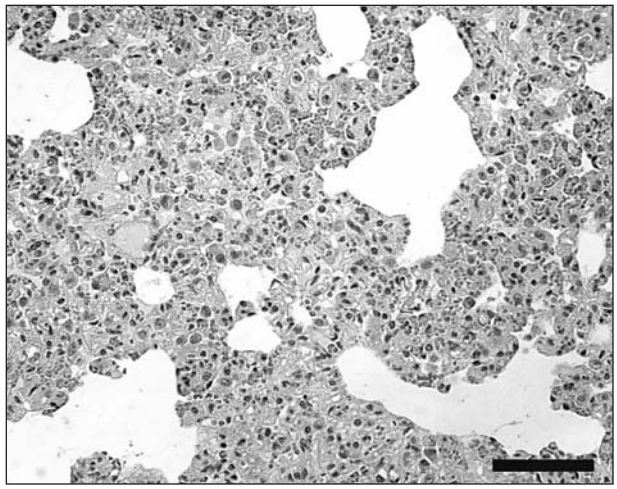

Figure 1—Photomicrograph of a section of lung obtained from a cat with chronic, diffuse interstitial pneumonia attributable to infection with coronavirus. Notice that the interstitium is diffusely thickened by macrophages and that neutrophilic infiltrates compress the alveolar lumina. H&E stain; bar = 75 μm.

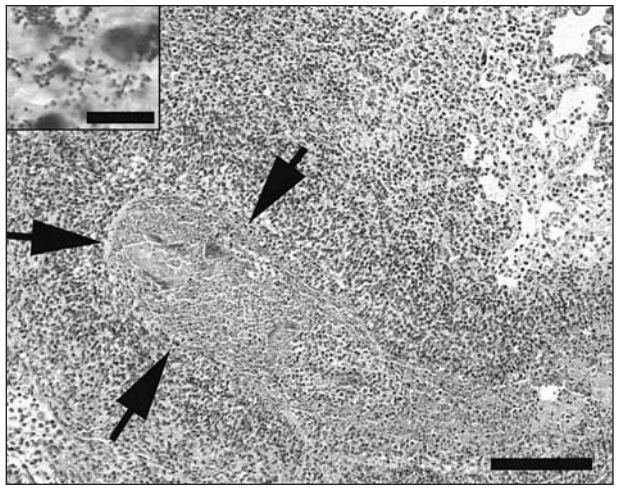

Figure 2—Photomicrograph of a section of lung obtained from a cat with acute multifocal necrotizing vasculitis and interstitial pneumonia as a result of sepsis from bite wounds. Microbial culture of the lung specimen yielded a β-hemolytic *Streptococcus* sp. Notice that the large vessel (black arrows) is obliterated by neutrophilic inflammatory infiltrates and transmural necrosis. H&E stain; bar = 150 μm. Inset: higher magnification of vessel lumen with coccoid gram-positive bacteria. Brown and Brenn stain; bar = 10 μm.

Viral infection was implicated as the primary cause of pneumonia in 11 cats. Viral infection was identified more frequently in juvenile cats (8/18) than in adult cats (3/21, 14%), although these values did not differ significantly ($P = 0.072$). Viruses isolated included coronavirus (n = 9) and feline herpesvirus (1); in 1 additional cat, the specific viral agent was not identified, but intranuclear inclusion

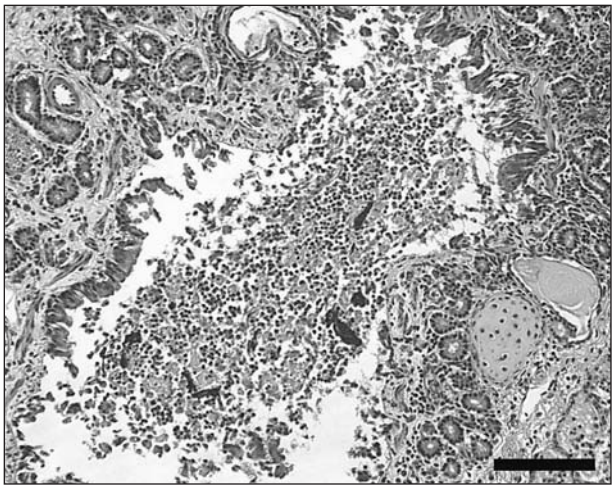

Figure 3—Photomicrograph of a section of lung obtained from a cat with acute diffuse fibrinopurulent bronchopneumonia. Microbial culture of the lung specimen yielded *Bordetella bronchiseptica*. Notice that the bronchus has sloughed the mucosal lining and is filled with intraluminal necrotic cellular debris, fibrin, and neutrophils. H&E stain; bar = 150 µm.

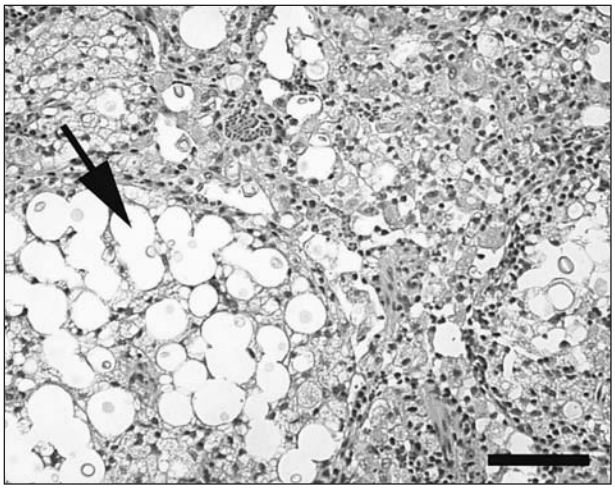

Figure 4—Photomicrograph of a section of lung obtained from a cat with multifocal granulomatous alveolitis. Alveoli are effaced by large numbers of foamy macrophages and numerous round refractile bodies surrounded by clear capsules (arrow), which is consistent with *Cryptococcus neoformans* infection. Cryptococcal organisms were also identified in the brain of this cat. H&E stain; bar = 75 µm.

bodies were detected during histologic examination. Feline infectious peritonitis accounted for pneumonia in 5 of 8 purebred cats, which was significantly (P = 0.01) different from the incidence in domestic mixed-breed cats (4/29, 14%). This difference was most pronounced among young cats in which FIP was identified in 3 of 3 juvenile purebred cats, which differed significantly (P = 0.04) from the incidence in juvenile domestic mixed-breed cats (3/13). In adults, FIP was identified in 2 of 5 purebred cats, which did not differ significantly (P = 0.13) from the incidence in domestic mixed-breed cats (1/16). The 3 adult cats in which FIP was diagnosed were relatively young, ranging from 1 to 3 years of age. Of the 11 cats with a viral infection of the respiratory tract, 2 had concurrent pulmonary bacterial infection (1 had a combination of herpesvirus and *Bordetella* infection, and the other had aspiration pneumonia with an unidentified viral infection in conjunction with a mixed population of bacteria).

Fungal, protozoal, and parasitic organisms constituted the remainder of the infectious etiologic agents that caused pneumonia. Five cats were infected with *C neoformans*; intralesional organisms were identified in 4 of these cats during histologic examination **(Fig 4)**. Three of these 4 cats did not have samples submitted for culture of the organism, whereas the remaining cat had positive results for culture of *C neoformans*. One of the 4 cats had an antigen titer of 1:16,384. In the fifth cat, culture was not performed, and cryptococcal organisms were not found in the lung sections during histologic examination. However, histologic changes in the pulmonary sections were consistent with fungal infection, the cat had a positive result when tested to determine the antigen titer (1:64), and cryptococcal organisms were observed during histologic examination of tissues obtained from elsewhere in the body. One cat had a fungal infection that was consistent with *Candida albicans*, as determined by intralesional hyphae detected during histologic examination. Fungal cultures were not performed for this cat. Fungal infections were significantly (P = 0.02) more likely to occur in adult cats (6/21, 29%) than in juvenile cats (0/18).

Protozoal organisms (*Toxoplasma gondii*) were identified in 2 cats (1 juvenile and 1 adult). There was 1 adult cat with parasitic pneumonia attributable to infestation with *Aelurostrongylus* organisms.

Histologic specimens were reviewed by a pathologist. One cat had a poor-quality histologic specimen; the specimen was adequate to enable the pathologist to make a histopathologic diagnosis of pneumonia, but further qualifications (ie, severity, duration, anatomic location, and distribution of lesions) were not possible. For the other 38 cats, most had severe pulmonary lesions (n = 25), and the remainder had moderate (10) and mild (3) lesions. Cats that had clinical signs related to the respiratory tract (19/24, 79%) were significantly (P = 0.04) more likely to have a histologic grade of severe than were cats that did not have clinical signs of respiratory tract disease (6/14). Cats that had clinical signs of systemic illness (13/23, 57%) were somewhat less likely to have pulmonary lesions classified as severe than were cats that did not have signs of systemic illness (12/15), but these values did not differ significantly (P = 0.18). Four cats had results of a CBC that were considered normal, and 3 cats had thoracic radiographic findings that were unremarkable. Of these 7 cats, 4 had severe, 2 had moderate, and 1 had mild pulmonary lesions, as determined on the basis of histologic examination.

Duration of lesions was characterized as acute (n = 17), chronic (16), subacute (2), and peracute (1); in the other 2 cats, lesions were of mixed duration, depending on the location that was examined. Lesions associated with bacterial infections (2/19) were significantly ($P < 0.001$) less likely to be characterized as chronic than were lesions associated

with other causes (14/19). All infections attributable to fungal and protozoal organisms were characterized as chronic.

Distribution of lesions was classified as diffuse (n = 16), multifocal (12), focal (2), focal diffuse (lesions limited to a single lobe but having a diffuse distribution within that lobe [5]), or a mixture of several types (3). Lesions were identified in the interstitium (n = 18); interstitium and alveoli (7); interstitium, alveoli, and airways (5); alveoli and airways (4); airways (3); and interstitium and airways (1). Lesions in the interstitium were associated with bacterial (n = 15), viral (9, all of which were FIP), fungal (6), protozoal (1), and parasitic (1) organisms. Lesions in the alveoli were associated with bacterial (n = 7), fungal (5), viral (2), parasitic (1), and a combination of viral and bacterial organisms (1). Lesions in the airways were associated with bacterial (n = 7), protozoal (2), and a combination of viral and bacterial organisms (1).

Histologic evidence of systemic infection was detected in 29 cats, whereas histologic evidence of infection was limited to the lungs and thoracic cavity in 9 cats. Evaluation of the specific types of inflammatory cells associated with infectious pneumonia revealed a mixed population of 2 or more cell types (consisting of neutrophils, macrophages, lymphocytes, and plasma cells) in 22 cats. In the remaining 16 cats, the predominant cell type was neutrophils (n = 12) or macrophages (4). Neutrophilic inflammation was associated with bacterial (n = 10) or viral infections (2). Macrophages were exclusively associated with fungal infections (n = 4). Most cats also had evidence of type-II pneumocyte hyperplasia.

On the basis of histologic examination of specimens from the lungs and other organs obtained during necropsy, pneumonia was considered the primary cause of death in 27 of 39 cats (19/27 were euthanatized, whereas the remaining 8 died as a result of pneumonia). Pneumonia was believed to be a secondary factor as a cause of death in 11 cats. In only 1 cat was pneumonia considered to be an incidental finding during necropsy. Pneumonia in that cat was attributed to infestation with *Aelurostrongylus* organisms.

Discussion

Pneumonia is uncommon in cats. Correspondingly, there are few reports documenting this disorder. Classification schemes for pneumonia are often confusing and hampered by a lack of uniform use in case descriptions. Broad categories include classification on the basis of primary cause (eg, noninfectious or infectious and specific type of infectious microorganism involved), gross anatomic distribution of inflammation (eg, bronchopneumonia vs lobar pneumonia), and microscopic anatomic distribution of inflammation (eg, bronchopneumonia affecting the bronchoalveolar junction, interstitial pneumonia affecting the alveolar septa and vasculature, and bronchointerstitial pneumonia affecting both regions).[7] One of the more common methods used to classify pneumonia in small animals is on the basis of cause, whereby pneumonia is defined as inflammation of the pulmonary parenchyma attributable to noninfectious inflammatory factors or infectious agents. In cats, documented causes of noninfectious pneumonia include interstitial lung diseases (eg, interstitial pulmonary fibrosis, bronchiolitis obliterans with organizing pneumonia, and lymphocytic interstitial pneumonitis),[2-4,8] pneumonia attributable to exogenous and endogenous lipids,[1,9,10] and aspiration pneumonia.[11] Infectious agents include bacteria, viruses, fungi, protozoa, rickettsia, and parasites. However, we are not aware of any reports comparing clinicopathologic, radiographic, and histologic features in cats with a spectrum of infectious agents that caused the pneumonia. The only large retrospective study[12] of infectious pneumonia in cats focused on the histologic description of infectious pneumonia in 207 cats. However, in 37 (18%) of those cats, an etiologic agent could not be found, and in 23 (11%) of those cats, an infectious cause was suspected but not confirmed. Furthermore, associated clinical signs and diagnostic data were not reported in that study.

In the cats of the study reported here, histologic examination was used as the inclusion criterion to definitively confirm a specific infectious organism as the causative factor for the pneumonia. Although antemortem culture of airway lavage fluid is traditionally used in the diagnosis of infectious pneumonia, it has several inherent limitations, many of which can be overcome by the use of histologic examination for definitive confirmation of pneumonia. First, bacteria cultured from lavage fluid could be a contaminant or part of the resident microflora. Aerobic growth has been detected in 44 to 77% of cultures of lavage fluid from healthy cats, which suggests that resident microflora may be responsible for bacterial colonization of the bronchioles and alveoli in the respiratory tract of cats despite a lack of illness.[13,14] Second, a positive result for bacterial culture of a lavage sample may not be sufficient evidence to identify those bacteria as being secondary to a primary noninfectious lung disease (eg, aspiration pneumonia or chronic bronchitis) or to infectious pneumonia attributable to another organism (eg, viral infection). Third, an organism could fail to grow for several reasons, such as inappropriate selection of growth media, organisms that require special culture media for growth, insufficient amount of time allowed for growth (especially for some fungal organisms), organisms sequestered in a granuloma, or organisms that are localized to a specific compartment of the lungs that was not lavaged (which is especially true when an endotracheal technique is used for collection of lavage fluid). Although concurrent cytologic examination can help overcome some of these limitations, collection of lung tissue during necropsy for histologic examination made the inclusion criteria more stringent and a definitive diagnosis more likely.

Although it is recognized that histologic examination of lung tissue is not the ideal or typically recommended procedure to diagnose infectious pneumonia, results of this study are important to provide further understanding of the clinicopathologic features of this disease in cats. Cats with infectious pneumonia, especially of bacterial and fungal origin, have been successfully treated when an appropriate diagnosis has been

made.[15-19] If there is ample clinical and radiographic evidence of infectious pneumonia, diagnosis through standard means should be straightforward. However, as documented in this study, diagnostic challenges remain in those cats that lack clinical signs or hematologic or radiographic abnormalities that support the diagnosis of infectious pneumonia. Antemortem diagnostic tests for infectious pneumonia, including endotracheal washes, collection and examination of **bronchoalveolar lavage fluid (BALF)**, and fine-needle aspiration of the pulmonary parenchyma to provide specimens for cytologic examination and microbial culture, have been described. For example, BALF has been used successfully for the cytologic identification of bacterial, protozoal, and fungal infections in cats with or without positive results for microbial cultures.[16,18,20,21] Fine-needle aspiration of the lungs has been advocated as a safe and efficient diagnostic tool for diagnosis of solitary pulmonary lesions (eg, fungal granulomas) in dogs and cats.[22,23] Moreover, cytologic examination of specimens obtained by use of fine-needle aspiration is a successfully used diagnostic tool for detection of diffuse pulmonary lesions, such as infectious and noninfectious pneumonia, and results of cytologic examination of fine-needle aspirates correlate well with results of histologic examination.[24,25] In situations in which radiography and cytologic examinations are inadequate to obtain a definitive answer, use of thoracoscopic or key hole biopsy techniques to obtain specimens for histologic examination may prove to be necessary to achieve a correct diagnosis.[2,26]

Bacterial causes of infectious pneumonia in cats have generally been reported as small case series or isolated case reports. Those studies[17,18,27-29] describe antemortem diagnosis of pneumonia caused by *Salmonella* spp, eugonic fermenter 4a, mycobacteria, *Bordetella* spp, *Nocardia* or *Corynebacterium* spp, *Pasteurella* spp, and *Bacteroides* spp and document the clinical features, diagnostic protocol, and therapeutic regimens used in cats. Similarly, there are case reports of cats with viral pneumonia associated with FIP,[30] fungal pneumonia,[16,31] and protozoal pneumonia.[20,21,32]

Fourteen of 39 (36%) cats with infectious pneumonia in the study reported here lacked clinical signs referable to the respiratory tract. However, the lack of respiratory signs is consistent with other reports[1,33,34] of cats with pulmonary disease. For example, it was documented in other studies[1,33,34] that 7 of 12 cats with bronchiectasis, 16 of 29 (55%) cats with pulmonary thromboembolism, and 8 of 24 (33%) cats with pneumonia attributable to endogenous lipids did not have signs of respiratory tract disease despite the fact that they had substantial pulmonary disease. In particular, lack of coughing as a clinical indicator of pneumonia in the cats of this study was remarkable, because only 3 of 39 (8%) cats with infectious pneumonia coughed. This is consistent with other reports[17,27,30,35] of infectious pneumonia in cats. Clinicians should use respiratory signs as a clinical indicator of potentially advanced respiratory tract disease, because cats in this study that had signs of respiratory tract disease were more likely to have severe histologic changes.

Anorexia, lethargy, and fever have been described in cats with infectious pneumonia.[17-19,27,30] However, 16 (41%) cats in our study did not have signs of systemic illness, which also agrees with results in other reports[19,27,28,35] of cats with pneumonia. We did not detect a significant correlation between severity of pneumonia on histologic examination and evidence of signs of systemic illness in the cats of this study.

In addition to the fact that 14 (36%) cats lacked clinical signs referable to the respiratory tract, it was also remarkable that 4 of 18 cats with infectious pneumonia in which a CBC was performed had normal leukogram results. One of the 4 cats was receiving systemically administered steroids as treatment for a previously diagnosed chronic bronchitis. In this cat, it is possible that the immunosuppressive effects of steroid treatment inhibited a typical inflammatory response to the infectious insult. Normal results for the leukogram have been reported[19] in cats with bacterial pneumonia. Thus, lack of abnormalities on a CBC is not adequate to rule out infectious pneumonia in cats.

Infectious pneumonia in cats is most commonly associated with an alveolar pattern on thoracic radiographs.[17,19,27,30] Thoracic radiographic abnormalities in the study reported here were usually interstitial or mixed radiographic patterns, regardless of the infectious agent. However, despite histologic evidence of infectious pneumonia, thoracic radiographs were unremarkable in 3 of 13 cats. Lack of radiographic abnormalities in conjunction with infectious pneumonia has been rarely reported in cats.[36,37]

It should be mentioned that the 4 cats with normal results for CBCs and the 3 cats with unremarkable results for thoracic radiographs constituted 7 cats. Lack of evidence of pneumonia on diagnostic tests, however, was not an accurate predictor of severity of lesions, because 4 of 7 had severe, 2 of 7 had moderate, and only 1 of 7 had mild histopathologic lesions of the respiratory tract.

Not surprisingly, bacterial pneumonia was the most common infectious cause, representing 20 of 39 (51%) cats in this study. Similar percentages have been reported[29] in dogs with regard to the prevalence of bacterial pneumonia, compared with other infectious causes. In comparison to other types of infectious pneumonia, cats with bacterial pneumonia were less likely to have chronic lesions. The majority (12/20) of cats developed bacterial pneumonia as a result of hematogenous spread, although inhalation and local extension were seen in 4 of 20 and 2 of 20 cats, respectively. Most infections were attributable to aerobes (17/21, 80%), and 8 of 13 were single isolates. This is similar to results of a study[38] in which transtracheal aspirates were collected from 264 dogs with bacterial pneumonia. Aerobic bacteria were most common (206/264, 78%), and most infections (150/264, 57%) were attributed to a single species of bacteria. Although the number of infected cats was small, the most prevalent bacterial agents in the study reported here were *Streptococcus* spp (6/21, 29%), *Pasteurella* spp (5/21, 24%), and anaerobes (2/21, 10%). These results contrast to results of a study[38] of bacterial pneumonia in dogs. In that study, *E coli* (36/116, 31%) was isolated

most commonly; however, similar to cats, *Pasteurella* spp (26/116, 22%) and anaerobes (25/116, 22%) were the next most common isolates.

Interestingly, there was 1 cat with infectious pneumonia attributable to eugonic fermentor 4a; that cat had severe gingivitis. These gram-negative organisms have been recognized as a causative agent of pneumonia in cats.[39] In 1 review[39] of 6 cats, gingivitis had been diagnosed in 5 prior to the outbreak of pneumonia. Eugonic fermentor 4a is considered to be an oropharyngeal contaminant, and pneumonia may result from inhalation of the bacteria or introduction into the vascular system with localization in the lungs.[39] It is speculated that the organism is more likely to cause necrotizing pneumonia in those cats that are compromised by stress or immunosuppression or that have concurrent viral infections such as FeLV.[27]

Viral pneumonia was identified in 11 of 39 (28%) cats in the study reported here, and FIP was associated with 9 of the 11 cats. Similar to another report,[40] risk of infection with coronavirus was significantly higher in juveniles and purebred cats. Although lung lesions are commonly found during necropsy in cats that die as a result of noneffusive FIP,[41] it is unusual (ie, estimated to be < 10% of noneffusive cases) for cats to be examined primarily because of clinical signs associated with pulmonary involvement.[42] For 1 cat in our study, herpesvirus was the causative viral agent of pneumonia, but it was found in conjunction with *Bordetella* infection. For another cat, the causative viral agent was observed (intranuclear inclusion bodies) but not identified; that cat also had a combination of a mixed viral-bacterial infection, with the bacterial component probably resulting from aspiration. Although herpesvirus is a common cause of nasopharyngeal, laryngeal, and tracheal infections in cats, pneumonia attributable to herpesvirus is rare in cats[43]; this was supported by results of the study reported here. It is more common for calicivirus than herpesvirus to cause interstitial pneumonia in cats,[44] although none of the cats in our study had calicivirus-induced pneumonia.

Fungal pneumonia was documented in 6 of 39 (15%) cats, although the incidence of fungal infection is influenced by geographic location, and the highest infection rates for diseases are caused by primary pathogens (cryptococcosis, coccidioidomycosis, blastomycosis, and histoplasmosis) in endemic areas. Opportunistic fungi are often ubiquitous in the environment and cause disease when the host is immunosuppressed.[22] Most cats in our study had fungal pneumonia attributable to *Cryptococcus* organisms, and only 1 cat had pneumonia attributable to an opportunistic pathogen, *C albicans*. This latter cat also had trauma to the gastrointestinal tract. Fungal septicemia is theorized as the source of infection in the lungs. Although rare, systemic candidiasis has been reported[45] in 8 cats, including 1 with *C albicans* infection (pyothorax secondary to migration of a foreign body). Gastrointestinal infection with *Candida* organisms has also been linked to primary viral infection with feline panleukopenia.[45]

Histopathologic changes in the lungs were diverse, but most cats had lesions that were severe with mixed populations of inflammatory cells. Pneumonia was most often located in the interstitium (31/38, 82%), which could, in part, be the reason that the radiographic alveolar pattern was a less common hallmark of pneumonia in the cats of this study, compared with results for another study.[46] There was not a strong association between the location of lesions (interstitial, alveolar, or airways) and type of infectious organism. There are multiple infectious causes of interstitial pneumonia that have been documented in animals, including infection with bacteria, viruses (eg, coronavirus), protozoa (eg, *Toxoplasma* spp), or parasites (eg, *Aelurostrongylus* spp).[7]

The type of damage induced by a pathogen and the host immune response to the infectious microorganism dictate the type of inflammatory cell infiltrates in the lungs. For example, pneumonia caused by bacterial infection is generally associated with neutrophilic inflammation,[7] which was seen in 10 of 12 cats in the study reported here. Neutrophils are considered the first line of defense against most bacterial pathogens, and they are attracted to invading bacteria by chemotactic peptides produced by the bacteria, as well as complement components, chemokines, and leukotrienes elaborated from injured tissues.[47] Certain types of fungal infection are associated with granulomatous inflammation (macrophages that attempt to engulf and kill the organisms).[48] Granulomatous inflammation was a consistent finding in all cats of our study that had fungal pneumonia, even though cryptococcal lesions may be evident without a substantial inflammatory response. Cryptococcal organisms have a gelatinous capsule that can inhibit phagocytosis, plasma cell function, and leukocyte migration, which allow them to evade the immune system.[49] In contrast to bacterial and fungal pneumonia, the pulmonary lesions seen in viral pneumonia are often more variable. Whereas coronavirus (ie, FIP) is identified on the basis of mixed inflammatory-cell infiltrates (typically in peribronchiolar locations), herpesvirus may cause neutrophilic inflammation with or without macrophages in the bronchoalveolar junction.[7,50] Caliciviruses more frequently cause pneumonia than do herpesviruses. Furthermore, caliciviruses cause accumulations of neutrophils (during the acute phase) and mononuclear cells (during later stages) in the pulmonary interstitium.[50] Protozoal infections, such as toxoplasmosis, cause mixed inflammatory-cell infiltrates that often have a prominent neutrophilic component leading to diffuse interstitial pneumonia or bronchopneumonia.[51] Early during infection, pneumonia attributable to parasites (eg, *Aelurostrongylus* spp) is associated with eosinophils and neutrophils, but in later stages, populations of mixed mononuclear cells are seen.[52] In the majority (22/38, 58%) of cats from the study reported here, mixed populations of inflammatory cells predominated, documenting the diverse pathogenic mechanism of damage to the lungs and the host responses to these pathogens.

Necropsy specimens served as a criterion for selection of cases for confirmation of a diagnosis of infectious pneumonia in this study and also provided information on the distribution of the microorganisms in

other parts of the body. Histologic examination revealed that most (29/38, 76%) cats had evidence of systemic disease, whereas the remaining cats had lesions limited to the respiratory tract. In cats with disease in other organ systems, clinicians should maintain an index of suspicion for infectious pneumonia, and a thorough systematic evaluation of the respiratory tract should be performed in these cats.

Retrospective studies have inherent limitations, and this study was no exception. Standardization of evaluations, diagnostic tests, and treatments for cats included in the study was not possible. Clinical history, physical examination findings, and the diagnostic tests performed were dependent on the attending clinicians, and complete antemortem evaluation of the respiratory tract was not performed in many cats. Specifically, a CBC was not performed for 21 cats, and thoracic radiography was not included as part of the evaluation for 26 cats. Antemortem procedures to address clinical, clinicopathologic, or radiographic evidence of respiratory tract disease, such as examination of BALF or fine-needle aspirates of the pulmonary parenchyma, were performed in only 1 cat.

Examination of the medical records revealed several reasons for the lack of complete evaluation of the respiratory tract. Nineteen cats were in a critical state and subsequently died or were euthanatized prior to diagnostic tests being performed; 2 kittens (from catteries) were provided only for necropsy. Despite histologic findings to the contrary, another 4 cats did not have overt clinical signs associated with the respiratory tract that would warrant associated diagnostic evaluation, and they were euthanatized or died as a result of causes not directly related to pneumonia. Four other cats were strays that needed extensive diagnostic tests and supportive care; because of a poor prognosis, they were euthanatized.

Despite the relative paucity of diagnostic testing in many cats, important information can still be derived from this retrospective study. Cats with infectious pneumonia were often not recognized as having signs suggestive of respiratory tract disease until the pneumonia was in an advanced stage. In this study, cats that had noticeable clinical signs of respiratory tract disease were those that also had severe histologic evidence of infectious pneumonia, and this critical clinical status frequently precluded a thorough evaluation of the respiratory tract.

It is recognized that several populations of cats were excluded from this initial study, including those with subclinical disease or those surviving an episode of infectious pneumonia in which histologic examination was not available. Stringent criteria for case selection resulted in relatively few cases of pneumonia attributable to certain etiologic agents (eg, protozoal or parasitic) for evaluation, limiting conclusions regarding diagnosis, treatment, and pathologic characteristics of pneumonia determined on the basis of the type of infectious agent. It is our hope that the conclusions of this initial retrospective study will lead to future prospective studies of cats with infectious pneumonia. With a high suspicion for possible infectious respiratory tract disease, those cats with mild to moderate disease, which likely would have a better chance for successful use of diagnostic testing and therapeutic outcomes, could be identified and objectively evaluated by use of standardized diagnostic and therapeutic protocols.

[a]SPSS software, version 10.0, SPSS Inc, Chicago, Ill.

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