Journal of Feline Medicine and Surgery (2004) **6**, 167–180

jfms

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Lower respiratory tract infections in cats: 21 cases (1995–2000)

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Revised 11 November 2003; accepted 14 November 2003

Summary Twenty-one lower respiratory tract infections diagnosed in cats at University of Sydney Veterinary Centre between 1995 and 2000 were identified retrospectively. Patient records were analysed to determine historical, clinical, clinicopathologic and radiographic features of lower respiratory tract infections. Response to therapy was also assessed. Infectious agents identified were *Mycoplasma* spp., *Pasteurella* spp., *Bordetella bronchiseptica*, *Salmonella typhimurium*, *Pseudomonas* sp., *Mycobacterium thermoresistible*, *Cryptococcus neoformans*, *Toxoplasma gondii*, *Aelurostrongylus abstrusus* and *Eucoleus aerophilus*. The study provides a detailed retrospective analysis of infectious lower respiratory tract disease in this population of cats.
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Introduction

Lower respiratory tract (LRT) disease in cats may be caused by infectious agents (viruses, bacteria, fungi, parasites), cardiac disease, neoplasia, trauma, toxins or irritants. Most cats with LRT infection (LRTI) have pneumonia (inflammation of the lung parenchyma), although occasionally pathology is limited to the airways (Bart et al., 2000).

Common bacterial causes of feline pneumonia are reported to include *Pasteurella multocida*, *Escherichia coli*, *Klebsiella pneumoniae*, *Bordetella bronchiseptica*, and *Streptococcus canis* (Henik and Yeager, 1994). However, published reports of pneumonia are invariably restricted to case reports and a literature search revealed only one detailed retrospective study of infectious causes of pneumonia in cats (Bart et al., 2000). In that study, bacteria were isolated post-mortem from feline lungs in cases of bronchitis, pneumonia and septicaemia. The majority of cases were kittens and no clinical details were provided. The bacteria identified as causing bronchitis and pneumonia were *B. bronchiseptica*, *Pasteurella* spp., *Mycoplasma* spp., *E. coli* and *Streptococcus* spp. The bacteria isolated from lungs in cases of septicaemia were *E. coli*, *Streptococcus* spp. and *Pasteurella* spp. Other infectious agents identified as causing pneumonia in the study were viruses (herpesvirus), lungworm (*Aelurostrongylus abstrusus*), *Toxoplasma gondii* and fungi (*Mucor* sp. and *Aspergillus* sp.).

Viral causes of LRTI are unlikely to be diagnosed without lung histopathology and specific viral detection techniques. Parasitic, bacterial and fungal LRTIs can be diagnosed by routine investigation of LRT disease. The aim of this study was to provide clinical, clinicopathologic, radiographic and therapeutic details of 21 non-viral cases of feline LRTI

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1098-612X/04/$ - see front matter © 2004 Published by Elsevier Ltd on behalf of ESFM and AAFP.
doi:10.1016/j.jfms.2003.11.006

identified at University of Sydney Veterinary Centre (UCVS) between 1995 and 2000.

Materials and methods

Nineteen cases of feline LRTI that presented to UVCS between 1995 and 2000 were identified from a retrospective study of bronchoalveolar lavage (BAL) cytology and microbiology (Foster et al., 2004a). In that study, pure culture of any bacterium or fungus was considered significant as was moderate to heavy growth of any microbe with minimal growth of oral contaminants. However, the infectious agents in cases with a positive microbial culture were only considered the aetiological agents if historical, clinical, radiographic and cytologic findings were supportive and if there was an unambiguous response to appropriate antimicrobial therapy. Parasitic LRTIs were identified from unstained wet preparations of BAL fluid. Two other LRTIs were diagnosed during the same time by means other than BAL, both of which have been published previously (Foster et al., 1998a, 1999).

Signalment was analysed for the 21 cases. Statistical comparisons for data on sex and breed were performed using Statistix for Windows (Analytical software, Tallahassee, FL, USA). Breeds were classified as domestic, Siamese, Burmese, purebred shorthair (other than Burmese and Siamese) and purebred longhair for comparison with the hospital population of cats at the time of the study (Gabor et al., 1998).

Historical and clinical data were also analysed. Clinical data was recorded as peracute if signs had been present for 72 h or less, acute, if signs had been present for less than a month, and chronic, if signs had been present for a month or longer. Tachypnoea was defined as a respiratory rate greater than or equal to 60 breaths per min as effects of temperament, transport and ambient temperature could not be assessed retrospectively. Date of presentation and, if known, date of onset of clinical signs were also analysed. The seasons in Sydney are defined as summer (December to February), autumn (March to May), winter (June to August) and spring (September to November).

Haematology, serum biochemistry and serological test results from commercial ELISA or immunomigration kits for feline immunodeficiency virus (FIV) antibody, feline leukaemia virus (FeLV) antigen and heartworm antigen were analysed. Cytologic and microbiological findings for the 21 cases were also analysed. Differential cell counts for BAL cytology were classified by the predominant inflammatory cell type, if the cell type comprised at least 50% of the total white cells, or described as mixed, if no cell type comprised at least 50% of the total.

Radiographs for 19 cases were reviewed by a specialist radiologist who was blinded as to the clinical diagnosis (GA). For two cases, only the specialist reports from the original radiographs were available. Bronchial signs were defined as mild (first generation of bronchi visible), moderate (second generation visible) and severe (third generation visible). Alveolar patterns were defined as mild (isolated fluffy infiltrates), moderate (well defined with air bronchograms) and severe (lobar sign). Nodular interstitial patterns were recorded as nodular. Reticular interstitial patterns were recorded as interstitial and defined as mild (interstitial framework visible but could be bronchial pattern), moderate (interstitial framework can be distinguished from bronchial) and severe (undisputed reticular interstitial pattern).

Therapeutic agents, response to therapy and long term follow-up in all survivors, were recorded.

Results

Signalment, history, physical findings

Nineteen LRTIs in 18 cats were diagnosed by BAL cytology and microbiology. Two further cases in two cats were diagnosed by other means: mycobacterial LRTI by ultrasound-guided fine-needle aspirate cytology and microbiology (Foster et al., 1999) and toxoplasmosis, by lung squash-preparation cytology and lung histology (Foster et al., 1998a). The LRTIs were due to *Mycoplasma* spp. (11), mycoplasmas and *P. multocida* (1), mycoplasmas and *B. bronchiseptica* (1), *Pasteurella* sp. and mixed anaerobes (1), *Pasteurella* sp. and an unidentified Gram negative bacterium (1), *Salmonella typhimurium* and *A. abstrusus* (2, one of which also had *Pseudomonas* sp. cultured), *Mycobacterium thermoresistibile* (1), *T. gondii* (1), *Cryptococcus neoformans* var. *grubii* (previously var. *neoformans* serotype A) (1) and *Eucoleus aerophilus* (previously *Capillaria aerophila*) (1). The cases are detailed in Table 1; cases 1, 4, 6, 11, 16, 18–21 have been published previously (Barrs et al., 1999, 2000; Foster et al., 1998a,b, 1999).

The median age was 10 years. Fifteen cats were male and six were female. The sex difference was not significant (P=0.07 with Chi-square test) but using odds ratios (Martin et al., 1987), males were 2.4 times more likely to have LRTIs than females (95% confidence interval 0.9, 6.1). There were no significant differences between any of the breeds

or between domestic and purebred cats. However, compared to the hospital population, purebred shorthair cats (other than Burmese and Siamese) were four times more likely to have LRTIs than domestic cats (95% confidence interval 1.2, 12.7).

Historical complaints, main presenting complaints and physical examination findings are detailed in Table 1. The cases presented throughout the year: winter (10), summer (6), spring (2), autumn (3). The date of onset of clinical signs was only accurately recorded in 10 cases: four in summer, four in autumn, one in winter and one in spring. Clinical signs in the cats with mycoplasmal LRTIs commenced in autumn in 4/8 cases for which a date of onset was known with the others recorded as spring (1), winter (1) and summer (2).

Haematology, serum biochemistry and serology

Haematological and serum biochemical data are listed in Table 2. Seven cats had serum biochemistry performed; only the more commonly abnormal analytes were listed.

Serological testing for FIV antibody was performed in 12 cases (3, 7, 10–12, 15–21) and was positive in four (11, 18, 19, 21). Serological testing for FeLV antigen in seven cases (7, 12, 15, 16, 18, 19, 20) was negative in each. Heartworm antigen tests in four cases (3, 10, 11, 15) were negative.

Radiology

Radiographic findings for each case are detailed in Table 3. Lung patterns were classed as bronchial (5), bronchoalveolar (4), alveolar (4, one with concurrent pneumothorax), bronchointerstitial (3, two of which also had right middle lung lobe consolidation) and mixed (5, four of which had one or more nodules). In total, 17 cats had bronchial changes and 14 had alveolar changes.

Cytology and microbiology

BAL cytology revealed large numbers of inflammatory cells in 18 cases and moderate numbers in one. Inflammation was neutrophilic in 17 cases (15 of which had 80% or more neutrophils) and histiocytic in two. The two cases with histiocytic inflammation were both from the same FIV-infected cat (Cases 18 and 19). Eosinophils comprised less than 20% of the cell population in all samples except one, in which certain areas of the smear had up to 34% of eosinophils. Infectious agents were observed cytologically except in the cases of mycoplasmal infections.

Two cats with persistent coughing despite therapy had BALs performed to check microbiological cure: Case 17 (salmonellosis) and Case 20 (mycobacteriosis). Both had many inflammatory cells and there was mixed inflammation (predominantly macrophages and neutrophils) in Case 17 and histiocytic inflammation in Case 20. Culture was negative in both cases.

Three cats had lung fine-needle aspirate cytology and culture. Ultrasound-guided lung fine-needle aspirates of a focal mass in Case 3 (Fig. 1a and b) yielded numerous inflammatory cells, of which the majority were neutrophils. A heavy pure growth of mycoplasmas was cultured from the sample and a mycoplasmal abscess was diagnosed. Lung fine-needle aspirate cytology in Case 10 revealed numerous inflammatory cells, of which the majority were neutrophils. There were also clusters and sheets of relatively uniform epithelial cells and this was attributed to epithelial cell hyperplasia or well-differentiated neoplasia. A moderate growth of mycoplasmas was obtained from a very small amount of diluted sample and heavy growth of mycoplasmas was also cultured from BAL fluid in this cat. As long-term follow-up eliminated the possibility of neoplasia, mycoplasmal LRTI was diagnosed. Fine needle aspirate cytology in the cat with mycobacterial LRTI (Case 20) revealed large numbers of inflammatory cells, the majority of which were intact and degenerate neutrophils. Numerous Gram-positive, acid-fast bacteria, which tended to occur in lipid vacuoles, were also noted.

Cytology on post-mortem squash preparations of lung in Case 21 (toxoplasmosis) revealed numerous inflammatory cells, mainly neutrophils. Epithelial cells were very pleomorphic with marked anisocytosis, anisokaryosis, large nuclei and prominent nucleoli (Fig. 2a). Intracellular tachyzoites were discovered in one oil immersion field (Fig. 2b). Histopathology on the necropsy samples was consistent with disseminated toxoplasmosis (subacute to chronic necrotising encephalitis and suppurative interstitial pneumonia with bradyzoites and tachyzoites in lung and brain and tachyzoites also in tracheobronchial lymph nodes) (Foster et al., 1998a).

Therapy and outcomes

Therapy and outcome for each case are detailed in Table 1. Antibiotic therapy for the mycoplasmal LRTIs included fluoroquinolones (ciprofloxacin and enrofloxacin), doxycycline, gentamicin, azithromycin or combinations of these; bronchodilators were

Table 1 Case data for twenty-one cases of feline lower respiratory tract infection

Case	Age	Sex	Breed	Main complaint	Other complaints	Physical examination findings	Culture / infectious agent	Outcome after specific therapy for aetiological agent
1	10 years	MN	Domestic	Chronic cough	Weight loss	Dyspnoea, sneezing, POD	Light to moderate mycoplasma	Treated with doxycycline and terbutaline. Resolved (3 year follow-up).
2	1 year	MN	British shorthair	Peracute cough	Peracute dyspnoea	Cough, inspiratory stridor	Heavy mycoplasma, some mixed contaminants	Treated with doxycycline and theophylline. Resolved (3 year follow-up).
3	10 years	MN	Australian Mist	Chronic cough		Inspiratory wheeze, epiphora, obesity	Light to moderate mycoplasma from lung FNA; heavy mycoplasma from BAL	Initially responsive to doxycycline. Recurrence of mycoplasmal LRTI 10 months later and doxycycline ineffective. Required azithromycin for complete resolution.
4	6 months	FN	Burmese	Chronic cough	Regurgitation	Cough, pyrexia, tachypnoea	Heavy mycoplasma	Treated with ciprofloxacin (and amoxycillin initially). Resolved but occasional cough; cat has megaoesophagus.
5	4 years	MN	Abyssinian	Acute cough	Occasional vomiting	Not possible	Heavy mycoplasma	Treated with oral doxycycline and parenteral enrofloxacin. Resolved but occasional recurrence of self limiting cough.
6	7 months	FN	Australian Mist	Chronic cough		Cough, wheezing, pyrexia	Heavy myoplasma	Treated with doxycycline. Resolved but occasional recurrence of self limiting cough.
7	11.5 years	MN	Oriental	Chronic cough	Weight loss, acute dyspnoea	Dyspnoea, tachypnoea, cyanosis, weakness, hypothermia	Heavy mycoplasma	Failed to respond to enrofloxacin, terbutaline and prednisolone. Resolved after doxycycline, terbutaline and prednisolone. Occasional terbutaline-responsive cough.
8	15 years	MN	Domestic	Chronic cough	Nasal discharge, sneezing	Wheezing, expiratory grunt, bilateral nasal discharge, URT stertor, cardiac murmur (previously hyperthyroid)	Heavy mycoplasma	Treated with doxycycline. Resolved. Recurrent doxycycline (tylosin)-responsive coughing each winter.
9	middle-aged	MN	Domestic	Peracute dyspnoea	Inappetence, weight loss	Dyspnoea, POD, cardiac arrhythmia	Heavy mycoplasma, some mixed contaminants	Treated with doxycycline and terbutaline. Resolved but recurrent doxycycline-responsive cough, especially in cold weather.
10	9 years	MN	Persian	Acute dyspnoea	Weight loss	Dyspnoea, tachypnoea, cyanosis, pyrexia, poor body condition, fleas	Heavy mycoplasma	Poor response to clindamycin and enrofloxacin. Responded to gentamicin. Oral enrofloxacin and nebulised gentamicin only partially successful. Good response to azithromycin and constant azithromycin required.
11	aged	MN	Domestic	Acute cough	Nasal discharge	Cough, POD, ocular discharge, nasal SCC	Heavy Mycoplasma, FIV	Treated with doxycycline and terbutaline. Resolved initially but diagnosed with FBD disease 16 months later.

Table 1 (continued)

Case	Age	Sex	Breed	Main complaint	Other complaints	Physical examination findings	Culture / infectious agent	Outcome after specific therapy for aetiological agent
12	9 years	MN	Domestic	Peracute cough	Chronic sneezing	Cough, tachypnoea, pyrexia, tachycardia	Heavy mycoplasma, *Bordetella bronchiseptica*	Treated with enrofloxacin. Cough resolved. URT signs continued (15 month follow-up).
13	16 years	FN	Domestic	Chronic cough	Occasional vomiting	Cough, dyspnoea, crackles, nasal discharge, hyperthyroidism	Heavy mycoplasma, moderate *Pasteurella multocida*	Treated with doxycycline. Resolved. Coughing recurred 8 months later but attributed to cardiac disease.
!4	11 years	FN	Siamese	Chronic cough	Anorexia	POD	*Pasteurella* sp., unidentified Gram negative bacterium	Treated with enrofloxacin. Resolved but had two further episodes of coughing: 8 months later (neutrophilic BAL and negative culture; resolved after amoxcillin-clavulanate and terbutaline) and 15 months later (resolved spontaneously). Died 6 months later due to unknown cause.
15	2.5 years	MN	Domestic	Acute anorexia	Straining to defaecate	Dyspnoea, poor body condition	*Pasteurella* sp., mixed anaerobes	Treated with amoxycillin and enrofloxacin. Responded but died 9 days later due to potassium bromide-induced FBD.
16	14 wks	M	Domestic	Peracute dyspnoea	Acute cough	Dyspnoea, tachypnoea, pyrexia	*Salmonella typhimurium*, *Aelurostrongylus abstrusus*	Treated with chest drainage, amoxycillin (initially), enrofloxacin and fenbendazole. Resolved.
17	1.5 years	MN	Domestic	Chronic cough	Dyspnoea	Dyspnoea, tachypnoea, wheezing, expiratory grunt	*Salmonella typhimurium*, *Pseudomonas* sp., *Aelurostrongylus abstrusus*	Treated with enrofloxacin (initially) ciprofloxacin (when susceptibilities known). Still coughing 4.5 weeks later but BAL negative for bacteria and larvae. Terbutaline required for one month then resolved (2 y follow-up).
18[a]	12 years	MN	Domestic	Chronic cough	Sneezing	Dyspnoea, cough	*Cryptococcus neoformans*, FIV	Treated with itraconazole. Resolved. One year later second LRTI (see case 19).
19[a]	13 years	MN	Domestic	Chronic cough	Sneezing, ocular discharge	Cough, bilateral ocular discharge	Mixed contaminants, *Eucoleus aerophilus*, FIV	Treated with abamectin. Resolved. Euthanased two months later with mast cell neoplasia.
20	1.3 years	FN	Domestic	Acute cough	Depression	Dyspnoea, tachypnoea, poor body condition	*Mycobacterium thermoresistibile*	Treated with rifampicin, clarithromycin and doxycycline. Resolved (12 month follow-up).
21	8 years	FN	Domestic	Acute neurologic signs	Anorexia, weight loss	Neurologic signs, cardiac murmur, pale mucous membranes, dyspnoea, thin	Not cultured. *Toxoplasma gondii*, FIV	Euthanased. No treatment.

Abbreviations: MN=desexed male; FN=desexed female; M=male; POD=periodontal disease; URT=upper respiratory tract; SCC=squamous cell carcinoma; FBD=feline bronchial disease; FNA=fine needle aspirate; BAL=bronchoalveolar lavage.

[a]Cases 18 and 19 were from the same cat on two different occasions.

Table 2 Haematological and serum biochemical data for twelve cases of feline lower respiratory tract infection

Case	Infection	Analyte with reference range										
		PCV 0.30–0.45 l/l	TPP 59–78 g/l	WCC 8–14× 10^9/l	Neutrophils 3.8–10.1× 10^9/l	Bands 0–0.4× 10^9/l	Lymphocytes 1.6–7×10^9/l	Monocytes 0.1–0.6× 10^9/l	Eosinophils 0.2–1.4× 10^9/l	Globulin 26–51 g/l	ALT <60 U/l	CK <200 U/l
2	mycoplasma	N	N									
5	mycoplasma	0.23	N	5.5	3.4	0.9	1.1	N	N			
6	myoplasma	N	N	18.1	10.2	N	N	1.1	N	N	84	N
7	mycoplasma	0.25	95	28.3	23.8	N	N	N		60	N	2616
9	mycoplasma	0.28	97	26.3	20	N	N	N	2.1	61	N	N
10	mycoplasma	N	93	16	14.2	N	1.1	N	N	52	N	N
12	mycoplasma, *Bordetella bronchiseptica*	N	88									
13	mycoplasma, *Pasteurella multocida*	0.28	96	32.4	24.3	N	N	1.6	1.9	71	166	223
14	*Pasteurella*, Gram negative bacterium	N	89	24.6	13.0	N	9.1	N	1.7			
15	*Pasteurella*, mixed anaerobes	N	87	N	12.0	N	0.5	1.1	N	N	97	239
16	*Salmonella typhimurium*, *Aelurostrongylus abstrusus*	N	N	25.6	16.1	N	N	N	3.1			
19	*Eucoleus aerophilus*	N	90	17.1	15.6	N	0.9	N	N	54	81	1020

Abbreviations: N=normal (value in reference range); PCV=packed cell volume; TPP=total plasma protein (measured by refractometry); WCC=white cell count; ALT=alanine aminotransferase; CK=creatine kinase.

Table 3 Thoracic radiographic features of 21 cases of lower respiratory tract infection

Case	Infection	Radiographic features						
		Bronchial	Alveolar	Interstitial	Nodular	Cardiovascular	Pleural	Comments
1	mycoplasma	Severe						Improved after treatment.
2	mycoplasma	Moderate						
3	mycoplasma	Moderate	Mild, focal, R cranial lobe		15 mm nodule in L cranial lobe			Changes persisted for 10 months. No radiographs after clinical cure.
4	mycoplasma	Moderate	Severe, focal, R cranial lobe	Moderate				Bronchointerstitial pattern resolved with treatment. R cranial lobe consolidation persisted.
5	mycoplasma		Moderate (diffuse) to severe (lobar)					Alveolar pattern resolved with treatment. Residual mild bronchial pattern.
6	myoplasma	Moderate	Mild to severe multifocal. Consolidation cranial part of L cranial lobe					Improved with treatment to mild alveolar pattern but mild broncho-interstitial pattern developed 19 months later.
7	mycoplasma	Moderate	Severe multifocal	Mild	5 mm nodule in R cranial lobe			
8	mycoplasma	Severe	Lobar sign R middle lobe	Severe				
9	mycoplasma	Severe	Lobar sign R middle lobe	Severe				Air trapping, overinflation evident.
10	mycoplasma		Severe diffuse					Alveolar pattern improved with treatment but severe bronchial pattern then evident.
11	mycoplasma	Mild	Mild, focal, dorsocaudal margins of caudal lobes			Caudal lobar pulmonary artery dilation and tortuosity		Alveolar pattern resolved with treatment. Vascular changes increased in severity.
12	mycoplasma, *Bordetella bronchiseptica*	Mild		Mild				
13	mycoplasma, *Pasteurella multocida*	Severe				Cardiomegaly		Bronchial pattern improved after treatment.
14	*Pasteurella* sp., unidentified Gram negative bacterium	Moderate						
15	*Pasteurella* sp., mixed anaerobes	Severe	Mild diffuse					Mild broncho-interstitial pattern five months prior to this.
16	*Salmonella typhimurium*, *Aelurostrongylus abstrusus*		Severe diffuse				Severe pneumo-thorax	Improved with treatment to severe interstitial and moderate bronchial pattern one month later.
17	*Salmonella typhimurium*, *Pseudomonas* sp., *Aelurostrongylus abstrusus*	Severe	Patchy R middle lung lobe atelectasis					
18*	*Cryptococcus neoformans*	Moderate			Two focal nodules, 3–5 mm diameter			Nodules resolved with treatment.
19*	*Eucoleus aerophilus*	Severe						
20	*Mycobacterium thermoresistibile*		Severe diffuse					
21	*Toxoplasma gondii*	Moderate	Mild		Six to ten nodules, 2–5 mm diameter			

Abbreviations: R=right; L=left.

*Cases 18 and 19 were from the same cat on two different occasions.

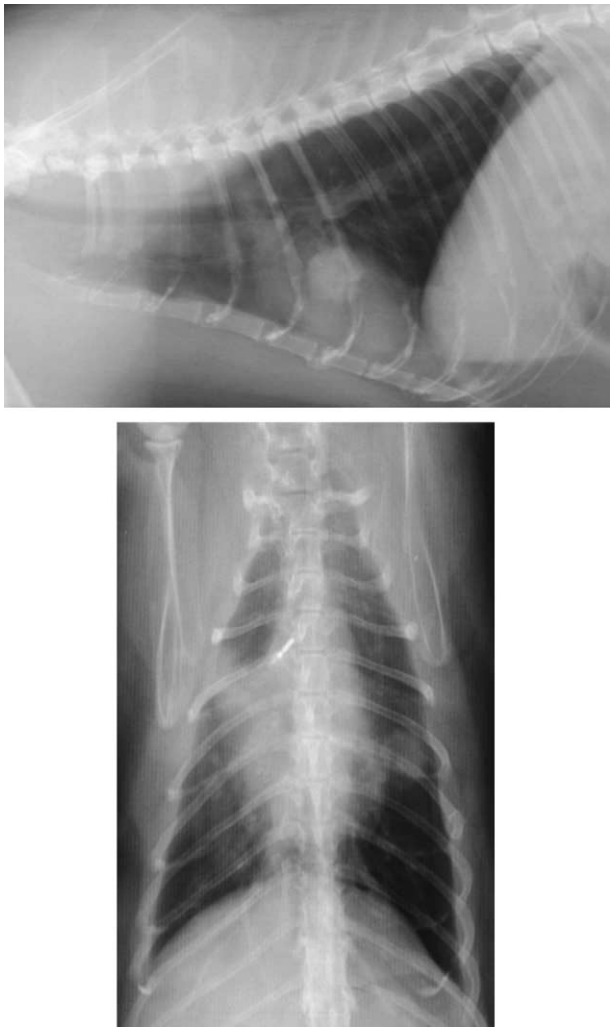

Figure 1 Right lateral and ventrodorsal radiographs from Case 3 (mycoplasmal abscess). A well circumscribed opacity is superimposed upon the cardiac silhouette at the level of the fifth and sixth intercostal space (Figure 1a). It has clearly defined margins and matches the soft tissue opacity visible in the caudal part of the left cranial lung lobe (Figure 1b). An ill-defined pulmonary opacity in the right cranial lobar region is also evident (Figure 1b).

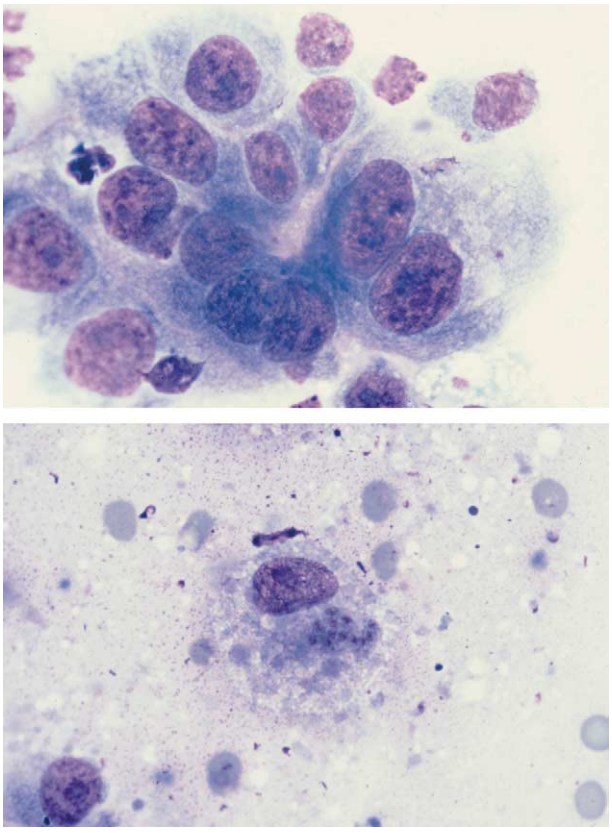

Figure 2 (a) Diff Quik-stained squash preparation of pulmonary parenchyma from Case 21 illustrating dysplastic bronchoalveolar epithelial cells. Note the variation in cell and nuclear size, the presence of prominent large nucleoli and one binucleate cell. Magnification ×735. (b) *T. gondii* tachyzoites within a macrophage in a squash preparation of pulmonary parenchyma from Case 21 (Diff Quik stain). Magnification ×735.

also used initially in five cases. Response to doxycycline (VibraVet and Vibra-Tabs 50; Pfizer) with doses approximating 5 mg/kg twice daily orally (length of treatment variable) appeared uniformly successful except in Case 3 which responded initially then required azithromycin (Zithromax; Pfizer). Enrofloxacin (Baytril; Bayer) was used in four cases and response was poor in two of these, one having heavy growth of mycoplasmas cultured from BAL whilst receiving enrofloxacin, prednisolone and terbutaline therapy.

Of the 13 cases of mycoplasmal LRTIs, two cases (1 and 2) resolved completely (both with three-year follow-up). Four cases have had occasional coughing episodes that require no treatment (cases 4, 5 and 6) or terbutaline (case 7); case 4 had a concurrent oesophageal motility disorder. Cases 5 and 6 had BALs performed 12.5 and 18.5 months later respectively, with numerous inflammatory cells noted in both cases. Inflammation was neutrophilic in Case 5 and mixed in Case 6. Neither sample had significant bacterial growth.

Case 8 had a three-year history of tylosin-responsive coughing every winter prior to having a BAL; there was no response to amoxycillin-clavulanate on the occasions it was administered. When the BAL was eventually performed there was a heavy pure growth of mycoplasmas and signs resolved after two-weeks of doxycycline therapy. Signs recurred again in the following winter and again, rapidly resolved with two weeks of

doxycycline therapy. Case 9 also had recurrent doxycycline-responsive coughing when the weather was cold.

The cat with the mycoplasmal lung abscess (Case 3) was treated with a 10-week course of doxycycline (6 mg/kg twice daily orally (PO)). A repeat fine needle aspirate of the nodule 14 weeks after initial diagnosis did not yield inflammatory cells or mycoplasmas. Coughing recurred five months after this and a further course of doxycycline of unspecified duration was ineffective. A BAL performed six weeks after this course of doxycyline was prescribed (10 months after initial diagnosis) demonstrated the presence of mycoplasmas. An eight-week course of azithromycin (7 mg/kg twice weekly PO) led to complete resolution of the clinical signs and there has been no recurrence (18 month follow-up).

One cat with very severe clinical and radiographic signs that had mycoplasmas cultured both from lung fine-needle aspirate and BAL (Case 10), required gentamicin initially (2 mg/kg thrice daily intravenously for five days) as there was minimal clinical response to enrofloxacin (3 mg/kg twice daily subcutaneously (SC) for seven days) and clindamycin (Antirobe; Pharmacia and Upjohn; 15 mg/kg twice daily PO for four days). This cat was treated after discharge with gentamicin nebulisation and oral enrofloxacin (8 mg/kg once daily PO) for one month before being treated with azithromycin (5–6 mg/kg twice weekly PO). Continuous azithromycin therapy was required until its death from unrelated causes 29 months later; any withdrawal of the drug resulted in relapse.

One cat with mycoplasmal LRTI (Case 11) developed severe feline bronchial disease (FBD) that required continuous treatment with prednisolone, bronchodilators or both. A second BAL performed 16 months later demonstrated histiocytic inflammation and no significant bacterial growth. This cat was a FIV-positive stray and it is not known whether it had had FBD prior to its mycoplasmal LRTI. There was no bronchial pattern evident on the initial radiographs but radiographs taken at the time of diagnosis of FBD revealed a mild bronchointerstitial pattern. Throughout, there was consistent enlargement of the caudal lobar pulmonary arteries but heartworm infection was excluded on the basis of echocardiography and heartworm antigen and antibody testing.

Anthelminthic treatment was successful in the three cases of parasitic LRTI. Oral fenbendazole (Panacur; Intervet Australia; 50 mg/kg daily PO for three days) was used to treat one case of *A. abstrusus* (Case 16) and two doses of abamectin (Avomec Antiparasitic Injection for Cattle; Merial Australia), 300 µg/kg SC two weeks apart, were used for the other two parasitic LRTIs: *A. abstrusus* (Case 17) and *E. aerophilus* (Case 19).

Discussion

Published case reports of pneumonia are invariably restricted to case reports or small case series. An extensive literature search revealed only one detailed retrospective study of infectious causes of pneumonia in cats (Bart et al., 2000). That study reported microbiological, parasitic and histological findings from autopsied cats and identified bacteria, fungi, parasites and viruses as causes of feline LRTIs. It included no clinical data on the cats.

This study would appear to be the first clinical study of feline LRTIs. There is no "gold standard" that can be used to make a clinical diagnosis of LRTI (Peeters et al., 2000). Historical, haematologic and radiographic findings known to be compatible with LRTI are often non-specific or are inconsistently present (Hawkins, 2000). In addition, many cases of LRTI have concomitant, predisposing respiratory tract or systemic diseases, the presence of which does not preclude a diagnosis of LRTI (Peeters et al., 2000).

In this study, diagnosis of LRTI was not based solely on identification of an infectious agent. The infectious agent was only considered the aetiological agent if historical, clinical, radiographic and cytologic findings were supportive and if there was an unambiguous response to appropriate therapy. Each case was considered individually and then the group examined as a whole in an attempt to provide useful clinical data about both diagnosis and management of feline LRTIs.

The most common presenting complaint was coughing and the most common abnormalities detected during physical examination were dyspnoea, tachypnoea and coughing (or increased tracheal hypersensitivity). Pyrexia only occurred in five cats (24%) indicating it is an unreliable sign of LRTI. However, as mild pyrexia was only recorded in one of 25 cases (4%) of feline bronchial disease diagnosed during the same time (unpublished data), presence of pyrexia may be of assistance when trying to distinguish between the two disease categories if BAL microbiology is not feasible. Crackles on auscultation are reported as a clinical sign in cases of feline pneumonia (Henik and Yeager, 1994) but were only present in one case in this series (5%) and in three of 25 cases of FBD (12%) diagnosed during the same study period (Foster et al., 2004b). Twenty nine per cent of the cats, including 38% of

cats with mycoplasmal LRTIs, had ocular or URT signs at the time of presentation. *Mycoplasma felis* is a recognised cause of URT and or ocular signs in cats (Campbell et al., 1973; Haesebrouck et al., 1990; Tan, 1974) and it is tempting to speculate that ocular discharge and URT signs in the cats with mycoplasmal infections may also have been due to mycoplasmosis. In another study of mycoplasmal respiratory infections in small animals, upper respiratory tract signs were present in all three cats reported (Chandler and Lappin, 2002).

Although not statistically significant there was a trend towards a male sex predisposition. Two desexed male cats (three cases) and one desexed female cat were infected with FIV. Seroprevalence of FIV is reportedly two to three times higher in males than females (Sellon, 1998). As testing for FIV was not routine, it may be that FIV infection was underestimated in this group of cats.

Data on season of admission was not available for hospital cats in the years 1995–2000 which makes any conclusions about dates of presentation tenuous. Date of onset of signs is more useful than date of presentation but there were very few cats, for which this information was known. More cats presented in winter than the other seasons and for mycoplasmal infections, onset of clinical signs was frequently in autumn.

The most common haematological abnormalities were leucocytosis and neutrophilia, which would not be unexpected findings in bacterial infections. The most common biochemical abnormalities were hyperproteinaemia, hyperglobulinaemia increased ALT and increased CK. Hyperproteinaemia and hyperglobulinaemia, consistent with antigenic stimulation, were present in the majority of tested samples. Increased ALT in four of seven cats tested was unexpected, however, one of the cats was being treated with phenobarbitone and another had concurrent hyperthyroidism; the other two cases had very mild increases. Increased CK concentrations were also not expected. In one case, the increase was negligible and in Case 7 the cat had recently had seizures but the increased CK concentration was unexplained in the third cat (Case 19).

Radiographically, all lung patterns were represented and whilst 67% of cases had alveolar changes, 81% of cases had a bronchial pattern either alone or in combination with another pattern. This is consistent with the histological diagnoses of bronchitis, bronchointerstitial pneumonia or bronchopneumonia in non-septicaemic cases of bacterial pneumonia (Bart et al., 2000). A predominantly nodular pattern was noted in the cases of cryptococcosis, toxoplasmosis and mycoplasmal abscess.

All BALs except for those from one FIV-positive cat (cases 18 and 19), were neutrophilic. The three lung aspirate samples also had neutrophilic cytology suggesting that the normal response to pulmonary bacterial or protozoal infection is neutrophilic unless there is concurrent immunosuppression. None of the three cats with confirmed parasitic infections had an eosinophilic BAL although other factors may have influenced this: the presence of concurrent salmonellosis in two and FIV infection in the other.

Lung aspirate cytology has been reported in one study as 100% specific for neoplasia (De Berry et al., 2002). The lung cytology in the case of toxoplasmosis in our study, however, demonstrated that care needs to be taken with interpretation of hyperplastic and dysplastic epithelial changes when there is concurrent inflammation. As published previously, the dysplastic epithelial changes in the cat with toxoplasmosis were initially attributed to neoplasia as tachyzoites were sparse (Foster et al., 1998a). Cytological diagnosis of toxoplasmosis in both this cat, and another in the literature (Litster et al., 1999), was made retrospectively once a histological diagnosis was available and the slides reviewed.

The bacteria reported as occurring in the airways of healthy cats include *Pasteurella* spp., *Pseudomonas* spp., *Staphylococcus* spp., *Streptococcus* spp., *E. coli* and *Micrococcus* spp. (Padrid et al., 1991). Anaerobic bacteria and mycoplasmas have not been isolated from the lower airways of healthy cats (Padrid et al., 1991; Randolph et al., 1993). The most commonly reported bacterial causes of feline pneumonia include *P. multocida*, *E. coli*, *K. pneumoniae*, *B. bronchiseptica*, *Streptococcus canis*, mycobacteria and Eugonic Fermenter-4 (Bart et al., 2000; Henik and Yeager, 1994). In the present study infectious bacterial agents identified were mycoplasmas, *Pasteurella* spp., *Salmonella typhimurium*, *B. bronchiseptica*, *Pseudomonas* sp. and *Mycobacterium thermoresistibile*.

Mycoplasmas are known pulmonary pathogens in other species and have been recorded as causing pyothorax, pneumonia and pulmonary abscessation in cats (Crisp et al., 1987; Foster et al., 1998b; Malik et al., 1991; Wong and Noor, 1984). Mycopolasmas were identified in a recent study as the third most common cause of bacterial pneumonia in cats; the majority of cases in the study were kittens up to 12 weeks old (Bart et al., 2000). Mycoplasmas were the most common cause of LRTIs in our study, which included no patients younger than 14 weeks old.

Mycoplasmas were also identified as the cause of pulmonary abscessation in one cat, the second such case in the feline veterinary literature (Crisp et al., 1987).

Response of the mycoplasmal LRTIs to appropriate antimicrobial therapy in this study would appear to be compelling evidence for the pathogenicity of mycoplasmas. However, the most commonly used antibiotic in these cases was doxycycline. In addition to its antibiotic effects, doxycycline has been shown to have immunomodulatory effects and a recent study demonstrated suppression of in vitro induction of immunoglobulin E responses of peripheral blood mononuclear cells obtained from asthmatic humans (Smith-Norowitz et al., 2002). It is possible that the responses to doxycycline in our cases were, at least in part, due to the immunomodulatory effects of the drug, however, it is unlikely that the responses should have been so consistently dramatic and sustained if mycoplasmas had been incidental to FBD. In addition, no similar effects would be expected of the other agents employed: fluoroquinolones, aminoglycosides and azalides.

Mycoplasmal LRTIs are often considered to be a consequence of pre-existing pulmonary diseases although pulmonary pathology other than FBD would appear to be inadequate for mycoplasmal colonisation (Foster et al., 2004a). It is possible that the mycoplasmal infections in this study, whilst of clinical significance, were secondary to FBD especially as clinical signs only resolved completely in two cases. However, it is possible that the mycoplasmas caused serious pathology and resulted in bronchial inflammation and airway hyperresponsiveness similar to *Mycoplasma pneumoniae* in humans (Sabato et al., 1984). Certainly, LRTIs caused by other agents also caused clinical signs that persisted after the infections cleared, as evident in Cases 17 and 20.

The role of mycoplasmas is being increasingly examined in human asthma where there are strong associations between (i) mycoplasmal infection and exacerbation of asthma (ii) chronic mycoplasmal infections and asthma and (iii) induction of asthma subsequent to mycoplasmal infection (Gil et al., 1993; Kraft et al., 1998; Micillo et al., 2000; Petrovsky, 1990; Sabato et al., 1984; Seggev et al., 1986, 1996; Teo et al., 1986; Yano et al., 1994). We believe that mycoplasmal LRTIs in cats should be regarded as significant irrespective of any pre-existing pathology as even in cats with known FBD, there is the possibility of acute exacerbation by mycoplasmas. Evidence in the human literature also suggests that the role of mycoplasmas as causal agents of asthma/bronchial disease requires investigation.

The history in one case of mycoplasmal LRTI suggested recurrent infection every winter. Other owners noted recurrence of signs when the weather became cold. As known onset of clinical signs showed a trend for autumn, this would be consistent with the seasonal data and suggest that mycoplasmal LRTI may be more common in cold conditions. Alternatively, the cats may remain indoors in cold weather so signs are more obvious to owners.

Treatment of mycoplasmal infections in veterinary medicine is usually empirical. Antibiotic susceptibility profiles are not available for feline mycoplasmal isolates. Mycoplasmas are generally reported to be sensitive to macrolides (erythromycin and tylosin), fluoroquinolones (enrofloxacin and ciprofloxacin), tetracyclines, chloramphenicol and gentamicin (Greene, 1998). However, species differences are noted in human isolates with *M. hominis* being resistant to erythromycin and some of the other macrolides whilst *M. pneumoniae* is invariably sensitive. *M. hominis* is sensitive to ciprofloxacin whilst *M. pneumoniae* may or may not be (Taylor-Robinson, 1995). Doxycycline, used at approximately 5 mg/kg twice daily orally, appeared effective in most cases in this study, however, the cat with the mycoplasmal abscess responded initially and then required azithromycin, suggesting that resistance might have developed. Resistance of mycoplasmas can develop through chromosomal mutations or through acquisition of antibiotic resistance transposons. Tetracycline resistance mediated by the latter mechanism has been noted in some human mycoplasmal species (Taylor-Robinson, 1995).

Enrofloxacin did not appear as effective as doxycycline and one cat had mycoplasmas cultured whilst being treated with the drug, albeit with concurrent corticosteroid therapy. Enrofloxacin has the advantages of being bactericidal and requiring once daily administration but increasing reports of idiosyncratic retinopathy and blindness, even at normal dose rates (Gelatt et al., 2001; Wiebe and Hamilton, 2002), would suggest that this drug should be reserved for infections where it is specifically indicated. Azithromycin was used effectively in two cases and may be a better choice, especially in those cases where less frequent dosing is desirable.

It is difficult to comment on the role of *Pasteurella* spp. in feline LRTIs as in the three cases in this study, infections were mixed, one occurring shortly before death due to potassium

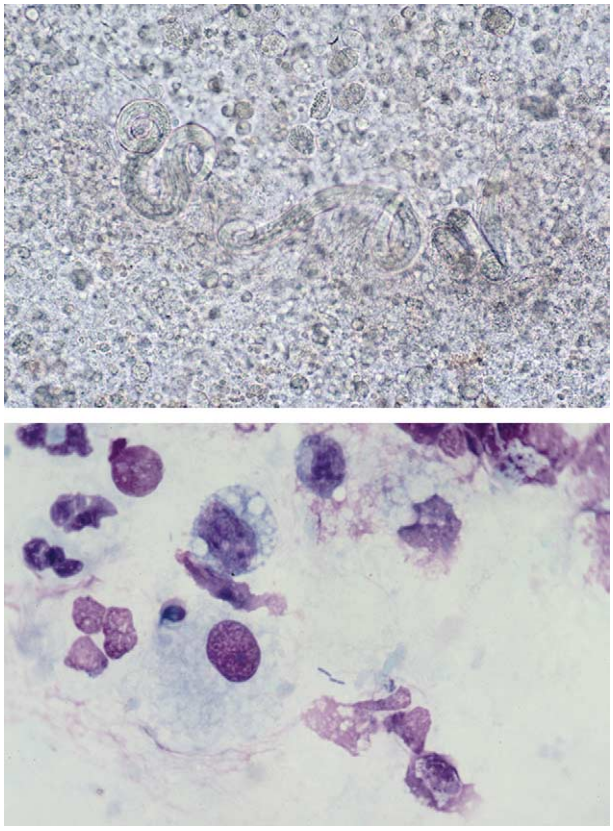

Figure 3 (a) Unstained wet preparation of the bronchoalveolar lavage from Case 17 illustrating larvae of *A. abstrusus* surrounded by inflammatory cells. Magnification ×147. (b) Diff Quik-stained smear of bronchoalveolar lavage from the same case illustrating bacterial rods of *S. typhimurium* surrounded by bronchoalveolar macrophages and intact and degenerate neutrophils. Magnification ×735.

bromide-induced FBD. *P. multocida* is a common inhabitant of the oral and upper respiratory mucous membranes in cats, with a carrier rate of over 30%, (Biberstein and Holzworth, 1987) and has been reported as a cause of pneumonia (Bart et al., 2000; Henik and Yeager, 1994).

Salmonellosis occurred twice in association with *A. abstrusus* (Fig. 3a and b) and it has been postulated that migrating lungworm larvae may act as carriers for intestinal bacteria (Barrs et al., 1999). Unlike the previously reported kitten (Case 16; Barrs et al., 1999), Case 17 was an apparently healthy adult cat with no signs of enteric salmonellosis. Pneumonia due to *Salmonella choleraesuis* has also been reported in a cat with no signs of gastrointestinal tract disease (Rodriguez et al., 1993).

In a previous Australian survey, *A. abstrusus* was found only in adult animals in autumn and winter (Wilson-Hanson and Prescott, 1982). The kitten in the present series would appear to be an exception to this with respect to both age and season; it presented in autumn, having shown signs in summer. The adult cat with *A. abstrusus* presented in winter and date of onset of signs was thought to be either summer or early autumn. The reason for this discrepancy may just be a result of insufficient sample size in the original survey or because it was performed in Brisbane, which has different seasonal conditions than Sydney.

Ivermectin, a semi-synthetic analogue of avermectin B_1, is often recommended for treatment of *A. abstrusus* as a single dose of 400 μg/kg orally or SC (Hawkins, 2000; Pechman, 1994). Presumably this recommendation is made because ivermectin administered at 200 μg/kg SC proved ineffective in treating *A. abstrusus* in one case report and a second dose of 400 μg/kg SC was required 2.5 weeks later (Kirkpatrick and Megella, 1987). Whilst the second dose was effective, it may be that two doses were in fact required for complete resolution. In another study, a single dose of oral ivermectin at 300 μg/kg was ineffective in three cats (Blagburn et al., 1987). Two doses of abamectin (a natural fermentation product of avermectin) at 300 μg/kg SC, two weeks apart, were used successfully for treatment of *A. abstrusus* and *E. aerophilus* in this study. Administration of ivermectin or abamectin is considerably easier than fenbendazole although use of these drugs is "off-label" and care needs to be taken in kittens (Plumb, 2002). The bioavailability of ivermectin may be lower in cats than dogs (Plumb, 2002) thus parenteral administration is preferable to oral.

Parasitic causes of LRTIs commonly cited include *A. abstrusus* and *T. gondii* (Bart et al., 2000). *E. aerophilus* is rarely mentioned despite the fact that in Australia at least, a similar prevalence of 3–5% has been reported for both *E. aerophilus* and *A. abstrusus* (Barrs et al., 2000). Presumably this is because prevalence of clinical disease due to *E. aerophilus* appears to be low (Pechman, 1994). Diagnosis of infection with this parasite should be straightforward as the ova are passed in the faeces and routine faecal flotation is adequate for detection. However, the double operculated ova of *E. aerophilus* may be mistaken for *Trichuris* spp. when found in faecal preparations (Barrs et al., 2000).

Diagnosis of *T. gondii* is probably the most difficult of the three parasites. The lung appears to be a target organ in both primary and reactivated toxoplasmosis in cats (Dubey and Carpenter 1993; Parker et al., 1981). Radiology and pulmonary cytology in both Case 21 and another cat in the

literature (Litster et al., 1999) were consistent with neoplasia. Case 21 was euthanased due to its poor neurological and systemic status but the decision was influenced by the radiographic changes. Diagnosis is possible by BAL (Brownlee and Sellon, 2001; Eddlestone et al., 1996) but both BAL and lung biopsy evaluation may fail to identify *T. gondii* in human patients. Immunohistochemistry and tissue culture have been recommended for lung biopsies and BAL specimens from human patients with AIDS (Derouin et al., 1989; Nash et al., 1994).

Fungal causes of feline LRTIs include *Cryptococcus* spp., *Sporothrix schenkii*, *Aspergillus* sp., *Mucor* sp., *Candida* sp., *Histoplasma capsulatum*, *Coccidioides immitis* and *Blastomyces dermatitidis* (Bart et al., 2000); the latter two are exotic to Australia. The lungs are considered the primary site of infection for cryptococcosis in humans (Malik et al., 2001) but pulmonary cryptococcal infections appear to be quite rare in cats (Gerds-Grogan and Dayrell-Hart, 1997; Malik et al., 1992; Medleau et al., 1995). In this study, cryptococcal LRTI was only identified in a single FIV-positive cat which had the hallmarks of AIDS-like disease: opportunistic infections and, terminally, neoplasia (Sellon, 1998).

Whilst this study has much information that may be pertinent only to cats in Sydney, it would appear to be the first clinical study of feline LRTIs. The typically cited bacteria in feline pneumonia were not identified commonly in these cats and the majority of LRTIs were caused by mycoplasmas. The diversity of causes even in this small number of cats, suggests that empirical therapy in coughing cats is not recommended and that BAL cytology and microbiology should be performed in all cases. If specimen transport and culture methods for mycoplasmal detection are sub-optimal, empirical therapy with two weeks of doxycycline at 5 mg/kg twice daily orally is recommended. Should BAL be impossible due to financial or patient constraints then therapy should at least address potential mycoplasmal and nematode infections before corticosteroids are administered. Bronchodilators such as terbutaline and theophylline may be needed as supportive therapy in any case of LRTI.

Acknowledgements

This study would not have been possible without the enthusiastic assistance of Rhian Foster and Karen Kilpatrick in medical records and Leanne Fitzsimmons from Veterinary Imaging Associates, Sydney. The clinicians who managed the cases are gratefully acknowledged as is Professor Ian Robertson, Murdoch University, for his assistance with statistics. Richard Malik is supported by the Valentine Charlton Bequest of the Post Graduate Foundation in Veterinary Science of the University of Sydney.

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