

Airway microbial culture and susceptibility patterns in dogs and cats with respiratory disease of varying severity

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Abstract

Objective – To compare airway microbiological culture and susceptibility results in 2 groups of dogs and cats: 1 with respiratory failure requiring positive pressure ventilation (PPV) and 1 with respiratory disease.

Design – Retrospective study.

Setting – University teaching hospital.

Animals – Fifty-two dogs and cats requiring PPV that had an airway microbiologic culture submitted from October 1, 2003 to October 31, 2008 were included. One hundred and four airway microbiologic cultures from dogs and cats with respiratory disease not requiring PPV were randomly sampled for comparison.

Interventions – None.

Measurements and Main Results – Patients with respiratory failure were more likely to have a gram-negative enteric isolate identified ($P < 0.001$), while patients with respiratory disease were more likely to have a gram-negative nonenteric isolate ($P < 0.001$) or anaerobic isolate ($P < 0.001$) identified. Aerobic bacterial isolates from patients with respiratory failure were less likely to be susceptible to ampicillin ($P = 0.006$), amoxicillin/clavulonate ($P < 0.001$), chloramphenicol ($P = 0.004$), enrofloxacin ($P < 0.001$), ticarcillin/clavulonate ($P = 0.004$), and the combination of ampicillin with enrofloxacin ($P < 0.001$) than were aerobic bacterial isolates from patients with respiratory disease.

Conclusions – Canine and feline patients with respiratory failure severe enough to require PPV exhibit a different pattern of bacterial isolates cultured from their airways when compared with isolates from patients with respiratory disease that has not resulted in ventilator dependence. These isolates are more likely to be resistant to commonly used antimicrobials/antimicrobial combinations than patients in the respiratory disease group. These findings suggest that in canine and feline patients with infectious lower respiratory tract disease, consideration of the severity of the pulmonary insult may allow for better prediction of likely isolates and their antimicrobial susceptibilities. Further prospective studies with a standardized collection technique are warranted.

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Introduction

Lower respiratory tract infections are a common clinical diagnosis in dogs and cats. They may be due to infec-

tious bronchitis, lobar pneumonia, or bronchopneumonia. Bacterial pneumonia may be due to aspiration of gastrointestinal or oropharyngeal contents,¹ colonization by resident microflora, hematogenous spread, or from a community acquired source.² The incidence of pneumonia in dogs and cats in the general population is unknown. In dogs, recent reports show the incidence of pneumonia to range from 4.6% to 24% following surgery for thoracolumbar intervertebral disc herniation or laryngeal paralysis.^{3–6} Pneumonia from any source is 1 of the leading causes of death in people.^{7,8} Although there are no mortality statistics in veterinary medicine, recent studies have shown the need for positive pressure ventilation (PPV) in 35 dogs⁹ and 2 cats¹⁰ due to respiratory failure from pneumonia.

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Hospital-acquired pneumonia (HAP) in human medicine is defined as pneumonia that occurs 48 hours or more after admission, which was not incubating at the time of admission^{11,12} and frequently leads to respiratory failure and the need for PPV. Ventilator-associated pneumonia (VAP) refers to pneumonia that arises >48–72 hours after endotracheal intubation.¹² To the authors' knowledge, in regards to animals requiring mechanical ventilation due to respiratory failure, there are no reports of airway cultures in cats, a single report in dogs containing 3 antemortem cultures⁹ and 1 report of 6 dogs suspected to have VAP.¹³

The most recent guidelines from the American Thoracic Society and the Infectious Disease Society of America stress the clinical importance of adequate initial therapy for HAP and VAP to decrease mortality and hospital stay.¹⁴ Empiric antimicrobial therapy for HAP or VAP is based on whether the onset is late (≥ 5 d in hospital), and if there are risk factors for multidrug-resistance present.¹⁴ Current guidelines recommend consideration of local microbiologic data if possible, when selecting empiric therapy. Current guidelines in veterinary medicine are based on suspected pathogens and the severity of the illness.^{15,16}

Bacterial identification, rather than susceptibility results, has been the focus of previous veterinary studies reporting microbial culture results from airway samples.^{17–21} Bacterial identification, while valuable information, can only guide treatment when accompanying susceptibility patterns are known. Bacteria have, over time, developed increased resistance to antimicrobials, and many multidrug-resistant bacteria have emerged making such information all the more necessary to guide appropriate antimicrobial selection. Consequently, recent data on bacterial identification and susceptibility would be of value to clinicians treating animals with pneumonia or other lower respiratory tract infectious diseases. Such data would be particularly useful in the treatment of animals with lower respiratory tract infections requiring PPV. In these cases, appropriate initial antimicrobial selection may help to reduce the overall time the patient requires ventilatory support and reduce the associated risks and costs.

For the present study we have elected to separate the patients into 2 distinct groups: those patients requiring mechanical ventilation will be hereafter referred to as 'respiratory failure' patients while those patients who had respiratory tract infections but did not require mechanical ventilation will be referred to as 'respiratory disease' patients. At our institution, the 3 primary indications for PPV are as follows: (1) hypoxemia ($\text{PaO}_2 < 60$ mmHg) despite supplemental oxygen therapy, (2) persistent hypoventilation ($\text{PaCO}_2 > 60$ mmHg), or clinical suspicion of impending respiratory muscle

exhaustion.⁹ While there are many causes of noninfectious respiratory disease and failure, in this study we only evaluated patients in which, at the time the culture sample was obtained, a bacterial infectious component was suspected to be contributing to their respiratory compromise. This could include both patients placed on the ventilator for pneumonia as well as patients who were placed on the ventilator for another cause of respiratory failure, but were suspected of having developed VAP. The purpose of this retrospective study is to compare the airway microbial cultures results obtained from patients with respiratory disease to those obtained from patients in respiratory failure. The secondary goal is to characterize the differences in antimicrobial susceptibilities in isolates obtained from these 2 groups of patients to help provide guidelines for empiric therapy. We hypothesized that patients in respiratory failure would have both different predominant bacterial species as well as different patterns of antimicrobial resistance relative to patients with respiratory disease.

Materials and Methods

Patient identification

Respiratory failure: The intensive care unit (ICU) census of all dogs and cats admitted to the UC Davis William R. Pritchard Veterinary Medical Teaching Hospital small animal ICU from October 1, 2003 to October 31, 2008 was searched. Patients were identified in which PPV was utilized. The digital medical record was reviewed for both an aerobic and anaerobic bacteriologic culture of the airways. Patients were excluded if no airway culture was submitted, or if a jet ventilator was used briefly to facilitate the performance of a diagnostic procedure.

Respiratory disease: The hospital computer database was searched for the same time period for all bacterial culture submissions from dogs and cats. To achieve a randomly sampled cohort, search results were numerically ordered by the last 2 digits of a sequentially numbered 6-digit medical record system. These numbers are assigned automatically upon scheduling the first ever appointment to see a clinician at our institution and are not linked in any way to presenting complaints, signalment, or any aspect of the case other than the time and date of the first visit. Digital medical records were reviewed for results of an airway culture. Patients were included if an airway aerobic and anaerobic culture was present and excluded if they were also in the respiratory failure group. During the 5-year period of this study, over 4,000 airway sample culture requests were submitted from this patient group.

Following randomization as described above, a subset of patients numbering twice the size of the respiratory failure group (104 versus 52 cultures) was selected. Twice the number of patients was included in the respiratory disease group due to a lower predicted frequency of positive culture results in this group relative to the respiratory failure group.

Data retrieval

The medical records of these patients were retrospectively reviewed and data were imported into a computer spreadsheet application.^a Variables included in the electronic data included: age, sex, breed, antimicrobial usage, timing of culture (antemortem versus postmortem), bacteriologic culture source, bacteria isolated, if *Mycoplasma* cultures were obtained, and minimum inhibitory concentration (MIC) susceptibility results. If more than 1 positive culture occurred in the same patient, only the first positive culture was recorded, as subsequent positive culture results could not be treated as independent data in this context. For the respiratory failure group, the record was also analyzed for presence of a CBC and thoracic radiographs within 24 hours of culture submission and for cytology submitted concurrently with the culture. For the respiratory disease group, the record was also reviewed for cytologic evaluation submitted concurrently with the culture.

Data analysis

For the purpose of data analysis bacterial isolates were subdivided into gram-negative enterics, gram-negative nonenterics, gram-positive cocci, and anaerobes. MIC data was classified as sensitive or resistant. Intermediate designations were placed into the resistant category. The MIC corresponding to 'susceptible' was described by the National Committee on Laboratory Standards. Bacterial isolates for which no susceptibility data was present, e.g., anaerobes and postmortem samples, were not included in MIC analysis.

The MIC susceptibility results were reviewed to determine if there was a difference in susceptibility between the respiratory failure and respiratory disease groups for the antimicrobials commonly used empirically for respiratory tract infections in our hospital. Each subgroup was compared as well as the bacterial isolates as a whole. We also evaluated the common combination therapies of ampicillin with enrofloxacin and ticarcillin/clavulonate with enrofloxacin for individual bacteria that both data points were available.

CBC data was analyzed for presence of an inflammatory leukogram according to the systemic inflammatory response syndrome criteria. An inflammatory leukogram was considered present if the total WBC count $>16.0 \times 10^9/L$ ($>16,000/\mu L$), $<6.0 \times 10^9/L$ ($<6,000/\mu L$),

or $>3\%$ of the WBC count compromised of immature neutrophils.²² Thoracic radiographs were scrutinized for evidence of pneumonia as described on the finalized radiology report. Cytology reports were scrutinized for the presence of suppurative inflammation and evidence of oropharyngeal contamination read out by a board-certified clinical pathologist.

Statistical analysis was performed using a commercially available statistical analysis software package.^b Data were tabulated into contingency tables and analyzed using a χ^2 or Fisher's exact test depending on sample size. Age distribution in both groups was tested for normality using the Kolmogorov-Smirnov test.

Results

Patient populations

A total of 184 dogs and cats were identified as having received PPV therapy during the study period from October 1, 2003 to October 31, 2008. Of those, 53 animals met the inclusion criteria. One dog was excluded because the medical record was incomplete leaving a final population of 52 in the respiratory failure group. In the respiratory disease group 104 animals were included.

The respiratory failure group consisted of 45 dogs and 7 cats. The median age was 5 years (range 0.16–15 y). Represented dog breeds included: mixed ($n = 5$), Labrador Retriever ($n = 4$), German Shepherd ($n = 3$), Golden Retriever ($n = 3$), Dachshund ($n = 2$), Pug ($n = 2$), Rottweiler ($n = 2$), Standard Poodle ($n = 2$), Yorkshire Terrier ($n = 2$), and 1 each of 20 other breeds. Represented cat breeds included: Domestic shorthair ($n = 3$), Domestic mediumhair ($n = 2$), Domestic longhair ($n = 1$), and Siamese ($n = 1$). Fifty percent of the patients were male (22 castrated and 4 intact), and 50% were females (18 spayed and 8 intact).

The respiratory disease group consisted of 84 dogs and 20 cats. The median age was 6 years (range 0.25 to 17 y). Represented dog breeds included: mixed ($n = 13$), Labrador Retriever ($n = 10$), Jack Russell Terrier ($n = 5$), German Shepherd ($n = 4$), Australian Shepherd ($n = 3$), Bichon Frise ($n = 3$), Chihuahua ($n = 3$), Border Collie ($n = 2$), Boxer ($n = 2$), Dachshund ($n = 2$), French Bulldog ($n = 2$), Pug ($n = 2$), Rottweiler ($n = 2$), Yorkshire Terrier ($n = 2$), and 1 each of 30 other breeds. Represented cat breeds included: domestic shorthair ($n = 13$), domestic longhair ($n = 4$), domestic mediumhair ($n = 2$), and Siamese ($n = 1$). Forty-nine percent of the patients were male (42 castrated and 9 intact), and 51% were female (40 spayed and 13 intact).

Antimicrobials were in use at the time of culture in 42 of 52 (81%) patients in the respiratory failure group.

The most common antimicrobials were: ampicillin with enrofloxacin ($n = 12$), ticarcillin/clavulonate with enrofloxacin ($n = 12$), and ticarcillin/clavulonate ($n = 7$).

Antimicrobials were in use at the time of culture in 40 of 104 (38%) patients in the respiratory disease group. The most common antimicrobials were: amoxicillin/clavulonate ($n = 14$), ampicillin with enrofloxacin ($n = 11$), and doxycycline ($n = 5$).

Bacterial isolates

Forty-seven of the 52 cultures submitted (90%) were positive in the respiratory failure group. A total of 89 bacterial isolates were identified with 56 (63%) obtained antemortem and 31 (37%) postmortem. Collection methods included: necropsy ($n = 17$), endotracheal tube swab ($n = 12$), blind bronchial lavage ($n = 8$), protected specimen brush ($n = 6$), and bronchoalveolar lavage (BAL) ($n = 5$).

In the respiratory disease group, 56 of the 104 cultures submitted (54%) were positive. A total of 109 bacterial isolates were identified with 102 (94%) obtained antemortem and 7 (6%) postmortem. Collection methods included: BAL ($n = 72$), endotracheal wash ($n = 10$), surgical biopsy ($n = 9$), necropsy ($n = 6$), transtracheal wash ($n = 5$), and lung aspirate ($n = 1$).

There were 81 aerobic (91%) and 8 anaerobic (9%) isolates from patients with respiratory failure. Aerobic isolates were: gram-negative enterics ($n = 32$), gram-positive cocci ($n = 28$), or gram-negative nonenterics ($n = 19$, Table 1). No *Simonsiella sp.* were cultured. A *Mycoplasma* culture was submitted in 17 patients and

Table 1: Bacterial isolates from dogs with respiratory failure

Bacteria	Number of isolates
Gram-negative enteric	
<i>Escherichia coli</i>	18
<i>Enterobacter sp.</i>	8
<i>Klebsiella pneumoniae</i>	6
Gram-negative nonenteric	
<i>Acinetobacter sp.</i>	6
<i>Pseudomonas sp.</i>	5
<i>Pasteurella sp.</i>	4
<i>Bordetella bronchiseptica</i>	2
Other	2
Gram-positive	
<i>Enterococcus sp.</i>	14
Coagulase+ <i>Staphylococcus</i>	6
<i>Streptococcus sp.</i>	5
Coagulase- <i>Staphylococcus</i>	3

The bacterial species isolated most frequently from the respiratory failure patient group are listed by subgroup in order of descending frequency. Species names for isolates that were cultured only once are not listed and are categorized as 'other.'

Table 2: Bacterial isolates from dogs with respiratory disease

Bacteria	Number of isolates
Gram-negative enteric	
<i>Escherichia coli</i>	8
<i>Klebsiella pneumoniae</i>	3
<i>Enterobacter sp.</i>	2
<i>Citrobacter braakii</i>	1
Gram-negative nonenteric	
<i>Pasteurella sp.</i>	18
<i>Bordetella bronchiseptica</i>	8
<i>Pseudomonas aeruginosa</i>	2
Other*	12
Gram-positive	
<i>Streptococcus sp.</i>	9
Coagulase+ <i>Staphylococcus</i>	4
Coagulase - <i>Staphylococcus</i>	3
<i>Corynebacterium sp.</i>	1

*Species or type of bacteria classified as other include: gram-negative nonenteric ($n = 5$), Nonfermenter group 3 ($n = 2$), *Sternotrophomonas maltophilia* ($n = 2$), *Alcaligenes faecalis* ($n = 1$), *Chryseobacterium indologenes* ($n = 1$), and *Ralstonia pickettii* ($n = 1$).

The bacterial species isolated most frequently from the respiratory disease patient group are listed by subgroup.

was positive in 2. Two fungi were cultured: *Coccidioides immitis* and *Candida glabrata*.

There were 77 aerobic (71%) and 32 anaerobic (29%) isolates from patients with respiratory disease. Aerobic isolates were: gram-negative enterics ($n = 14$), gram-negative nonenterics ($n = 40$), and gram-positive cocci ($n = 17$, Table 2). No *Simonsiella sp.* were cultured. A *Mycoplasma* culture was submitted in 87 patients and was positive in 6. Four fungi were cultured: 2 *Coccidioides immitis*, 1 *Aspergillus niger*, and 1 *Scedosporium apiosermum*.

Patients with respiratory failure were more likely to have a gram-negative enteric isolate cultured (32 versus 14 isolates, $P < 0.001$). Patients with respiratory disease were more likely to have a gram-negative nonenteric (40 versus 19 isolates, $P < 0.001$) or an anaerobic isolate cultured (32 versus 8 isolates, $P < 0.001$).

Clinical findings

In the respiratory failure group 28 patients, all with positive culture results had both a CBC and thoracic radiographs performed within 24 hours of obtaining a culture. Twenty-seven of 28 (96%) had evidence of systemic inflammation. Nineteen of 28 (68%) also had thoracic radiographs consistent with the diagnosis of pneumonia. Thirteen patients had concurrent cytology submitted with their culture and 12 (92.3%) were interpreted as suppurative inflammation. None of these patients had oropharyngeal contamination suspected on cytology.

In the respiratory disease group 88 of 104 (84.6%) had concurrent cytology submitted with their cultures. Sixty-one (69.3%) had suppurative inflammation present. Five of 88 (5.7%) had oropharyngeal contamination suspected on cytology.

MIC findings

Overall antimicrobial susceptibilities are summarized in Table 3. Although no single antimicrobial would have been effective across all organisms, amikacin and imipenem had the highest percent susceptibilities (>90% for both groups). Bacterial isolates from respiratory failure patients were less susceptible to amoxicillin/clavulonate (35% versus 84%, $P < 0.001$), ampicillin (33% versus 69%, $P = 0.006$), chloramphenicol (57% versus 90%, $P = 0.004$), enrofloxacin (48% versus 88%, $P < 0.001$), and ticarcillin/clavulonate (47% versus 83%, $P = 0.004$) than isolates from respiratory disease patients.

Isolates from patients with respiratory failure were more likely to be resistant to the combination of ampicillin and enrofloxacin (52% versus 6%, $P < 0.001$) than isolates from patients with respiratory disease. Respiratory failure patients also had a higher proportion of infections resistant to the combination of ticarcillin/clavulonate and enrofloxacin (28% versus 10%), but this difference failed to reach statistical significance ($P = 0.15$).

Table 3: Susceptibility among all aerobic bacterial isolates

Antimicrobial	Isolate susceptibility (%) in respiratory failure	Isolate susceptibility (%) in respiratory disease
Amikacin	98	96
Amoxicillin/clavulonate	35	84 ^a
Ampicillin	33	69 ^b
Chloramphenicol	57	90 ^a
Enrofloxacin	48	87 ^a
Imipenem	91	93
Ticarcillin/clavulonate	47	83 ^c
Ampicillin and Enrofloxacin	48	94 ^a
Ticarcillin/clavulonate and Enrofloxacin	72	90

Proportion of isolates susceptible to the individual antimicrobial or antimicrobial combination are listed.

^aSignificant difference between susceptibility frequency in isolates from respiratory failure versus respiratory disease patients ($P < 0.001$).

^bSignificant difference between susceptibility frequency in isolates from respiratory failure versus respiratory disease patients ($P = 0.006$).

^cSignificant difference between susceptibility frequency in isolates from respiratory failure versus respiratory disease patients ($P = 0.004$).

In the subgroup analysis, gram-negative enteric isolates from patients with respiratory failure were less frequently susceptible to amoxicillin/clavulonate than those from respiratory disease patients (30% versus 80%, $P = 0.02$). Similarly, gram-negative nonenteric isolates from patients with respiratory failure were also less frequently susceptible to amoxicillin/clavulonate than those from respiratory disease patients (38% versus 85%, $P = 0.002$). In addition, gram-negative enteric isolates from respiratory failure patients were less frequently susceptible to chloramphenicol than those from respiratory disease patients (61% versus 100%, $P = 0.032$). Lastly, gram-negative nonenteric isolates from respiratory failure patients were also less frequently susceptible to chloramphenicol than those from respiratory disease patients (38% versus 84%, $P = 0.006$).

Discussion

To the authors' knowledge, this is the first study to retrospectively evaluate both bacterial isolate types and their antimicrobial susceptibilities in a group of patients with respiratory failure requiring PPV. In addition, the authors know of no prior veterinary studies comparing airway microflora and their antimicrobial susceptibilities between patients with lower respiratory tract infections of varying severity. Despite the wide range of disease severity observed in patients in the present study, the overall patient population characteristics were remarkably similar between the 2 groups with respect to median age, species, breed distribution, and sex.

As described above, a greater proportion of patients with respiratory failure received antimicrobials before an airway sample was submitted for bacterial culture than did patients with respiratory disease. Frequently patients in veterinary medicine that are felt to be unstable from respiratory disease will have empiric antimicrobial therapy started without cultures being submitted due to the potential risks associated with obtaining a culture sample; this may explain the higher preculture antimicrobial usage rate in the respiratory failure group, but this cannot be confirmed retrospectively. Despite the frequent use of empiric antimicrobial therapy before obtaining cultures in our respiratory failure patients, positive cultures results were common.

Swabbing of the end of the endotracheal tube accounted for 12 of the 52 (23%) culture sources in the respiratory failure group. Lower tracheal cultures do not always correspond with pneumonia and it is known that up to 40% of cultures of the lower trachea are positive for growth in clinically healthy dogs.²³ The respiratory failure group had clinical signs of pneumonia 68% of the time based on an inflammatory leuko-

gram and radiographic changes taken within 24 hours of submission of the culture. Seven of the 10 (70%) patients with the culture being obtained from the endotracheal tube had clinical signs of pneumonia based on the above criteria. Cytology was available from 2 of these patients and showed suppurative inflammation in both. These findings show a correlation with the culture results and clinical signs of pneumonia. However, caution should be used when interpreting culture results from the lower trachea if clinical signs of pneumonia are not present as colonization of the trachea can be observed.

In the present study, ampicillin with enrofloxacin and ticarcillin/clavulonate with enrofloxacin were the antimicrobial combinations used most frequently before cultures being submitted. These combinations of empiric therapies theoretically provide broad-spectrum coverage when susceptibility data are not yet available. The authors believe that these combinations are also widely used at other institutions. In a recent study of bacterial culture results in critically ill canine patients (from a different institution) ampicillin with enrofloxacin was the most common antimicrobial regime used pending culture results.²⁴ Current recommendations in human medicine for empiric therapy in HAP and VAP are broken into 2 categories: patients with no known risk factors for multidrug-resistant (MDR) pathogens and early onset disease, or patients with risk factors for MDR pathogens or late onset disease (≥ 5 d in hospital).¹⁴ Multiple studies have shown in hospitalized human patients with pneumonia, incorrect initial empiric antimicrobial therapy increases morbidity and mortality.²⁵⁻²⁷ In 1 study of VAP patients, it was found that delaying appropriate antimicrobial therapy until after bronchoscopy is performed (or until BAL results are known) results in higher mortality than if appropriate antimicrobials had been given at the time of first establishing a clinical diagnosis.²⁷

In order to provide appropriate empiric antimicrobial therapy, one must have knowledge of the common bacteria isolated. Textbooks frequently list empiric antimicrobial recommendation based on expected bacterial isolates.^{15,28,29} In the present study, patients in the respiratory disease group had a gram-negative nonenteric bacteria (e.g., *Bordetella bronchiseptica*) isolated most frequently. Using our grouping system, this is similar to previous reports of dogs with lower respiratory tract infections.¹⁸⁻²⁰ In contrast to patients with stable respiratory disease, the predominate isolate from our patients with respiratory failure was a gram-negative enteric. This likely reflects aspiration of oropharyngeal or gastrointestinal contents as the most common underlying mechanism. Aspiration pneumonia in dogs can be associated with severe respiratory

compromise and in 1 recent study a mortality rate of 23% was reported.¹ Patients with an endotracheal tube in place are at risk of leakage of bacteria around the endotracheal tube cuff as a route of bacterial entry into the trachea.^{30,31} In addition, the development of biofilms may allow bacterial colonization of the endotracheal tube surface that increases the risk of VAP; in this setting, gram-negative enteric bacteria are the most common isolates.³² In the respiratory disease group more anaerobic bacteria were isolated than in the respiratory failure group. One possible cause of this is contamination from the upper airway at the time of the culture. Cytologically there were patients in the respiratory disease group in which oropharyngeal contamination was deemed likely, but not in the respiratory failure group. This can partially account for the increased number of anaerobes cultured in the respiratory disease group. Another contributory factor could be the increased use of anaerobic drugs in the respiratory failure group at the time of culture.

An understanding of the common bacterial species isolated from the respiratory tract of veterinary patients may be insufficient to guide therapy. Knowledge of the susceptibility patterns of commonly isolated bacteria is of additional benefit in prescribing empiric antimicrobial therapy. When bacteria such as *Pseudomonas aeruginosa*, *Acinetobacter sp.*, or *Enterococcus sp.* are isolated their intrinsic resistance must be considered when choosing antimicrobials pending susceptibility results. This study demonstrates a decreased susceptibility for ampicillin, amoxicillin/clavulonate, chloramphenicol, enrofloxacin, and ticarcillin/clavulonate in patients with respiratory failure compared with those with respiratory disease across all aerobic isolates. Thus, there was a difference in antimicrobial susceptibilities between our patient groups when aerobic bacteria were looked at as a whole. However, when antimicrobial susceptibilities are compared for these agents across patient groups but within bacterial subgroups (gram-negative enterics, gram-negative nonenterics, gram-positives), subgroup analysis did not find a difference in susceptibilities to ampicillin, enrofloxacin, and ticarcillin/clavulonate; this is most likely due to low sample numbers in each individual subgroup. These results suggest that commonly recommended antimicrobials such as enrofloxacin, amoxicillin/clavulonate, or ticarcillin/clavulonate would provide inadequate coverage for many patients with respiratory failure, but may be suitable empiric choices for patients with respiratory disease who are not in respiratory failure. In the present study, the combination therapy of ampicillin with enrofloxacin or ticarcillin/clavulonate with enrofloxacin in respiratory disease patients provided excellent coverage ($\geq 90\%$ susceptibility), while providing marginal

to good coverage in patients with respiratory failure (72% susceptibility). In light of this, the authors suggest that patients with respiratory failure be classified as a distinct group when making decisions on empiric antimicrobial therapy. However, current guidelines appear appropriate to guide antimicrobial selection in patients with stable respiratory disease.

In this study, the increased resistance pattern noted in patients with respiratory failure compared with respiratory disease suggests that obtaining an airway culture early in the course of illness may be beneficial to help guide antimicrobial therapy. Further, the results suggest that for patients requiring PPV, imipenem (or another carbapenem) or amikacin in combination with a β -lactam (to cover potential anaerobes) would be appropriate initial choices while awaiting susceptibility results from airway cultures if clinical signs of systemic inflammation or radiographic signs of pneumonia are present. Metronidazole or clindamycin (at bactericidal concentrations) could also be used to improve coverage of anaerobes when amikacin is selected.

There are inherent limitations of this study due to its retrospective nature. In this retrospective study, there was no way to control the administration of antimicrobials before acquisition of culture samples. The increased antimicrobial use in the respiratory failure group must be considered as a possible explanation for the increased antimicrobial resistance observed. Use of β -lactams and fluoroquinolones has been shown to contribute to the creation of MDR.³³ A study in critically ill canine patients demonstrated increased likelihood of MDR samples after patients had been hospitalized for 48 hours.²⁴ In addition, third-generation cephalosporins were not evaluated due to the low number of susceptibility data available. They may represent a reasonable antimicrobial choice for patients with respiratory failure when empiric antimicrobial therapy is clinically indicated. Further studies would be needed to evaluate this. In the respiratory failure group, the patients were all housed in the same ICU. This introduces the possibility of nosocomial clones as an underlying cause of the increased resistance observed. When the antimicrobial susceptibility results for gram-negative enterics were evaluated temporally, potential clones were not identified. Pulsed-field gel electrophoresis would have been optimal to assess for the presence of clones, but was not possible due to the retrospective nature of the analysis. Another possible limitation to the study is that endotracheal tube swabs represented a large portion of the data collected in the respiratory failure group. This may represent colonization of the trachea, which is common in intubated patients, rather than true lower respiratory tract infection. In human patients, it is recommended that airway cul-

tures be obtained via endotracheal aspiration, BAL, or a protected specimen brush.^{14,34}

In summary, this study highlights the differences in airway microflora and in their associated antimicrobial susceptibility patterns in patients with respiratory failure versus those with respiratory disease. Empiric antimicrobial therapy in patients with infectious respiratory disease should be selected based on disease severity and known resistance patterns whenever possible. Further prospective studies with a standardized technique for obtaining an airway culture sample would be beneficial.

Footnotes

^a Excel, Microsoft Inc, Redmond, WA.

^b Sigmastat, SyStat Software Inc, San Jose, CA.

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