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An updated description of bacterial pneumonia in adult horses and factors associated with death

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Abstract

Background: Available descriptive studies on equine pneumonia are outdated or focus on specific horse or bacterial populations.

Objectives: To describe the clinical presentation and bacterial isolates of adult horses with bacterial pneumonia and identify factors associated with death.

Animals: One hundred sixteen horses >2 years old with bacterial pneumonia.

Methods: Retrospective case series. Data regarding history, physical examination, clinicopathologic features, treatment, bacterial culture and sensitivity, and outcome were collected and analyzed retrospectively.

Results: Historical risk factors were present for 60% of cases, whereas abnormal vital signs on intake were present for <50%. Most horses (58%) underwent at least 1 change of antimicrobial treatment, and 67% received the highest-priority critically important antimicrobials. *Streptococcus zooepidemicus* was the most isolated bacteria (44%), followed by *Escherichia coli* (19%), *Klebsiella* spp. (18%), other *Streptococcus* species (17%), and *Bacillus* spp. (13%). *Fusobacterium* spp. were the most common anaerobic isolates (11%). Antimicrobial susceptibility varied widely. Survival to discharge was 73%. Heart rate at presentation (odds ratio [OR] 1.08, 95% confidence interval [CI] 1.008-1.17, $P = .03$) and higher creatinine (OR 14.1, 95% CI 1.56-127.6, $P = .02$) increased the risk of death. Higher lymphocyte count (OR 0.27, 95% CI 0.08-0.94, $P = .04$) reduced risk.

Conclusions and Clinical Importance: Contrasting older literature, *Fusobacterium* spp. were the most common anaerobes. *Streptococcus zooepidemicus* remained the most common isolate and was predictably susceptible to penicillin. Antimicrobial susceptibility was otherwise variable and broad applicability is limited as this was a single-center study. Increased risk of death associated with tachycardia and abnormally high serum creatinine concentration is consistent with previous studies.

KEYWORDS
anaerobes, antimicrobials, bronchopneumonia, creatinine, lymphocytes, pleuropneumonia

Abbreviations: HPCIA, highest-priority critically-important antimicrobial; NSAID, non-steroidal anti-inflammatory; TTW, transtracheal wash.

1 | INTRODUCTION

Bacterial pneumonia is a major cause of morbidity and death in adult horses.[1-4] Reported survival rates for pneumonia and pleuropneumonia range from 38% to 100%, likely because of varying inclusion criteria.[1,5-15] Factors previously associated with increased risk of death include primary infection with *Escherichia coli* or *Klebsiella* spp., presence of anaerobic organisms on transtracheal wash (TTW) culture, and higher serum creatinine at the time of presentation.[1,5,7,8,15]

Risk factors for the development of bacterial pneumonia in horses include transportation, previous or concurrent respiratory illness, general anesthesia, and aspiration of feed material.[4,16-20] Consistent with these risk factors, commensal bacteria of the nasopharynx are the most common etiologic agents, followed by enteric organisms. *Streptococcus zooepidemicus* is consistently the most commonly identified isolate followed by coliforms such as *E. coli*, *Klebsiella* spp., and *Enterobacter*, other *Streptococcus* species, *Bacillus* species, and *Actinobacillus* species.[3,5,7,8,11,15,21-26] The reported prevalence of infection with anaerobic bacteria varies from 5% to 38%, and common isolates include *Bacteroides*, *Fusobacterium*, *Clostridium*, and *Peptostreptococcus* species.[3,5,7,9,15] Fewer reports are available regarding the antimicrobial susceptibility of common isolates. Historically, *S. zooepidemicus* isolates have been highly susceptible to various antimicrobial agents, whereas *Klebsiella* spp. and *E. coli* isolates show greater resistance rates.[5,8,15,27]

Although the body of literature describing the presentation, management, and outcome of pneumonia and pleuropneumonia is robust, many of the larger scale studies are outdated or focus on specific horse or bacterial populations.[3,5,7,8,10,16,23] Bacterial populations and their antimicrobial susceptibility patterns are dynamic, with antimicrobial resistance being a growing problem in both human and veterinary medicine.[28-34] In addition to continuously emerging resistance patterns, there are significant differences in bacterial populations and antimicrobial susceptibility patterns across regions and even between ambulatory practices and referral hospitals from similar geographic locations.[33-35] Although therapy is ideally guided by culture and sensitivity, initial therapy for bacterial pneumonia is often empiric because of the risk of delaying treatment while awaiting results.[1,21,26] As such, availability of recent data regarding the presentation and management of cases of bacterial pneumonia is essential to rapid and efficacious treatment.

The objectives of this study were to describe the clinical presentation, bacterial isolates, treatment regimens, and case outcomes of a group of adult horses with a diverse range of ages and breeds diagnosed with bacterial pneumonia and identify factors associated with death. We hypothesized that the most common bacterial isolates would show altered antimicrobial resistance patterns as compared to previous research, and that clinical variables could be used as indicators for death.

2 | MATERIALS AND METHODS

Medical records of adult horses diagnosed with bacterial pneumonia at the North Carolina State University Veterinary Teaching Hospital between January 1, 2010 and December 31, 2021, were identified. Records were included for horses greater than 2 years of age with septic suppurative inflammation identified on cytology of TTW fluid with clinical signs and imaging findings consistent with bacterial pneumonia, or with a diagnosis of bacterial pneumonia on postmortem examination. Retrospective analysis of records was performed and data recorded including signalment, history, physical examination findings, clinicopathologic data at the time of diagnosis, diagnostic imaging results, culture and sensitivity data, treatment, complications, and case outcome.

Previous antimicrobial therapy was not considered criteria for exclusion but was recorded when noted in the history. As is standard hospital policy antimicrobial therapy was withheld for at least 24 hours before TTW sampling. Method of sampling was based on clinician preference and was not regularly recorded in medical records though percutaneous TTWs are most commonly performed at our institution. For horses diagnosed with pneumonia at the time of presentation to the hospital, results of physical examination, initial clinicopathologic testing, and imaging were recorded. For horses that developed pneumonia while hospitalized for another reason, variables from the day of diagnosis were used. For horses with multiple culture samples submitted throughout hospitalization only the intake samples were included. Fever was defined as a temperature ≥101.5°F, tachycardia as a heart rate ≥60 beats per minute, and tachypnea as a respiratory rate ≥32 breaths per minute. Complications were defined as laminitis, thrombophlebitis, pneumothorax, and antimicrobial-associated diarrhea. Outcome was defined as survival to discharge from the hospital.

Because of the retrospective nature of this study, not all data points were available for all horses. Clinicopathologic variables included for analysis were limited to glucose, lactate, albumin, total protein, creatinine, blood urea nitrogen, total white blood cell count, segmented and band neutrophil count, lymphocyte count, and fibrinogen. No standard form for thoracic ultrasound findings was present, so interpretation was limited to findings described in the horse's case summary. All cultures were submitted to an in-house, hospital microbiology laboratory and processed within 24 hours in accordance with their standard operating procedures. All samples were cultured onto tryptic soy agar media with 5% sheep blood (Remel), and MacConkey agar (Remel) and enriched in 10 mL of tetrathionate medium (Remel). All bacterial isolates were semi-quantified and struck for isolation before identification by MALDI-TOF MS (BioMerieux). Genus and species were reported as available and antimicrobial susceptibly was determined by microbroth dilution on a commercial system (Sensititre; ThermoFisher). Interpretations were based on available interpretations by the Clinical Laboratory and Standards Institute (CLSI) at the time of culture. The version of CLSI guidelines used varies over the course of the study because of available updates.

Antimicrobial therapy for each horse was recorded by agent and route. For horses that underwent a transition in antimicrobial therapy during hospitalization, the reason for transition was recorded. Possible reasons included de-escalation of therapy, development of complications from previous therapy, clinical failure to respond to previous

therapy, and based on antimicrobial susceptibility testing. The use of high-priority, critically important antimicrobials (HPCIAs) as designated by the World Health Organization was also recorded, along with any justifications provided for their use.[36] Possible justifications included azotemia, continuation of previous antimicrobial therapy, clinical failure to respond to other antimicrobials, and based on antimicrobial susceptibility testing. Some cases had multiple concurrent reasons for change in therapy or for use of HPCIAs and all reasons provided were recorded.

Data sets were tested for normality with the Shapiro-Wilk test and found to be not normally distributed. Therefore, descriptive data are presented as medians and ranges. Multivariate logistic regression was performed to predict death based on clinical and laboratory findings. Data analyzed in univariate and multivariate logistic regression included heart rate, respiratory rate, temperature, glucose, lactate, albumin, total protein, creatinine, blood urea nitrogen, total white blood cell count, segmented and band neutrophil count, lymphocyte count, and fibrinogen concentrations. Because of missing data and a significant correlation between some of the variables (creatinine/BUN $\rho = 0.7$ [$P < .001$], creatinine/lactate $\rho = 0.6$ [$P < .001$]); 5 variables were included in the calculation of the final model. These variables were screened, and those with a $P < .25$ were tested in a backward stepwise multivariate logistic regression to determine the final model. Variables with P values <.05 were retained in the model. The Hosmer and Lemeshow Goodness-of-Fit test indicated that the data fitted the model (Step 1, $x^2 = 2.4$, degree of freedom = 8, $P = .96$; Step 2, $x^2 = 13$, degree of freedom = 8, $P = .11$). Commercial software was used for statistical analyses with significance established at $P < .05$ (SPSS 22, IBM Corporation).

3 | RESULTS

3.1 | Signalment and history

A total of 116 horses met the inclusion criteria of the study, including 44 mares, 68 geldings, and 4 stallions. Median age was 13.5 years (range, 2-30 years). Breeds included 40 Quarter Horses/Paints, 19 Warmbloods, 17 Thoroughbreds, 8 Arabians, 7 Saddlebreds, 6 Tennessee Walking Horses, 6 Draft horses, 5 Morgans, 4 Standardbreds, 2 Ponies, 1 American Miniature Horse, and 1 Rocky Mountain Horse.

Duration of clinical signs before presentation was available for 109/116 horses. The median duration was 10.5 days (range, 0-150 days). Data on historical risk factors for pneumonia were available for all horses, and 68/116 (59%) horses had 1 or more. History of travel was identified in 23/116 cases (20%), general anesthesia in 11/116 (9.5%), esophageal obstruction in 23/116 (20%), and other respiratory illness in 14/116 (12%) horses. Three horses had 2 concurrent risk factors. Sixty-nine out of 116 horses (59%) had documented treatment with antimicrobials before presentation. Antimicrobials administered included ceftiofur (35/116 cases, 30%), gentamicin (25/116 cases, 22%), trimethoprim sulfa (23/116 cases, 20%), penicillin (13/116 cases, 11%), metronidazole (10/116 cases, 8.6%), enrofloxacin (8/116 cases, 6.9%), doxycycline (1/116 cases, 0.86%), chloramphenicol (1/116 cases, 0.86%), and rifampin (1/116 cases, 0.86%).

3.2 | Initial evaluation

For horses with vital signs recorded at time of pneumonia diagnosis (110/116), fever was present in 28/110 (26%), tachycardia in 43/110 (39%), and tachypnea in 48/110 (44%) cases.

Ultrasonography of the thorax was performed in 96/116 horses. Of these 96 horses, 94 (98%) had 1 or more reported abnormalities. Comet tails were reported in 65/96 cases (68%), 14 of which were unilateral and 51 bilateral. Consolidation or abscessation was reported in 73/96 cases (76%), 27 unilateral of which were unilateral and 46 bilateral. Pleural effusion was reported in 36/96 cases (38%), 12 of which were unilateral and 24 bilateral.

Intake clinicopathologic data are presented in Table 1. Median values for the study group were within reference range for all

TABLE 1 Clinicopathologic data from horses at time of diagnosis with bacterial pneumonia.

Variable	N	Median (range)	Reference range	Below RR (n and % of N)	Above RR (n and % of N)
Glucose (mg/dL)	88	119 (64-344)	73-113	1 (1.1%)	58 (66%)
Lactate (mmol/L)	58	1.5 (0.3-9.7)	0.0-2.0	N/A	17 (29%)
Albumin (g/dL)	90	2.8 (1.6-3.9)	2.8-3.5	40 (44%)	2 (2.2%)
Total protein (g/dL)	94	6.7 (4.8-9.7)	5.9-8.0	14 (15%)	15 (16%)
Creatinine (mg/dL)	92	1.2 (0.4-4.2)	1.0-1.7	17 (18%)	15 (16%)
Blood urea nitrogen (mg/dL)	89	14 (7-45)	7-25	0 (0%)	7 (7.9%)
Total white blood cells (10^3 cells/μL)	104	8.82 (1.2-33)	4.69-10.36	19 (18%)	40 (38%)
Segmented neutrophils (10^3 cells/μL)	94	6.36 (0.05-31.02)	2.45-6.82	18 (19%)	44 (47%)
Band neutrophils (10^3 cells/μL)	94	0.14 (0-2.85)	0	N/A	60 (64%)
Lymphocytes (10^3 cells/μL)	94	1.52 (0.13-5.09)	1.33-4.57	41 (44%)	2 (2.1%)
Fibrinogen (mg/dL)	98	500 (0-1200)	100-400	1 (1.0%)	51 (52%)

Note: The number of horses for which data were available is indicated (N) along with laboratory reference ranges (RR).

variables except glucose, band neutrophils, and fibrinogen. The most common clinicopathologic abnormalities were hyperglycemia (58/88 cases, 66%), band neutrophilia (60/94 cases, 64%), hyperfibrinogenemia (51/98 cases, 52%), lymphopenia (41/94 cases, 44%), and hypoalbuminemia (40/90 cases, 44%).

3.3 | Treatment

Ten out of 116 horses were euthanized without any treatment. Of the 106 horses for which treatment was pursued, all received antimicrobials. Antimicrobial treatment was often adjusted during hospitalization based on culture and susceptibility results, treatment response, or to transition horses from injectable to oral antimicrobials when approaching hospital discharge. The most frequent route of administration of antimicrobials was oral (86/106 cases, 81%), followed by intravenous (77/106 cases, 73%), intramuscular (46/106 cases, 43%), nebulized (18/106 cases, 17%), and intrathoracic (5/106, 4.7%). Metronidazole was the most frequently prescribed antimicrobial (63/106 cases, 59%), followed by ceftiofur (59/106 cases, 56%), penicillin (53/106 cases, 50%), enrofloxacin (53/106 cases, 50%), and gentamicin (41/106 cases, 39%). Nebulization was most commonly performed with ceftiofur (18/18, 100%), although amikacin and gentamicin were additionally used in 1 case each (1/18, 5.6%). High-priority, critically important antimicrobials were used in 78/106 cases (67%). Forty-nine of those 78 cases (63%) had no recorded reason for use of an HPCIA. Recorded reasons for use included antimicrobial susceptibility testing (12/78 cases, 15%), continuation of therapy initiated before hospitalization (10/78 cases, 13%), azotemia (6/78 cases, 7.7%), and clinical failure to respond to other antimicrobial therapy (3/78, 3.8%). High-priority, critically important antimicrobial use was more frequent in the first half (2010-2015) of the study period, with 31/40 (78%) of cases receiving HPCIAs as compared to 48/77 (62%) in the second half (2016-2021). Use without documented reason was static across both halves of the study period (20/31, 65% vs 29/48, 60%).

Polytherapy was common, with 18/106 horses receiving 5 or more antimicrobials (17%), 23/106 receiving 4 (22%), 26/106 receiving 3 (25%), and 20/106 receiving 2 (19%). Nineteen out of 106 horses received only 1 antimicrobial (18%). The most common first-line antimicrobial combinations were penicillin, IV and enrofloxacin, IV with metronidazole, PO (22/106 cases, 21%), penicillin, IV and gentamicin, IV with metronidazole, PO (14/106 cases, 13%), ceftiofur, IV and gentamicin, IV with metronidazole, PO (7/106 cases, 6.6%), ceftiofur, IM alone (7/106 cases, 6.6%), and trimethoprim sulfa, PO alone (7/106 cases, 6.6%). Antimicrobial therapy was transitioned at least once in 62/106 cases (58%). Documented reasons for this transition included de-escalation of therapy (44/62 cases, 71%), antimicrobial susceptibility testing (36/62 cases, 58%), failure to respond to first-line therapy (8/62 cases, 13%), and complications of first-line therapy (3/62 cases, 4.8%). Ten out of 106 cases (9.4%) underwent a second transition in antimicrobial therapy, documented reasons for which were de-escalation of therapy (6/10 cases, 60%), antimicrobial susceptibility testing (3/10 cases, 30%), and clinical failure to respond to previous therapy (3/10 cases, 30%). Five out of 106 cases (4.7%) had their antimicrobial regimen changed a third time because of clinical failure to respond to previous therapy (3/5 cases, 60%), antimicrobial susceptibility testing (1/5 cases, 20%), complications of previous therapy (1/5 cases, 20%), and de-escalation of therapy (1/5 cases, 20%). Three out of 106 cases had a fourth antimicrobial transition, 1/3 cases (33%) for de-escalation of therapy, 2/3 cases (67%) for clinical failure to respond to previous therapy, and all 3 (100%) based on antimicrobial susceptibility results. One case out of 106 (0.94%) had a 5th antimicrobial transition for de-escalation of therapy based on antimicrobial susceptibility results.

After antimicrobials, non-steroidal anti-inflammatories (NSAIDs) were the next most frequently used type of medication, prescribed in 78/106 (74%) cases. Flunixin meglumine was used most often (75/106 horses, 71%). Phenylbutazone was administered in 4/106 (3.8%), and the NSAID used was unspecified in 2/106 cases (1.9%). Corticosteroids were administered to 17/106 horses (16%), with 13/106 (12%) receiving dexamethasone, 2/106 (1.9%) receiving prednisolone, and 2/106 (1.9%) receiving multiple types of corticosteroids. Anti-endotoxemic therapy (polymyxin B) was administered in 15/106 cases (14%). Bronchodilators were administered in 22/106 cases (21%), and supplemental oxygen was utilized in 16/106 cases (15%). Fifty-one out of 106 horses (48%) received intravenous fluids, and 18/106 (17%) received a plasma transfusion.

Thoracic drains were placed in 12/106 cases (11%), 6/106 (5.6%) of which were bilateral, and 6/106 (5.6%) unilateral. Eleven out of 106 horses (10%) underwent intermittent thoracocentesis, 5/106 (4.7%) underwent thoracotomy, and 5/106 (4.7%) received intrathoracic medication. Medications used for intrathoracic administration included ampicillin, potassium penicillin, gentamicin, meropenem, imipenem, ceftiofur sodium, N-acetylcysteine, tissue plasminogen activator, and platelet lysate (BIO-PLY).

3.4 | Culture and sensitivity

Culture data were available for 103/116 cases. Eleven cases had concurrent TTW and pleural effusion samples submitted, 1 of which with pleural effusion samples submitted from each side of the chest, resulting in a total of 115 samples. The characteristics of culture samples and most common bacterial isolates are presented in Table 2. The majority of samples were TTW fluid (80%), and polymicrobial infections were common with 58% of samples growing 2 or more organisms. Mixed gram-positive and gram-negative infections were most common (46%), and 14% of samples had anaerobic growth. *Streptococcus zooepidemicus* was the most common isolate, present in 44% of samples.

For the cases in which concurrent TTW and pleural effusion samples were submitted, bacterial growth was identical between samples in 3/11 cases (27%). In 5/11 cases (45%), including a sample from the horse with bilateral pleural effusion samples submitted, there was bacterial growth from the TTW sample but no growth from the pleural

TABLE 2 Description of bacterial culture samples and results for horses with bacterial pneumonia (N = 115).

	Number of samples (n and % of N)
Sample type	
Transtracheal wash	92 (80%)
Pleural effusion	15 (13%)
Pulmonary abscess aspirate	1 (0.87%)
Post-mortem lung tissue	7 (6.1%)
Overall growth	
No growth	16 (14%)
1 organism	33 (29%)
2 organisms	31 (27%)
3 organisms	25 (22%)
4 organisms	8 (7.0%)
5 organisms	2 (1.7%)
Type of bacteria present	
Gram positive only	32 (28%)
Gram negative only	14 (12%)
Mixed gram positive and gram negative	53 (46%)
Anaerobic growth	16 (14%)
Specific bacterial isolates	
Streptococcus zooepidemicus	51 (44%)
Escherichia coli	22 (19%)
Klebsiella spp.	21 (18%)
Non-*zooepidemicus Streptococcus* spp.	19 (17%)
Bacillus spp.	15 (13%)
Fusobacterium spp.	13 (11%)
Actinobacillus spp.	11 (9.6%)
Enterobacter spp.	11 (9.6%)
Staphylococcus spp.	9 (7.8%)
Pseudomonas spp.	9 (7.8%)

effusion. In 3/11 cases (27%), including the other sample from the horse with bilateral pleural effusion samples submitted, some but not all of the organisms identified on TTW culture were also identified on pleural effusion culture. Only 1 case (9.1%) had growth of an organism on pleural effusion culture that was not identified on TTW culture. The isolate was an anaerobic bacterium, *Fusobacterium necrophorum*.

The antimicrobial susceptibility data for the most common bacterial isolates are presented in Table 3. Antimicrobial susceptibility to amikacin, cefazolin, chloramphenicol, doxycycline, enrofloxacin, gentamicin, minocycline, penicillin, tetracycline, and trimethoprim/sulfa varied greatly across bacterial species.

3.5 | Complications and survival

For the 106 horses that underwent treatment, complications were reported in 13/106 cases (12%). Laminitis occurred as a sole complication in 4/106 cases (3.7%), antimicrobial-associated diarrhea in 2/106 (1.9%), pneumothorax in 1/106 (0.94%), and thrombophlebitis in 1/106 (0.94%). Thrombophlebitis and laminitis occurred concurrently in 1/106 cases (0.94%), and thrombophlebitis, laminitis, and pneumothorax occurred concurrently in 2/106 cases (1.9%). Because of the small number of individuals in each group, the association between complications and survival was not evaluated.

The overall case fatality rate was 27% (32/116). The multivariate logistic regression for factors associated with death is presented in Table 4. Factors associated with increased risk of death were heart rate at presentation (odds ratio [OR] 1.08, 95% confidence interval [CI] 1.008-1.17, $P = .03$) and higher creatinine (OR 14.1, 95% CI 1.56-127.6, $P = .02$). Lymphocyte count (OR 0.27, 95% CI 0.08-0.94, $P = .04$) was protective against death. Univariate logistic regression is presented in supplementary materials (Table S1). Factors associated with death in the univariate regression included heart rate and respiratory rate at presentation, higher creatinine, and higher band neutrophils. Higher segmented neutrophils were protective against death.

4 | DISCUSSION

This study provides an updated description of variables associated with the development, diagnosis, management, and survival of adult horses diagnosed with bacterial pneumonia. These data highlight differences in antimicrobial susceptibility from earlier studies and provide a current description of bacterial isolates in horses with pneumonia.

The overall survival rate for horses in this study was 73% consistent with earlier studies.[1,5-13] Our data analysis identified multiple risk factors associated with death. In contrast with previous reports, the presence of specific bacterial species such as *Klebsiella* spp. or *E. coli* were not associated with death, though this could have been a result of the small number of horses from which these bacteria were isolated. Previous literature has conflicting results on the association of anaerobes with death, but the presence of anaerobes was not associated with death in this study group.[5,7-9,13,14] Similar to previous reports on colic, colitis, neonatal bacteremia, and bacterial pneumonia, higher creatinine in our study was associated with death.[7,37-40] Higher heart rate at presentation was also associated with death, although the low OR (1.08) makes this variable unlikely to be useful clinically. The finding that higher lymphocyte count was protective against death has not been previously reported. Lymphopenia is a component of the stress leukogram, and circulating endotoxin causes lymphopenia in horses.[41] It is possible that the protective nature of higher lymphocyte count reflects the fact that horses with higher lymphocyte counts have less circulating endotoxin and therefore less severe disease. Complication rates associated with bacterial pneumonia in adult horses range from 19% to 65%, whereas this study found a complication rate of 12%.[6,8,10,42] Because of the lack of a standardized means of reporting complications in the medical record system, this number is suspected to be an underestimate of the true complication rate, especially for cases of mild thrombophlebitis that might have been

TABLE 3 Susceptibility of the most common bacterial isolates to selected antimicrobials in a group of horses with bacterial pneumonia.

	Antimicrobial									
Isolate	**AMK**	**CEF**	**CHL**	**DOX**	**ENR**	**GEN**	**MIN**	**PEN**	**TET**	**TMS**
Streptococcus zooepidemicus	1/1[a] 100[b]	14/14 100	29/42 69	4/5 80	0/4 0	1/1 100	4/4 100	43/45 96	10/44 23	2/3 67
Klebsiella spp.	18/20 90	—	14/20 70	14/20 70	4/7 57	13/20 65	1/1 100	0/8 0	11/18 61	11/20 55
Non-*zoo Strep* spp.	4/4 100	—	6/6 100	3/4 75	—	2/4 50	0/1 0	3/6 50	2/6 33.3	3/4 75
Escherichia coli	19/20 95	5/5 100	16/20 80	10/15 67	8/9 89	14/20 70	1/1 100	1/8 13	11/17 65	10/20 50
Actinobacillus spp.	9/9 100	—	9/9 100	9/9 100	1/1 100	9/9 100	4/4 100	0/2 0	2/2 100	9/9 100
Enterobacter spp.	8/9 88.9	1/1 100	7/9 77.8	6/8 75	3/3 100	6/9 66.7	—	1/3 33.3	7/9 77.8	6/9 67
Staphylococcus spp.	6/6 100	0/1 0	5/6 83	4/4 100	1/1 100	6/6 100	2/2 100	0/1 0	6/6 100	6/6 100
Pseudomonas spp.	9/9 100	0/2 0	0/9[c] 0	0/2[c] 0	1/3 33	7/9 78	—	0/1 0	0/4[c] 0	0/3[c] 0

Abbreviations: AMK, amikacin; CEF, ceftiofur; CHL, chloramphenicol; DOX, doxycycline; ENR, enrofloxacin; GEN, gentamicin; MIN, minocycline; PEN, penicillin; TET, tetracycline; TMS, trimethoprim/sulfa.

[a]Number of susceptible isolates/total number of isolates tested.

[b]Percentage of susceptible isolates.

[c]Per Clinical Laboratory and Standards Institute guidelines, intrinsic resistance to this antimicrobial is expected in the designated bacterial species and results should be treated differently than those with extrinsic resistance.

TABLE 4 Multivariate logistic regression for factors associated with death in horses with bacterial pneumonia.

Variable	*B*	S.E.	Wald statistics	OR for death	95% CI	*P*
Lymphocytes (10^3 cells/μL)	−1.3	0.63	4.2	0.27	0.08-0.94	.04
Creatinine (mg/dL)	2.6	1.12	5.5	14.1	1.56-127.6	.02
HR at presentation (beats/min)	0.08	0.04	4.8	1.08	1.008-1.17	.03
RR at presentation (breaths/min)	0.03	0.02	1.6	1.03	0.9-1.07	.2
Albumin (g/dL)	−1.56	0.8	3.46	0.21	0.04-1.08	.06

Abbreviations: *B*, regression coefficient; CI, confidence interval; HR, heart rate; OR, odds ratio; RR, reference range; S.E., standard error.

treated without documentation in the medical record. Additionally, included complications varied across studies, with some studies including additional complications such as formation of pulmonary abscesses.[6,10] Other studies also tended to focus on more severe presentations of pleuropneumonia rather than the broad inclusion of all cases of pneumonia in the present study. Because of the low number of horses with reported complications in this study, it was not possible to determine their association with survival.

The presence of clinical signs and clinicopathologic abnormalities commonly associated with pneumonia were variably present in our study group highlighting the insidious nature of pneumonia and potentially explaining why the condition can remain undiagnosed for an extended period. Fever (28/110, 26%), tachycardia in (43/110, 39%), and tachypnea (48/110, 44%) were inconsistent clinical findings in the study group. These numbers are lower than previous reports, which likely reflects the broad inclusion of all horses with pneumonia in our study vs the more severe pleuropneumonia and necrotizing pneumonia cases included in these other studies.[7,16,22]

Obtaining a through history could aid clinicians in the early diagnosis of pneumonia, as 59% (68/116) of horses in this study group had 1 or more historical risk factors for development of pneumonia. Travel, especially with the head restrained, is a well-documented risk factor for pneumonia.[16-18] Head restraint prevents horses from lowering their heads to promote normal mucociliary clearance, and travel for more than 6 hours increases bacterial loads in the lower airway and reduces phagocytic activity of alveolar macrophages.[17,18] In our study group, travel and esophageal obstruction were the 2 most common historical risk factors, each occurring in 20% of horses (23/116). Esophageal obstruction can result in aspiration of feed material which leads to significant lower airway contamination and secondary pneumonia.[43] Previous or concurrent respiratory illnesses, including viral infections and inflammatory airway disease, can increase the risk of pneumonia and were present in the history of 14 horses in this study.[4,16,44] Although general anesthesia is often cited as a risk factor for pneumonia in horses no studies have demonstrated a clear link, and a recent study showed no significant difference in

ultrasonographic changes in the thorax of horses pre- and post-anesthesia for an elective procedure.[45] Further research is needed to determine if a link truly exists between general anesthesia and the development of pneumonia in horses. More uncommon risk factors for pneumonia include dysphagia of etiologies other than esophageal obstruction, esophageal perforation, and thoracic trauma, all of which were encountered in this study group.[19,20,42,43] A thorough investigation of the thorax is warranted in horses with these historical risk factors and even vague clinical signs such as lethargy and anorexia.

The aerobic bacteria most commonly isolated from this study group align well with previous reports, with *S. zooepidemicus* being the most common followed by several enteric bacteria, other *Streptococcus* spp., *Actinobacillus* spp., and *Staphylococcus* spp.[3,5,7,8,11,15,21-26] Interestingly, *Fusobacterium* was the most commonly isolated anaerobic agent in our study, in contrast to several older reports identifying *Bacteroides* spp. as the most common anaerobe in equine pneumonia.[5,9,13,15] This difference could be because of regional differences in bacterial isolates or might represent a change in etiologic agents over time as 3 more recent studies also identified *Fusobacterium* spp. as the most frequently isolated anaerobe.[3,8,14]

The 4 most common aerobic isolates in this study (*S. zooepidemicus*, *Klebsiella* spp., other *Streptococcus* spp., and *E. coli*) had ≤75% susceptibility to trimethoprim sulfa, a commonly used first-line antimicrobial because of its relatively broad spectrum, ease of administration, and low cost. Additionally, these isolates showed varying degrees of resistance to chloramphenicol and enrofloxacin, antimicrobials typically reserved for more severe cases or cases with expected antimicrobial resistance. *Streptococcus zooepidemicus* isolates retained susceptibility of 95% or greater to all beta lactams and aminoglycosides tested, indicating that these antimicrobials remain good first-line choices for horses in need of intravenous antimicrobial therapy. However, *Klebsiella* spp. and *E. coli* isolates had ≤70% susceptibility to gentamicin, one of the most common first-line intravenous antimicrobials, emphasizing the need for culture and sensitivity in cases that are unresponsive to initial therapy. Most isolates were highly susceptible to amikacin, and as such this drug should be reserved for cases with demonstrated resistance to other more common antimicrobials. Availability of anaerobic antimicrobial susceptibility data was limited because of lab protocols, and therefore conclusions cannot be drawn on the prevalence of resistance in this subset of bacteria. The presence of anaerobic bacteria in approximately 15% of samples in this study supports continued use of antimicrobials that provide adequate anaerobic coverage in the initial empiric phase of treatment. Historically metronidazole is often prescribed for its anaerobic coverage as it is known to have better activity against *Bacteroides* spp. than penicillin. However, given the decreased prevalence of *Bacteroides* spp. isolates in recent studies evaluating pneumonia, metronidazole might provide limited additional benefit over penicillin in many cases.[46] Given previous literature demonstrating significant differences in bacterial isolates and their antimicrobial susceptibility patterns among different regions and between field and referral institution samples within the same region, broad application of data from this single referral center should be performed with caution.[33-35]

The majority of horses in this study received 3-4 antimicrobials throughout hospitalization, although in 17% of cases 5 or more antimicrobials were used. Initial empiric therapy typically includes intravenous agents for aerobic coverage along with metronidazole for improved anaerobic coverage. Metronidazole was the most frequently administered systemic antimicrobial, followed by ceftiofur, penicillin, gentamicin, and enrofloxacin. Fifty-eight percent of cases underwent at least 1 transition in antimicrobial therapy during hospitalization, most commonly for de-escalation of therapy to facilitate discharge from the hospital. Only 9.4% of cases underwent 2 or more transitions in antimicrobial therapy, but not all of these cases were transitioned based on antimicrobial susceptibility testing. In cases where there is a failure to respond to initial empiric therapy repeat sampling for culture and sensitivity should be pursued to ensure judicious use of antimicrobials.

The frequent use of a fluoroquinolone and a third-generation cephalosporin is concerning from an antimicrobial stewardship standpoint because of their inclusion on the World Health Organization's highest priority critically important antimicrobials list.[30,36] These agents were used in 67% of cases, and in 63% of those cases no justification for their use was provided. The frequency of HPCIA use decreased from 78% in the first half of the study period to 62% in the second half. Despite this reduction in use, 60% of cases in the second half still had no documented reason for use. Given the advances in knowledge regarding the importance of antimicrobial resistance, stronger efforts should be made to ensure these antimicrobials are only used in cases with documented resistance to first-line antimicrobials or those with comorbidities such as azotemia that preclude the use of first-line agents such as gentamicin. Ceftiofur was commonly administered by nebulization, likely because of literature available demonstrating higher pulmonary epithelial lining fluid concentrations in foals receiving the drug by nebulization as compared to intramuscular administration.[47] However, given the lack of evidence in adult horses or any clinical studies demonstrating efficacy in horses with pneumonia, the potential clinical benefit of this therapy should be weighed against the risk of encouraging the development of resistant bacterial strains. Given that there is evidence for use of nebulized gentamicin in healthy adult horses this might be a more appropriate first-line choice if nebulized therapy is desired to expand antimicrobial coverage.[48,49] Although the antimicrobial treatment strategies detailed in this report reflect the preferences of clinicians at the authors' institution, the widespread use of HPCIAs in equine practice has been documented in previous literature and reducing unnecessary use of these agents should remain a focus for improving antimicrobial stewardship moving forward.[30,50,51]

A number of adjunctive treatments were administered in addition to standard antimicrobial therapy. The use of intravenous fluid therapy, non-steroidal anti-inflammatories, nasal oxygen supplementation, anti-endotoxemic measures, and intermittent thoracocentesis or indwelling chest tubes has been well-described.[1,7,12,22,26,52] The use of intrathoracic medications has not been as well-detailed in the literature, although the use of antimicrobials and tissue plasminogen

activator have been reported.[26,53,54] Antimicrobials were the most used intrathoracic medications in this study group, including the use of more expensive, critically important antimicrobials such as meropenem and imipenem. These therapies were often used in conjunction with systemic antimicrobials based on antimicrobial susceptibility data, but because of a lack of evidence for efficacy of antimicrobials delivered in this manner their use should be questioned from an antimicrobial stewardship standpoint. It is important for clinicians to remember that the use of HPCIA antimicrobials for local therapy such as nebulization or intrathoracic treatment still counts as use of an HPCIA, and therefore should only be done in cases with documented resistance to first-line antimicrobials. Other intrathoracic medications included n-acetylcysteine, tissue plasminogen activator, and platelet lysate (BIO-PLY), all of which function to disrupt fibrin, bacterial biofilms, or both fibrin and bacterial biofilms.[55-57] This study includes the use of platelet-rich plasma lysate (BIO-PLY) in the thoracic cavity of a horse.[55] No difference in outcome was detected with the use of any of these treatments; however, the small number of horses receiving each type of treatment could have prevented detection of differences in outcome.

The limitations of this study were primarily because of its retrospective nature and the limited availability of certain types of data within earlier medical records. Standardized forms were not present for reporting of ultrasonographic findings or complications, limiting our ability to analyze the significance of these variables. Point-of-care clinicopathologic data such as blood lactate might be performed without being recorded in the medical record, reducing the number of horses for which those variables were present for analysis. Laboratory protocols for antimicrobial susceptibility testing changed throughout the study period, with antimicrobials being added or removed from standard analysis over time. This reduced the number of isolates tested against each antimicrobial, weakening any conclusions that could be drawn from that data set. Despite a reasonably large study group, the small number of horses in each subgroup for types or species of bacteria might have limited our ability to detect significant associations with survival. Additionally, the data presented in this report reflect only the cases and management strategies at the authors' institution and might not be transferrable to general practice populations or even other referral institutions. These findings cannot be broadly applied to other geographic locations or populations.

In conclusion, this study provides an updated description of bacterial pneumonia in a group of horses with a diverse range of ages and breeds at a referral hospital. Similar to other diseases, higher creatinine was associated with death and should be taken into consideration when determining prognoses. Individual bacterial species, types of bacteria, or treatment measures were not predictive of death. The most common bacterial isolates remain similar to previous reports, although differences in anaerobic bacterial isolates were present. Resistance to common first-line antimicrobials was present in this study group. Although broad application of culture and susceptibility findings should be performed with caution given the regional and institutional variability in bacterial isolates, these findings might be useful when making future empiric antimicrobial treatment decisions for horses with pneumonia.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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SUPPORTING INFORMATION

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