The Association of Fibrinous Pleural Effusion with Survival and Complications in Horses with Pleuropneumonia (2002–2012): 74 Cases

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Background: Fibrinous parapneumonic pleural effusions are associated with decreased efficacy of pleural fluid drainage and increased risk of medical treatment failure in people, but similar associations have not been established in horses.

Hypothesis/Objectives: We hypothesized that fibrin deposition in the pleural cavity of horses with parapneumonic effusions increases the risk of poor outcome.

Animals: Seventy four horses with bacterial pleuropneumonia diagnosed by culture and cytology of tracheal aspirates, pleural fluid, or both, and pleural effusion diagnosed by ultrasonographic examination.

Methods: Retrospective study of cases was from 2002 to 2012. Information obtained from the medical records included signalment, history, sonographic findings, treatments, and outcome. The primary outcome investigated was survival and secondary outcomes were development of complications and surgical intervention. Fisher’s exact test and logistic regression were applied for categorical variables. A t-test was used to find differences in continuous variables between groups.

Results: Seventy four horses met study criteria and 50 (68%) survived. Fibrinous pleural effusion was associated with higher respiratory rate and pleural fluid height at admission, necrotizing pneumonia, increased number of indwelling thoracic drains required for treatment, and decreased survival.

Conclusions and clinical importance: Fibrin accumulation in parapneumonic effusions is associated with increased mortality. Direct fibrinolytic treatment might be indicated in affected horses.

Key words: Equine; Fibrin; Pleuritis; Pneumonia.

Pleuropneumonia remains a substantial cause of morbidity and mortality in horses. Mainstays of treatment include systemic antimicrobial administration and thoracocentesis or indwelling tube drainage of parapneumonic effusions. Reported survival rates are 30–66% and surviving racehorses had a 61% probability of returning to racing in one study. Horses with anaerobic infection have been reported to have less than half the survival rate of horses without a detected anaerobic component. A 96% survival rate was reported in 140 horses treated for pleuropneumonia, but details of diagnostic criteria and treatment were lacking.

Loculated parapneumonic effusions in people are associated with larger effusions, longer hospitalization, more frequent tube thoracotomy procedures and increased requirement for surgical intervention. These associations have been presumed to be true for horses as well, and there has been increasing interest in developing novel treatments, such as intrapleural fibrinolytic treatment, to improve outcome. We hypothesized that fibrin deposition in the pleural cavity of horses with parapneumonic effusions increases the risk of poor outcome. The primary outcome evaluated was survival and secondary outcomes were development of complications and surgical intervention.

Materials and Methods

The imaging database at New Bolton Center, University of Pennsylvania was used to identify horses that underwent thoracic ultrasonographic examinations between January 2002 and December 2012. Horses were included if they had sonographic evidence of pulmonary parenchymal disease, pleural fluid accumulation at or above a line level with the point of the shoulder at some time during hospitalization, clinical evidence of pneumonia (eg, fever, tachypnea, tachycardia, cough, pleurodynia, adventitious lung sounds, or dull lung sounds) and a pleural fluid or tracheal aspirate that was purulent on gross or laboratory examination or positive on culture for bacterial infection. A sonographic pleural fluid height level with the point of the shoulder was chosen as the height at or above which placement of indwelling thoracic drains might be considered. Horses treated with intrapleural fibrinolytic treatment were excluded (n = 2).

Information collected from the medical record included signalment, duration of clinical signs before admission, details of the admission clinical examination, admission hematology findings,
sonographic findings at admission and during follow-up evaluations, duration of hospitalization, total inpatient hospital charges, bacterial isolates, medications used, adjunctive therapies, total number of drains placed, initial volume of drainage, total duration of drainage, complications, and survival to discharge. When horses had multiple inpatient visits (n = 5), the days of hospitalization and charges were combined. If pneumonia developed in hospital secondary to anesthesia (n = 2), duration of hospitalization and total charges were excluded from analysis and admission data was taken from the first day pneumonia was diagnosed.

Sonographic examinations were performed by the ultrasound service according to a standard protocol. All visible lung and the cranial mediastinum were imaged from caudal to cranial intercostal spaces. Pulmonary parenchymal pathology was defined as previously described and reported as consolidated, necrotic, or abscessed. Areas of hypoechoic lung were considered consolidated if the affected hypoechoic area maintained its normal size and wedge shape. Consolidated areas could contain hyperechoic linear structures filled with gas echoes (consistent with air bronchograms), hyperechoic linear structures filled with fluid (consistent with fluid bronchograms), pulmonary vessels, or some combination of these. If the affected area appeared gelatinous with respiration and contained no recognizable architecture, it was classified as necrotic. An abscess was diagnosed if a discrete cavitated area was identified containing a variable amount of fluid, gas, or both and no recognizable pulmonary architecture. Pleural abscesses were defined as discrete regions in the pleural space that contained fluid, gas, or both and were walled off from surrounding structures. For this report, horses were classified as having a bronchopleural fistula if there was a pleural abscess with a dorsal gas cap, a large dorsal pneumothorax, fluid observed draining from the nose during pleural lavage, or a fistula detected at postmortem examination. Fibrin in the pleural space was imaged as filmy or filamentous strands, hypoechoic relative to aerated lung, suspended in the pleural fluid, and separate from the pericardiodiaphragmatic ligament. In horses that were euthanized and had a necropsy performed, final classification included postmortem examination findings. On postmortem examination, a pulmonary sequestrum was defined as a walled-off necrotic focus of pulmonary parenchyma and an abscess was defined as a well-demarcated, but not necessarily walled-off accumulation of purulent material. Horses with sequestra were included in the necrotizing pneumonia classification. In cases for which ultrasound and postmortem examination findings disagreed, the following classification was made: the diagnosis of abscess or necrosis was based on postmortem examination, and the diagnosis of fibrin was made if fibrin was identified by sonography or necropsy. The maximal fluid height at admission was reported as the higher of the 2 fluid levels in the hemithoraces if they differed.

Complications recorded were pleural abscess, bronchopleural fistula, cranial mediastinal abscess, lamenitis (Obel grade ≥1 or radiographic evidence of rotation or distal displacement of the third phalanx), coagulopathy, colic, colitis, immune-mediated hemolytic anemia, seizure, cardiac arrhythmia, and pericarditis.

Two classification schemes were used for analysis based on the presence of pleural fibrin at admission (admission fibrinous [F₃] and admission nonfibrinous [NF₄] groups), or at any time during hospitalization (overall fibrinous [F₄] and overall nonfibrinous [NF₃] groups). The association of fibrinous effusion with the dichotomous variables survival, complication, surgical intervention, necrotizing disease, aerobic infection, E. coli infection, anaerobic infection, gas echoes in the pleural fluid, foul odor to breath or pleural fluid, treatment with any antibiotic before admission, treatment with metronidazole before admission, whether the horse was a racehorse or not, whether a surviving racehorse returned to racing or not, and whether a surviving racehorse won a race or not was investigated by Fisher’s exact test. The association of fibrinous effusion with the continuous variables age, admission findings (respiratory rate, heart rate, temperature, peripheral blood leukocyte count, plasma fibrinogen concentration, maximal pleural fluid height, pleural fluid nucleated cell count, and pleural fluid total solids), duration of clinical disease before presentation, number of indwelling drains placed, duration of pleural drainage, duration of hospitalization, and total hospital charges was investigated by independent samples t-test. Variables were interrogated by Tukey’s ladder test to determine the best transformations to achieve normality. Total hospital charges were transformed by natural logarithm. Duration of drainage and duration of hospitalization were transformed by square root. The association of fibrinous effusion with the categorical variables breed and sex (intact male, gelded male, female) was investigated with binary logistic regression. Duration of clinical disease before admission was investigated by natural logarithm transformation to normal data and alternatively by condensing into 3 categories based on descriptions of the stages of pleuropneumonia: 0–4 days, 5–14 days, and >14 days.9 The association between each type of complication and fibrinous effusion was investigated using Fisher’s exact test.

Variables that could affect the outcomes of survival, having a complicated course, and surgical intervention were interrogated with Fisher’s exact test for dichotomous variables, independent samples t-test for continuous variables, and binary logistic regression for categorical variables. Dichotomous variables were complication, surgical intervention, necrotizing disease, epistaxis, aerobic infection, E. coli infection, anaerobic infection, gas echoes in the pleural fluid, foul odor to breath or pleural fluid, use of indwelling thoracic drains, treatment with any antibiotic before admission, and treatment with metronidazole before admission. Because foul odor, gas echoes, and positive anaerobic culture can all indicate anaerobic infection,17 combinations of these variables (gas, odor, or both; culture, odor, or both; gas, culture, or both; or any of gas, culture, or odor) also were considered. Continuous variables were age, admission findings (respiratory rate, heart rate, temperature, peripheral blood leukocyte count, plasma fibrinogen concentration, maximal pleural fluid height, pleural fluid nucleated cell count, pleural fluid total solids), duration of clinical disease before presentation, number of indwelling drains placed, duration of hospitalization, and total hospital charges. Categorical variables were breed and sex. The same transformations were made for each variable as described above.

Significant associations between dichotomous variables were age, complication, surgery, and anaerobic infection were investigated using Fisher’s exact test. The association of necrotizing pneumonia with total hospital charges and duration of hospitalization was investigated with independent samples t-test using the transformations described above. The association of pleural gas echoes with anaerobic infection and survival was investigated using Fisher’s exact test separately for gas echoes identified at admission and for gas identified at any time during hospitalization.

Horses were identified as racehorses if the medical record referred to a recent race or race training, or they had raced within the previous year. Race records for all horses were followed until September 1, 2014.8 The previously published survival rates for horses with culture-confirmed anaerobic pneumonia were obtained from 3 previous studies published between 1985 and 1991.4,7,17 All 3 studies were performed at the same hospital as this study. These were compared with the current results using Fisher’s exact test to determine if the survival rate from anaerobic pneumonia has improved.

Statistical tests were performed with commercial software.9 Significance was set at P < .05.
Results

Signalment and Clinical Findings

Records of 74 horses were obtained for analysis. There were 31 (42%) females, 16 (22%) intact males, and 27 (36%) geldings. The median age was 5 years old (range, 14 days – 20 years). The breeds represented were 50 (68%) Thoroughbred, 10 (13%) Standardbred, 8 (11%) Quarter Horse, and 6 horses of other breeds. Clinical findings are presented in Table 1.

Seventy horses had aerobic bacterial culture performed and 63 (90%) cultures were positive. Thirtythree horses had anaerobic bacterial culture performed and 22 (35%) cultures were positive. Multi-bacterial infection was present in 21/63 (33%), with a median of 2 isolates cultured (range, 0–5; IQR, 1–3). The most common isolates were Streptococcus spp. (39; with 37 Streptococcus equi ssp. zooepidemicus), Escherichia coli (16), Actinobacillus equi (8), Enterococcus spp. (5), and Klebsiella spp. (5). The 2 most common anaerobic isolates were Prevotella spp. (12) and Bacteroides spp. (8).

Treatment

Antimicrobials were used in combination and frequently were switched from IV to PO route of administration during hospitalization. Horses in this study received penicillin (56), gentamicin (46), enrofloxacin (21), metronidazole (53), trimethoprim-sulfamethoxazole (23), chloramphenicol (17), rifampin (13), amikacin (5), ceftiofur (3), oxytetracycline (3), ampicillin (2), erythromycin (2), clarithromycin (1), ticarcillin (1), and doxycycline (1).

Indwelling thoracic drains were placed in 1 or both hemithoraces in 47/74 (64%) horses. Only 6 horses in the NF\textsubscript{A} and 1 horse in the NF\textsubscript{O} group underwent pleural fluid drainage with indwelling drains. The initial volume of pleural fluid drained was recorded in 44 horses and the median was 10 L (range, 0–60 L; IQR 6–16 L). Of horses that had indwelling drains, a median of 2 drains were placed during hospitalization (range, 1–5 drains) for a median duration of drainage of 4 days (range, 0–20 days; IQR, 2.75–7 days). Horses with NF\textsubscript{A} or NF\textsubscript{O} effusions had significantly fewer indwelling thoracic drains placed per horse (admission P = .039, overall P < .001) than horses with fibrinous effusions. When recorded, the reasons for removing or replacing drains were described as resolution of the pleural fluid to below the level of the drain (15), failure to drain loculated fluid (6), obstruction of the drain (3), or insertion site cellulitis (1).

Table 1. Description of findings for 74 horses with pleuropneumonia and pleural fluid at or above the point of the shoulder. Cases were subdivided into 2 groups based on the deposition of fibrin in the pleural space at any time during hospitalization. Data are expressed as number of horses (percent of the group) for dichotomous variables or median (IQR) for continuous data. Significant P-values are in bold. PF, pleural fluid; DPOS, dorsal to the point of the shoulder.

| Case                                | All Cases | NF\textsubscript{O} | FO | P-value |
|-------------------------------------|-----------|---------------------|----|---------|
| Cases                               | 74        | 11                  | 63 | .013    |
| Survived                            | 50 (68%)  | 11 (100%)           | 39 (62%) | .0024 |
| Duration prior (days)               | 7 (3–14)  | 4 (1.75–13)         | 7 (3–14) | .68    |
| Temperature (°C)                    | 38.6 (38.0–39.1) | 38.6 (38.3–39.2) | 38.6 (38.0–39.0) | .76    |
| Heart rate (bpm)                    | 53 (48–60) | 48 (40–56)         | 55 (48–60) | .44    |
| Respiratory rate (brpm)             | 30 (24–40) | 24 (21–27)         | 30 (20–44) | .0048  |
| White blood cell count (× 10\textsuperscript{9} cells/L) | 10.5 (6.25–15.5) | 8.70 (5.42–12.6) | 11.1 (6.45–15.7) | .13    |
| Fibrinogen (g/L)                    | 10.50 (7.77–12.39) | 8.55 (7.44–10.60) | 11.14 (7.88–12.58) | .15    |
| Max PF height (cm DPOS)             | 9 (0–14.5) | 0 (0–0)            | 10 (4–15.75) | .001   |
| PF nucleated cell count (× 10\textsuperscript{9} cells/L) | 50.0 (30.3–89.0) | 126 (98.6–134) | 47.8 (27.5–82.8) | .13    |
| PF total solids (g/L)               | 48 (45–55) | 45 (45–52)         | 48 (46–55) | .97    |
| Aerobic culture positive            | 63 (90%)  | 9 (11) (82%)       | 15 (92%) | .30    |
| E. coli                             | 16 (23%)  | 1 (11) (9%)        | 15 (25%) | .44    |
| Anaerobic culture positive          | 22 (35%)  | 4 (11) (36%)       | 18 (52%) | .018   |
| Necrotizing parenchyma              | 40 (54%)  | 2 (11) (18%)       | 38 (60%) | .024   |
| Foul odor at any time               | 22 (30%)  | 1 (11) (9%)        | 21 (34%) | .16    |
| Indwelling drains (no.)             | 1 (0–2)   | 0 (0–0)            | 1 (0–2) | .0024  |
however, necrotizing pneumonia was not significantly associated with F_A. The pleural fluid white blood cell count was significantly lower in the F_A group (n = 36, median 46.0 × 10⁹ cells/L, IQR 26.0–79.5 × 10⁹ cells/L) than the NF_A group (n = 5, median 120 × 10⁹ cells/L, IQR 110–126 × 10⁹ cells/L; P = .0052), however, there was no difference between the F_O and NF_O groups. For all other variables tested, the significance was the same for overall and admission fibrinous groupings. Horses with NF_A pleuropneumonia were more likely to survive than horses with F_A pleuropneumonia (88% versus 61%, P = .043).

There was no significant association between the presence of pleural fibrin at admission or overall and the occurrence of complications (Table 3), duration of hospitalization or total hospital charges (Table 4), or the rate of return to racing or winning a race after recovery for surviving racehorses (Table 5).

### Outcomes

Significant associations are presented for the outcomes of development of complication, surgical intervention, and survival (Table 6). The presence of any combination of gas echoes, odor, anaerobic infection, or some combination of these also was associated with an increased odd of complication (P ≤ .037). There was a trend toward decreased survival with necrotizing pneumonia (24/40, 59% versus 26/33, 79%, P = .083). All other variables tested were not significantly associated with these outcomes. Necrotizing pneumonia was not associated with total hospital charges or duration of hospitalization.

The majority of horses (48/74, 65%) developed at least 1 complication (Table 3) and there was no association between complications and survival (P = .60). An additional horse developed severe laminitis 1 week after discharge and was euthanized at home.

Three horses had both pleural abscesses and bronchopleural fistula and 2 survived. Eight horses had bronchopleural fistula and 3 survived. One was the horse that died 6 months later and 1 was a Thoroughbred racehorse.

### Table 2

Selected thoracic pathologic findings in 74 horses with pleuropneumonia as detected by sonography or postmortem examination. Presented as the number of horses that had the findings present at admission to the hospital, and the total number that developed the finding at some point during hospitalization.

| Pathologic Finding   | Present at Admission | Present at Any Time |
|----------------------|----------------------|---------------------|
| Consolidation        | 68                   | 70                  |
| Gas echoes suggestive of anaerobes | 29   | 43                  |
| Necrosis             | 25                   | 42                  |
| Pulmonary abscess    | 14                   | 29                  |
| Bronchopleural fistula | 4    | 8                   |
| Pleural abscess      | 2                    | 13                  |
| Pleural fibrin       | 57                   | 63                  |

### Table 3

The prevalence of and survival with complications in 74 horses with bacterial pleuropneumonia. The P-values for the association of pleural fibrin with the occurrence of complications are shown.

| Complication       | No. Horses (n = 74) | No. Survived (%) | NF_O (n = 11) | F_O (n = 63) | P-value |
|--------------------|---------------------|------------------|---------------|--------------|---------|
| No complication    | 25                  | 19 (76)          | 4             | 21           |         |
| Any complication   | 49                  | 31 (63)          | 7             | 42           | 1.0     |
| Coagulopathy       | 27                  | 17 (63)          | 3             | 24           | .74     |
| Pleural abscess    | 13                  | 9 (69)           | 0             | 13           | .19     |
| Laminitis          | 12                  | 6 (50)           | 2             | 10           | 1.0     |
| Colic              | 8                   | 7                | 2             | 6            | .34     |
| Bronchopleural fistula | 8   | 3                | 0             | 8            | .60     |
| Pericarditis       | 6                   | 2                | 0             | 6            | .58     |
| Colitis            | 5                   | 3                | 1             | 4            | .56     |
| Immune-mediated hemolytic anemia | 3 | 1 | 0 | 3 | 1.0 |
| Cardiac arrhythmia | 3                   | 3                | 0             | 3            | 1.0     |
| Seizures           | 1                   | 1                | 0             | 1            | 1.0     |
| Cranial mediastinal abscess | 1 | 1 | 0 | 1 | 1.0 |

### Table 4

Duration of hospitalization and total hospital charges for 74 horses with pleuropneumonia and pleural fluid at or above the point of the shoulder. Cases were subdivided into 2 groups based on the deposition of fibrin in the pleural space at any time during hospitalization. Data are expressed as median (IQR).

|                | All Cases | NF_O | F_O | P-value |
|----------------|-----------|------|-----|---------|
| Cases          | 74        | 11   | 63  |         |
| Duration (days)| 9 (5.25–16) | 8 (7–15) | 9 (4–17) | .91     |
| Inpatient charges ($US) | 5,314 (3,649–7,118) | 4,827 (3,725–5,507) | 5,687 (3,636–7,297) | .86     |
horse that returned to racing. Two horses suffered generalized seizures. In 1 horse, a seizure disorder was the primary complaint and pleuropneumonia was secondary. In the other horse, however, seizures were felt to be a complication of treatment. Coagulopathy was detected in 27 horses as evidenced by jugular vein thrombosis (14), abnormal coagulation profile (10), pulmonary thromboembolism (6), petechiation (6), or prolonged bleeding from venipuncture sites (2).

Surgical intervention (ie, thoracotomy) was performed in 5 horses for lung lobectomy (1) or drainage of pleural abscesses that had failed to resolve with medical management (4). One horse with a pleural abscess treated by thoracotomy died suddenly 6 months after discharge. No horse in the NF_F group required thoracotomy, although 1 horse in the NF_A group that subsequently developed fibrin underwent thoracotomy.

Fifty horses (68%) survived to discharge and 24 died or were euthanized. Six were euthanized before treatment because of poor prognosis (4) or the presence of concurrent medical problems (1 prior arytenoidectomy with ongoing aspiration, 1 arytenoid chondritis and guttural pouch mycosis) and 1 horse died spontaneously the first night of hospitalization. The reason for euthanasia was not clear from the medical record of 1 horse. Euthanasia was chosen in the remaining 16 because of poor response to treatment or deterioration (8), financial considerations (6), development of laminitis (1), and tibial fracture sustained during a generalized seizure (the horse with primary neurologic disease; 1).

Postmortem examination was performed on 20/24 horses that were euthanized. Eleven of 15 horses with necrotizing pneumonia confirmed at postmortem examination were identified sonographically ante-mortem. In the remaining 4 horses, the necrosis was focal and described as a developing sequestrum (n = 1) or was identified histologically and not on gross examination (n = 3). No case was falsely identified as necrotizing by sonography. Two of 6 pulmonary abscesses confirmed at postmortem examination were detected sonographically. In the other 4 cases, the abscessed region was described as necrotizing based on sonography in 3, and in the last case the abscess was ruptured at postmortem examination and was considered a pleural abscess sonographically. Two horses had pulmonary abscesses suspected sonographically that were not confirmed at

| Variable | Outcome Absent | Outcome Present | P-value | Odds Ratio (95% CI) |
|----------|----------------|----------------|---------|--------------------|
| Age (years) | 3 (2–5) | 6 (3–8) | .0096 | |
| Gas echoes | 8/25 (32%) | 35/48 (73%) | .0011 | 5.7 (2.0–16) |
| Foul odor | 3/25 (12%) | 19/48 (40%) | .017 | 4.8 (1.3–18) |
| Necrotizing | 7/24 (29%) | 33/49 (67%) | .0028 | 5.0 (1.7–15) |
| Total charges ($US) | 4887 (3208–6899) | 7338 (6239–20490) | .046 | |

| Variable | Outcome Absent | Outcome Present | P-value | Odds Ratio (95% CI) |
|----------|----------------|----------------|---------|--------------------|
| Age (years) | 5 (3–7) | 3 (3–3) | .05 | |
| Fibrinous overall | 24/24 (100%) | 39/50 (78%) | .013 | |
| Fibrinous admit | 22/24 (92%) | 35/50 (70%) | .043 | 0.21 (0.44–1.0) |
| Foul odor | 12/23 (52%) | 10/50 (20%) | .015 | 0.27 (0.097–0.78) |
| Had drains | 20/24 (83%) | 27/50 (54%) | .017 | 0.23 (0.070–0.77) |
| Max PF height (cm DPOS) | 13 (9.1–17) | 7.2 (4.5–10) | .016 | |
| Respiratory rate (brpm) | 38 (32–44) | 30 (26–34) | .044 | |
| Days in hospital | 3 (0–7) | 15 (8–17.5) | <.001 | |
| Total charges ($US) | 3747 (1385–4504) | 6334 (4815–8367) | <.001 | |

**Table 5.** Prognosis for survival and racing for horses treated for pleuropneumonia with pleural fluid at or above the point of the shoulder. Cases were subdivided into 2 groups based on the deposition of fibrin in the pleural space at any point during hospitalization. Data are expressed as number of horses (percent of the group). The P-value presented is based on the combined data for TB and SB. TB = Thoroughbred, SB = Standardbred.

| Variable | Outcome Absent | Outcome Present | P-value | Odds Ratio (95% CI) |
|----------|----------------|----------------|---------|--------------------|
| Age (years) | 3 (2–5) | 6 (3–8) | .0096 | |
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**Table 6.** Variables significantly associated with the outcomes of developing a complication, surgical intervention, and survival. Continuous data are presented as median (interquartile range).
postmortem examination; the pathology report for 1 of these described hyperinflation in the lung lobe where an abscess was suspected, and in the other horse a sequestrum was identified on postmortem examination in the region where an abscess was diagnosed sonographically. In 17 of 18 horses with consolidation confirmed at postmortem examination the consolidation was identified sonographically. In the other horse, 1 day had elapsed between the final sonographic examination and the time of euthanasia. In 1 horse, fibrin was detected at postmortem examination but not sonographically. In 2 horses, pleural lesions were fibrous by the time of euthanasia but had been diagnosed as fibrinous sonographically.

Gas echoes in the pleural fluid at admission or at any time during hospitalization were not associated with positive anaerobic culture or survival. Despite foul odor being significantly associated with decreased survival (Table 6), anaerobic culture results were not associated with survival. Ten horses had foul odor with no anaerobic growth on culture, and 15 had anaerobic culture growth but no odor. The survival rate from culture-confirmed anaerobic infection in this study (14/22, 64%) was higher than that reported in the 1980s (49/129, 38%, \( P = .0012 \)).

**Discussion**

The majority of horses with parapneumonic effusions (63/74, 85%) developed pleural fibrin, which was associated with increased mortality. Pleural inflammation induces production of tumor necrosis factor alpha (TNFα), which is associated with increased release of plasminogen activator inhibitor-1 (PAI-1). The imbalance between PAI-1 and tissue plasminogen activator (TPA) is thought to result in fibrin accumulation in the pleural space. At the time of pleural fluid analysis (admission), pleural fibrin (Fp) was associated with lower pleural fluid cell counts, but the cell count was not associated with, or predictive of, the presence of fibrin over the course of hospitalization (Fp). The low cell counts could be a spurious result because of low case numbers and multiple comparisons. Alternately, they could be because of a dilutional effect from the large volumes associated with fibrinous effusions, trapping of cells within the fibrin, or degeneration of neutrophils resulting in falsely lowered cell counts. In people, no association has been found between pleural fluid cell count and pleural fibrin.

As in people, fibrin deposition was associated with larger pleural effusions and increased use of tube thoracotomy. Larger pleural effusions could be a result of fibrin loculations trapping fluid in the pleural space and preventing natural reabsorption through the body’s lymphatics. Alternatively, large pleural effusions could be a consequence of a similar inflammatory mechanism underlying fluid and fibrin deposition in the pleural space. Based on our findings, pleural fluid above the level of the point of the shoulder at admission is a fairly accurate predictor of the presence or development of a fibrinous effusion and therefore could have prognostic implications. The increased number of thoracotomy tubes required for treatment could be consistent with decreased efficacy of drainage in the presence of fibrin or ongoing production of fluid.

We showed that fibrin accumulation is significantly associated with decreased survival. This could be because of decreased efficacy of drainage and the resultant difficulty clearing infection and removing inflammatory mediators, fibrin pleural fluid, and fibrin loculations trapping fluid in the pleural space. Larger pleural effusions could be a result of larger pleural effusions and increased use of tube thoracotomy. Larger pleural effusions could be a result of decreased survival. This could be because of the larger effusions, adhesions between the visceral and parietal pleura, or more severe parenchymal disease. If the cause of increased mortality is directly related to increased pleural fluid trapping and decreased efficacy of pleural drainage, then treatments aimed at decreasing pleural fibrin could have a positive effect on outcome.

Although surgical interventions (thoracotomy or thoracoscopy) have been proposed to remove pleural fibrin, to the authors’ knowledge few referral hospitals have adopted these approaches as routine treatment methods. This suggests that pursuing alternate medical treatments such as intrapleural fibrinolytic treatment could be warranted.

Complications were common and were more likely to occur in horses that had pleural gas echoes, anaerobic infection, foul odor, or necrotizing disease, which all can be signs of increased severity. However, surgical intervention remained a rare occurrence at this hospital. Although no horse in the NF group required thoracotomy, the study was underpowered to detect a statistically significant association with fibrin deposition. Other risk factors also might not have been detected by this investigation.

The overall survival rate from pleuropneumonia has not improved since previous reports. This population had a 67% survival compared to 30–66% reported previously. This is despite improved survival in the subpopulation of horses with culture positive anaerobic infection. There was a significant economic recession during the time period represented by this study, and financial considerations contributed to treatment and euthanasia decisions. In contrast, we report a higher percentage of surviving racehorses returning to racing (75%) than has been recorded previously (60%). All 3 studies have
small numbers, and this result could be spurious, or it could reflect increased attempts to return to racing by owners who have been counseled that a return to racing is possible after the previous reports. Of note, if horses with pleural fibrin survived, they were no less likely to return to racing or to win a race than horses without pleural fibrin. Given this observation and the fact that the hospital charges and duration of hospitalization were similar between fibrinous and nonfibrinous groups, treating owners with pleural fibrin could be justified despite the poorer prognosis.

Previously reported negative prognostic indicators were anaerobic infection,7,17 foul odor,7 pleural gas echoes,7,21 infection with E. coli,2,3 and necrotizing pneumonia.17 The survival with anaerobic pleuropneumonia has significantly improved and is now similar to that of horses with aerobic pleuropneumonia. This change could be because of increased awareness of and prompt treatment for anaerobic infection. In earlier reports, the survival rate of horses with anaerobic pneumonia was half that of horses with aerobic infection only.7,17,20 Though the reports emphasize the importance of specific anti-anaerobic treatment. In our hospital, horses are routinely treated with penicillin, which covers most aerobes except for Bacteroides fragilis. Because of the previous reports, however, metronidazole now is frequently used, with 72% of horses in this study receiving metronidazole during hospitalization and 22% of horses receiving metronidazole before admission. Interestingly, B. fragilis did not affect many horses in this group (only 8 horses had Bacteroides, and the organisms were not specified). Thus, it is unclear if the improvement in survival was because of increased anti-anaerobic spectrum, better ability of metronidazole than penicillin to reach necrotic tissue, or a synergistic effect of multiple anti-anaerobic antimicrobials, or some other factor.

Foul odor to the breath or pleural fluid was associated with increased mortality, but anaerobic culture results and any combination of culture, odor, and pleural gas echoes were not. Foul odor has been consistently associated with decreased survival,7,17 but the findings regarding the prognostic value of anaerobic culture and the presence of gas echoes in the pleural fluid have varied. Previously 62–63% of horses with anaerobic infections developed foul odors,7,17 whereas in our study only 35% developed foul odors. This difference could be because of increased use of antimicrobials with anti-anaerobic spectrum before and after admission to the hospital. Because our overall survival rate with anaerobic pleuropneumonia is improved and our rate of developing odor is decreased compared to previous reports, this observation suggests that odor could be related to severity of disease, possibly through the number of bacteria required to produce a noticeable odor, the pathogenicity of the bacteria, the location of infection, or the amount of necrotic tissue present.

The presence of gas echoes in the pleural fluid at admission was not associated with either anaerobic infection or decreased survival in contrast to a previous report.15 Anaerobic culture might be less sensitive now because of increased use of antimicrobial treatment with anti-anaerobic spectrum before admission. Fourteen horses that did not have pleural gas at admission developed pleural gas echoes after thoracocentesis, which could be caused by inadvertent introduction of air during the procedure. Pleural fluid culture was not repeated in these horses. E. coli infection was not associated with increased mortality in this study. In our study, 8/16 (50%) horses with E. coli infection survived, whereas previously 2/11 (18%) and 3/14 (21%)2 survived, respectively. The reason for this difference is not clear except that in all 3 studies, there were small numbers of horses with E. coli infection, which could have skewed the results. Also, E. coli infection was associated with chronic infection in a previous study,2 but this was not true in the current population, for which the median duration of clinical disease before admission for horses with E. coli infection was nearly the same as for horses without E. coli infection (7 days versus 6 days).

Necrotizing pneumonia and epistaxis (frequently presumed to be secondary to a necrotizing component of disease) were not associated with increased mortality in our study. This finding is surprising because necrotizing disease has been presumed to be more severe and would logically carry a more guarded prognosis. Also, previous results from this institution have suggested that necrotizing pneumonia was a significant risk factor for mortality21, which has influenced counseling of clients. In the current population, 40 horses were diagnosed with necrotizing pneumonia primarily based on sonographic findings, and 6 of these were euthanized with an attempt to treat because of multiple anti-anaerobic antimicrobials. Of the 34 horses with necrotizing pneumonia that were treated, however, 24 (70%) survived. It is impossible to know retrospectively whether those that were euthanized immediately had more severe disease, thus skewing this interpretation, but the survival rate of those treated suggests that clinicians should not consider sonographic evidence of necrotizing disease alone as a reason to recommend euthanasia.

In conclusion, the prognosis for horses with anaerobic pleuropneumonia appears to have improved in the last 2 decades. However, the overall survival rate for horses with pleuropneumonia has not improved. This study demonstrates that most horses with pleuropneumonia develop fibrinous effusions, and that fibrin accumulation is associated with decreased survival. Based on these findings, fibrinolytic treatment should be pursued as a next step in attempting to improve survival.

Footnotes

a Thoroughbred records from equibase.com last accessed September 1, 2014. Standardbred lifetime racelines from the United States Trotting Association on October 22, 2014.
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Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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