Case-control study of risk factors for development of pleuropneumonia in horses

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Summary: *Risk factors for development of pleuropneumonia were determined by reviewing medical records of 45 horses with pleuropneumonia and 180 control horses examined between Jan 1, 1980 and Jan 1, 1990. Factors considered included age, breed, sex, occupation, transport farther than 500 miles within the previous week, racing within the previous 48 hours, viral respiratory tract infection or exposure to horses with viral respiratory tract disease within the previous 2 weeks, and vaccination against influenza or rhinopneumonitis within the previous 6 months. Results indicated that Thoroughbreds were at a greater risk of developing pleuropneumonia than were other horses, and Standardbreds were at a reduced risk. Transport farther than 500 miles and viral respiratory tract disease or exposure to horses with respiratory tract disease were determined to be risk factors for the development of pleuropneumonia.*

In horses, pleuropneumonia is described as pleuritis or pleural effusion secondary to pneumonia or pulmonary abscesses and can be a devastating disease. In early reports, for instance, between 30 and 62% of affected horses died or were euthanatized,[1-5] and survivors were often unable to return to their previous level of performance because of residual effects of the disease.[1,2,6] More recently, authors of a retrospective study[7] reported a survival rate of greater than 95% for horses affected with pleuropneumonia. The high survival rate was attributed to early identification of pleural involvement, timely recognition of sequelae through the use of diagnostic ultrasonography, and early institution of appropriate treatment.

Although horses of any age, breed, or sex may develop pleuropneumonia, young Thoroughbred and Standardbred racehorses have most commonly been reported to be affected.[2,8] Pleuropneumonia has been associated with transport farther than 500 miles and with recent viral respiratory tract disease,[2,5,7,9,10] but controlled studies have not, to our knowledge, been performed to assess whether these factors increase the risk that horses will develop pleuropneumonia. The purpose of the study reported here was to determine whether age, breed, sex, occupation, recent transport farther than 500 miles, recent viral respiratory tract disease or exposure to horses with viral respiratory tract disease, or inadequate vaccination against respiratory tract viruses are significant risk factors for the development of pleuropneumonia in horses.

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Methods

Case selection—Medical and necropsy records of horses referred to the veterinary teaching hospital between Jan 1, 1980 and Jan 1, 1990 were reviewed. All horses with pleuropneumonia in which the diagnosis had been confirmed by means of thoracentesis, diagnostic ultrasonography, or necropsy were included in the study. Horses with pleural effusion secondary to neoplasia or penetrating thoracic wounds were excluded from the study, because risk factors would be different for these conditions.

Control selection—For each identified case of pleuropneumonia, 4 control horses (controls) were selected randomly from all horses referred to the veterinary teaching hospital during the study period that did not have infectious respiratory tract disease. A ratio of 4 controls/case represents the most efficient case:control ratio.[11]

Data collection—Information obtained for all horses included age, breed, sex, occupation, and reason the horse was referred to the veterinary teaching hospital. Additional information obtained for horses with pleuropneumonia included clinical signs, duration of illness, whether the horse had been transported more than 500 miles within the week prior to the onset of clinical signs of pleuropneumonia, whether the horse had raced within the 48 hours prior to onset, whether the horse had been exposed to horses with respiratory tract disease or had had viral respiratory tract disease in the 2 weeks prior to onset, and whether the horse had been vaccinated against influenza or rhinopneumonitis in the 6 months prior to the onset. Additional information obtained for control horses included whether the horse had been transported more than 500 miles within the week prior to admission to the hospital, whether the horse had raced within 48 hours prior to admission, whether the horse had been exposed to horses with viral respiratory tract disease or had had viral respiratory tract disease in the 2 weeks prior to admission, and whether the horse had been vaccinated against influenza or rhinopneumonitis in the 6 months prior to admission. All information was obtained from standard forms completed at the time the horses were first admitted to the hospital.

Data analysis—Unadjusted odds ratios (OR) and their 95% confidence intervals (CI) were calculated for each potential risk factor.[11,12] Stepwise multiple logistic regression was performed to adjust the OR for multiple risks and to identify the most important risk factors.[13,14] Only risk factors for which the Fisher exact test of whether the unadjusted OR was significantly different from 1 yielded a P value ≤ 0.30 were included in the logistic analysis.

Results

Our review yielded records of 45 horses in which pleuropneumonia had been diagnosed and that could be included in the study. Twenty-five of the 45 (56%) horses had been referred because of suspected chronic pneumonia or pleuropneumonia that was not responsive to treatment. Other reasons for referral included acute respiratory distress (6 horses), weight loss (5), recurrent fever (5), colic (3), chronic cough (2), laminitis (2), and myositis (1).

Table 1—Unadjusted odds ratios for development of pleuropneumonia among 45 horses with pleuropneumonia (cases) and 180 control horses (controls)

Risk factor	No. of cases n = 45	No. of controls n = 180	Odds ratio*	95% Confidence interval
Sex				
Male, sexually intact	9	36	1.0	0.4 to 2.3
Gelding	15	59	1.0	0.5 to 2.0
Female, sexually intact	21	85	1.0	0.5 to 1.9
Breed				
Thoroughbred	23	33	4.7	2.2 to 9.3
Standardbred	7	62	0.4	0.1 to 0.8
Quarter Horse	8	42	0.7	0.3 to 1.6
Other	7	43	0.6	0.2 to 1.4
Age				
< 2 Years old	5	28	0.7	0.2 to 1.9
2 to 6 Years old	31	104	1.6	0.8 to 3.2
> 6 Years old	9	48	0.7	0.3 to 1.5
Transport farther than 500 miles	16	10	9.4	3.9 to 22.7
Recent viral respiratory tract infection	7	7	4.8	1.5 to 13.7
Not vaccinated against influenza†	9	49	0.7	0.3 to 1.8
Not vaccinated against rhinopneumonitis†	10	57	0.6	0.3 to 1.7
Occupation				
Other	1	5	0.8	0.1 to 7.0
Racing	24	71	1.8	0.9 to 3.4
Showing	7	25	1.1	0.5 to 2.8
Breeding	4	23	0.7	0.2 to 2.0
Pleasure	4	22	0.7	0.2 to 2.2
None	5	34	0.5	0.2 to 1.5
Recent race‡	12	23	2.3	0.9 to 6.1

*Represents how much more likely a horse with the factor would be to develop pleuropneumonia, compared with all horses without the factor. †Information was available for only 24 of the 45 horses with pleuropneumonia and for only 113 of the 180 control horses. ‡Information regarding recent racing was limited to 24 of 45 horses with pleuropneumonia and to 71 of 180 control horses that were racehorses.

The most common clinical sign in these horses was tachypnea (43 horses). Abnormalities detected during thoracic auscultation included muffled lung sounds ventrally (37 horses), crackles over the dorsal lung fields (9), and pleural friction rubs (2). Percussion was helpful in identifying horses with pleuropneumonia, and a pleural fluid line was detected in 28 of the 29 (97%) horses for which percussion findings were recorded. Pleural fluid was bilateral in 31 horses and septic in 23 of the 36 horses for which bacteriologic culture results were available. Eighteen horses had a fever at admission (rectal temperature > 39 C). Other clinical signs included dyspnea (30 horses), nasal discharge (22), cough (21), ventral edema (20), and pleurodynia (16).

To allow comparisons with the 45 cases of pleuropneumonia, 180 randomly selected controls also were included. Most of the controls (79 horses) had been referred because of musculoskeletal abnormalities. Other reasons for referral included gastrointestinal tract abnormalities (25 horses), reproductive system abnormalities (19), respiratory tract disorders that were not infectious (13), traumatic wounds (13), neurologic disorders (8), ophthalmic disorders (6), and integumentary disorders (6). Six horses were referred for various other miscellaneous reasons, and 5 were referred for prepurchase examinations.

In the univariate analyses, age, sex, and occupation were not found to be risk factors for the development of pleuropneumonia (Table 1). However, Thoroughbreds were more likely than other breeds to develop pleuropneumonia, and Standardbreds were less likely. Horses that had a history of recent exposure to horses with a viral respiratory tract infection or that had a history of recent viral respiratory tract disease were at a greater risk for development of pleuropneumonia than were nonexposed and unaffected horses, but failure to vaccinate against influenza and rhinopneumonitis, 2 common respiratory tract diseases, was not found to be a risk factor. Recent transport farther than 500 miles was identified as a risk factor for development of pleuropneumonia, but having recently raced was not.

On the basis of results of univariate analyses, factors included in the logistic regression were breed (Thoroughbred, Standardbred, other), age (adult, other), occupation (racing, none, other), recent transport (yes, no), recent viral respiratory tract infection (yes, no), and recent race (yes, no). When these factors were considered simultaneously, recent transport remained the most important risk factor (OR, 14; 95% CI, 5 to 39.5). Recent exposure to horses with viral respiratory tract infection or recent viral respiratory tract disease increased the risk of developing pleuropneumonia by 10 times (OR, 10.1; 95% CI, 2.8 to 35.9). Thoroughbreds were at 3.3 times the risk of other horses (95% CI, 1.3 to 8.3), but Standardbreds had a third the risk of developing pleuropneumonia as did horses of other breeds (OR, 0.3; 95% CI, 0.1 to 1.0). Racing as an occupation was not identified as a significant risk factor when all other variables were taken into effect simultaneously and was not retained in the final logistic model. However, when the risk associated with racing was examined within breed groups, Thoroughbred racehorses were found to be 4.3 times (95% CI, 1.3 to 14.4) more likely to develop pleuropneumonia than were nonracing Thoroughbreds. Racing Standardbreds, however, were not more likely to develop pleuropneumonia than were nonracing Standardbreds (OR, 0.8; 95% CI, 0.1 to 7.3). When all horses were considered together, horses that had raced within the previous 48 hours had a 4.4 times higher risk of developing pleuropneumonia (95% CI, 1.4 to 13.2) than did horses that had not raced recently. Within breed groups, Thoroughbreds that had raced recently were 6.1 times more likely to develop pleuropneumonia than were Thoroughbreds that had not (95% CI, 1.3 to 38.7). However, Standardbreds that had raced recently were not more likely to develop pleuropneumonia than were Standardbreds that had not (OR, 0.3; 95% CI, 0.1 to 3.1). There was 84% agreement between observed outcomes and outcomes predicted on the basis of the logistic model.

Discussion

Diagnosing pleuropneumonia in horses can be difficult. Many horses with pleuropneumonia in this study were initially thought to have some other condition (eg, colic, laminitis, or myositis), and most had nonspecific clinical signs (eg, tachypnea, dyspnea, nasal discharge, recurrent fever, and coughing). Results of thoracic auscultation and percussion were valuable in identifying horses with pleuropneumonia, but not all horses had abnormal findings. Because pleuropneumonia can be difficult to diagnose, determining specific risk factors could aid in the earlier identification of horses with this condition.

Age and sex were not identified as risk factors for the development of pleuropneumonia. Most horses with pleuropneumonia were between 2 and 6 years old, but this reflected the general population of horses seen at our hospital. Thoroughbreds were more likely to develop pleuropneumonia than were horses of other breeds, but Standardbreds were less likely. This is in contrast to previous reports that identified both Thoroughbreds and Standardbreds as being predisposed to development of pleuropneumonia.[2,8] The reason for this difference in breed predisposition is unclear, but economic factors in our practice area may influence the decision to refer a horse for further evaluation. Differences in training schedules and the prevalence of exercise-induced pulmonary hemorrhage (EIPH) between the 2 breeds may also be important factors.

Stress associated with transport or athletic competition, coupled with viral respiratory tract disease, may predispose horses to develop pneumonia or pleuropneumonia.[15] In this study, horses transported more than 500 miles were much more likely to develop pleuropneumonia than were horses that had not been transported or were transported shorter distances. This finding is consistent with previous reports that identified an association between recent transport and development of pleuropneumonia.[2,3,9] Long-distance transport is believed to cause sufficient stress to impair pulmonary defense mechanisms, and it has been demonstrated that macrophage, neutrophil, and lymphocyte numbers decrease and cortisol concentrations increase in bronchoalveolar lavage fluid of healthy horses transported 1,200 miles.[15] Transport also results in increased exposure of the respiratory tract to potential pathogens. The number of bacterial and fungal colonies in the confined environments in which horses are transported increases over time.[16] This accumulation of organisms can represent a significant challenge to horses with transit-induced immunosuppression. A mixed population of bacteria, including anaerobes, is frequently isolated from horses with pleuropneumonia, suggesting that aspiration of pharyngeal contents may play a role in the pathogenesis of the disease. It has been suggested that cross-tying of the head during transport inhibits clearance of mucus from the trachea because lowering of the head is restricted. Feeding during transport also may lead to aspiration.[8]

The influenza virus impairs mucociliary clearance through local replication in and destruction of ciliated epithelium, and potentially pathogenic bacteria may gain access to the alveoli secondary to impaired mucociliary activity.[17] Viral infections also may impair alveolar macrophage activity, further compromising host defenses.[18] Therefore, it was not surprising that recent viral respiratory tract disease or recent exposure to affected horses was identified as a risk factor for development of pleuropneumonia in this study. However, there were some biases that might have contributed to this finding. History of disease exposure was obtained on admission to the veterinary teaching hospital, and owners of a horse with respiratory tract disease may have been more likely to recall and report recent exposure to viral respiratory tract disease. Also, owners of horses admitted for other reasons may have been less willing to volunteer information regarding possible disease exposure.

Although recent exposure to viral respiratory tract pathogens did increase the risk that a horse would develop pleuropneumonia, we did not detect any difference in risk between horses that had been vaccinated for influenza or rhinopneumonitis within the past 6 months and those that had not. It has been suggested that mucosal antibody production is more important in prevention of viral respiratory tract infections than is the systemic humoral response induced by available vaccines.[19] Also, influenza viruses undergo antigenic drift, and relevant field strains of virus, particularly those that have caused recent outbreaks, are only slowly incorporated into commercially available vaccines. Heterologous antibodies are not as effective as homologous antibodies in protecting horses from disease.[19] Herpesvirus, which causes rhinopneumonitis in horses, can establish latency and evade immune system destruction, which makes protection by vaccination difficult.[20] Vaccines for influenza and rhinopneumonitis do not provide long-lasting immunity, and protection wanes by 3 months after vaccination.[19,20] Use of an interval shorter than 6 months between vaccination and disease onset may have allowed us to demonstrate a protective effect associated with vaccination. However, our analysis was limited by the number of horses for which vaccination history was known. Vaccination history was not available for 21 of the horses with pleuropneumonia or for 67 of the control horses. Our findings might have been different if these horses had been included in the analysis.

Racing as an occupation was not identified as a risk factor when all other variables were considered simultaneously. When breed groups were examined, Thoroughbred racehorses were more likely to develop pleuropneumonia than were nonracing Thoroughbreds, but racing Standardbreds were not more likely to develop pleuropneumonia than were nonracing Standardbreds. This suggests that differences in training schedules or other racing factors may be important in the pathogenesis of pleuropneumonia. It has been suggested, for instance, that EIPH and inhaled dirt may overwhelm mucociliary clearance, and increase the risk of pleuropneumonia.[3] However, although EIPH is common in Great Britain, pleuropneumonia is not. On the other hand, most racing in Great Britain takes place on turf, which would greatly decrease the amount of dirt and debris inhaled, compared with racing on dirt.[9] Endoscopic surveys in the United States indicate that the prevalence of EIPH in racing Thoroughbreds is between 42[21] and 75%,[22] but that the prevalence of EIPH in racing Standardbreds is only 26%.[21] This difference between breeds may represent a partial explanation of why Thoroughbreds appear at greater risk for development of pleuropneumonia than do Standardbreds.

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Bovine immunodeficiency virus in stud bull semen

Eleven cryopreserved semen samples were procured from a stud semen repository. The DNA from purified leukocytes in the samples was used as a template in a polymerase chain reaction procedure to document presence of bovine immunodeficiency virus (BIV). Amplification of the target sequence, a 235-base pair, highly conserved domain of the BIV *pol* gene, along with nucleotide sequencing, confirmed its BIV specificity. The aforementioned target sequence was identified in leukocyte DNA from 9 of the 11 semen samples, providing evidence that stud bull semen may serve as a reservoir of BIV and suggesting that artificial insemination may have a major role in transmission and dissemination of this bovine lentivirus.—*Jerry W. Nash, Larry A. Hanson, Karen St. Cyr Coats, in Am J Vet Res (June 1995).*