Farm characteristics and management practices associated with development of *Rhodococcus equi* pneumonia in foals

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EQUINE

Objective—To identify farm characteristics and management practices associated with development of *Rhodococcus equi* pneumonia in foals.

Design—Prospective case-control study.

Animals—5,230 foals on 138 breeding farms with 9,136 horses.

Procedure—During 2003, participating veterinarians provided data from 1 or 2 farms with ≥ 1 foal with *R equi* pneumonia and unaffected farms. Data from affected and unaffected farms were compared by use of logistic regression analysis.

Results—A number of variables relating to farm size and desirable management practices were significantly associated with increased odds of farms being affected with *R equi* pneumonia. By use of multivariate logistic regression, affected farms were determined significantly more likely to have raised Thoroughbreds, housed ≥ 15 foals, used concrete floors in foaling stalls, and tested foals for passive transfer of immunity than unaffected farms. These results remained significant even after accounting for exposure of foals to other breeding farms during the first month of life.

Conclusions and Clinical Relevance—Breeding farms with large acreage and a large number of mares and foals have greater odds of being affected by *R equi* pneumonia. Clinical relevance of associations with Thoroughbred breed and concrete flooring in foaling stalls remains uncertain. Desirable management factors commonly used on farms were not effective for controlling or preventing development of *R equi* pneumonia. This finding indicates a need to focus on host factors that influence disease development. (*J Am Vet Med Assoc* 2005;226:404–413)

Pneumonia caused by *Rhodococcus equi* has a worldwide distribution and is considered the most common cause of severe pneumonia in foals.[1-4] The impact of this disease for affected farms is large for several reasons. Prevalence and case fatality rates are high.[2,5,6] Treatment is generally prolonged, expensive, associated with adverse effects, and often unsuccessful.[2] *Rhodococcus equi* pneumonia may negatively influence future performance.[7] Farms reputed to have endemic *R equi* pneumonia may lose clients and associated income because of the disease.

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For most infectious diseases, methods for control and prevention have a greater impact on the burden of disease than does treatment of individual affected animals. Methods for control and prevention of *R equi* pneumonia are limited. Presently, licensed vaccines to prevent disease caused by *R equi* are lacking. Prevention by use of transfusion of hyperimmune plasma is costly, labor-intensive, and not uniformly effective.[2] Understanding the epidemiology of the disease is essential in developing methods to control and prevent pneumonia caused by infection with *R equi*. Although epidemiologic studies of *R equi* have been performed, only 1 study conducted in a single state (Texas) describes systematic evaluation of breeding farm characteristics and management practices that distinguish affected from unaffected farms.[5,6] Results derived in Texas may not be applicable to other regions of the United States because of environmental, climatic, and other factors that may vary geographically. Because of the possibility of regional differences, clinical and economic importance of *R equi* pneumonia, and potential for prevention of the disease by identification of alterable farm management practices, we conducted a survey of veterinarians in the United States. The purpose of this study was to identify farm characteristics and management practices associated with development of *R equi* pneumonia in foals.

Materials and Methods

A listing of 5,162 member veterinarians residing in the United States was obtained from the American Association of Equine Practitioners during 2002. These veterinarians were contacted by mail to solicit participation in a study of farm characteristics and management factors associated with *R equi* pneumonia. Recipients of the initial contact were asked to respond with indication of their willingness to participate and preferred method of participation (postal or electronic submission of survey data). Each respondent was mailed instructions for participation, 2 data abstract forms, instructions for participation with study definitions, and a prepaid return envelope; those indicating preference for electronic submission also received an electronic mail message with instructions, including direction to the study Web site.

Participating veterinarians were requested to complete survey forms with information obtained during 2003 about affected and unaffected breeding farms. A breeding farm was defined as a farm that raised at least 5 foals during 2003. An affected farm was defined as a farm that had 1 or more foals affected with *R equi* pneumonia during 2003. An unaffected (control) farm was defined as a farm that had no history of *R equi* pneumonia and no foals affected during 2002 and 2003. Control farms were to be identified only after all foals on the farm were > 4 months of age to ensure that foals at these farms would be unlikely to develop *R equi* pneumonia subsequent to classification as control farms. An affected foal was defined as a foal that had either clinical signs of pneumonia and from which *R equi* was isolated from a **tracheobronchial aspirate (TBA)** or lung tissue (obtained postmortem) or clinical signs of pneumonia and at least 2 of the following: multifocal pulmonary opacities on thoracic radiographs, ultrasonographically visible pulmonary abscesses, cytologically visible gram-positive coccobacilli on transtracheal wash specimens, a history of endemic *R equi* disease on the premises, and a positive response to treatment directed against *R equi* infection. Veterinarians were asked to provide data from 1 affected and 1 unaffected farm; however, data from either type of farm were accepted. Survey questions were designed to include information about farm factors previously associated with *R equi* pneumonia in Texas.[5,6] Information for the year 2003 concerning the following was recorded for each study farm: veterinarian's study identification number; farm identification number; state; previous history of *R equi* pneumonia at the farm; predominant breed of horse at the farm; number of years the farm had been used for raising horses; total number of acres used for horses; number of horses (including foals) residing at the farm; total number of foals residing at the farm; total number of foals affected with *R equi* pneumonia; number of affected foals that died or were euthanatized because of *R equi* infection; number of resident mares at the farm; number of transient mares at the farm; percentage of mares that foaled at the farm; whether mares were shipped elsewhere for foaling; where mares foaled at the farm (specifically designated foaling stalls, paddocks, pastures, or other); type of flooring in foaling stalls (dirt, sand, concrete, rubber mats, other, or not applicable); type of bedding in foaling stalls (none, wood shavings, hay, straw, other, or not applicable); approximate percentage of foal births observed or attended by farm staff; age of foals (weeks) at the farm when first exposed to paddocks or pastures; age (weeks) at which foals were no longer housed in stalls; whether mare-foal pairs were housed in separate paddocks (yes, no, or some); if the answer to the preceding question was no or some; the mean number of mare-foal pairs in paddocks; age of foals at time of weaning (< 3 months, 3 to 5 months, or > 5 months); percentage of mare-foal pairs for which the mare is a transient mare (ie, a mare temporarily housed at the farm); estimated percentages of foals on the farm exposed to other breeding farms during the first month and the first 6 months of life, respectively; whether foals were tested for adequacy of **passive transfer of immunity (PTI)**; whether *R equi* immune plasma was administered to foals (and if so, the volume [mL], frequency, and age at which it was administered); the approximate frequency of anthelmintic administration to mares at the farm (daily or every 2, 4, 8, 12, or 16 weeks); whether mares or foals were vaccinated against *Streptococcus equi*; whether the farm had a program for removal of horse manure; whether horse manure was removed from pastures or paddocks; whether horse manure was spread on paddocks or pastures as fertilizer (and if so, was it spread as fresh material, composted material, or both); frequency that manure was removed from foaling stalls (≥ 2 times daily, daily, at least weekly, never, or not applicable); whether foaling stalls were disinfected between occupant mares; veterinarian's global assessment of the foals' environment with respect to dust (not dusty, slightly dusty, moderately dusty, or severely dusty); approximate percentage of grass and dirt in paddocks (100% grass and 0% dirt, 75% grass and 25% dirt, 50% grass and 50% dirt, 25% grass and 75% dirt, or 100% dirt); whether there were measures other than grass management used to decrease dust at the farm; and the veterinarian's assessment of the quality of ventilation in foals' stalls (poorly ventilated, average ventilation, well ventilated, or not applicable). A variable was created for region by grouping states into the following categories: midwest, northeast, southeast, southwest, and west. Veterinarians were requested to indicate the historical and clinical findings and diagnostic procedures used to diagnose *R equi* pneumonia among foals at affected farms.

Data forms that were returned by mail were hand-checked for apparent errors and unusual values; any errors or unusual values were resolved by direct communication between study investigators and participating veterinarians. Data from forms returned by mail were entered into a computerized database via the study Web site. Forms submitted electronically were checked for apparent errors and unusual values at the time of receipt; any errors or unusual values were resolved by direct communication between study investigators and participating veterinarians.

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Statistical analyses—To identify factors significantly associated with a farm being classified as affected with *R equi* pneumonia, affected farms were compared with unaffected farms. The association between categoric variables (eg, breed and *R equi* pneumonia status) was summarized by use of contingency tables for categoric data and medians and ranges for continuous data. These summaries neglected the correlation among observations from the same farm (ie, multiple farms submitted by the same veterinarian contributing to the *R equi* pneumonia-affected farm group and the unaffected farm group) and were used strictly for descriptive purposes. For purposes of logistic regression analysis, continuous data were often recoded as dichotomous variables by use of the median value for the population of farms studied.

To account for the correlation among farms contributed by the same veterinarian when examining the association between a given covariate and a farm being affected by *R equi* pneumonia, an extension of generalized linear modeling referred to as generalized estimating equations was used for analysis.[8] Modeling stipulated a dichotomous outcome (farm affected with *R equi* pneumonia group). Coefficients of the models had the interpretation of being the natural logarithm of the **odds ratio (OR)** of a farm affected by *R equi* pneumonia for the individual dependent variables evaluated. Robust standard errors were used to calculate 95% confidence intervals, and robust Z values were used to assess significance.[8] Each independent variable was examined separately for association with *R equi* pneumonia. Variables associated with *R equi* pneumonia at a value of $P \leq 0.05$ were included in multivariate modeling. A forward step-wise approach was used to select variables included in the multivariate model on the basis of the magnitude of the observed association. All possible bivariate interaction terms were examined for significance of those covariates retained in the final multivariate model. Data were analyzed by use of commercial software.[a] A value of $P < 0.05$ was considered significant for all analyses.

Results

Of the 5,162 veterinarians initially contacted, 400 (7.7%) responded and indicated a willingness to participate and 96 (24%) ultimately contributed data from at least 1 farm; data were obtained from 162 eligible farms (mean, 1.7 farms/veterinarian). Ninety-two veterinarians submitted data by mail, and 4 submitted data via an electronic Web site. Data were contributed from farms in 33 states including Alabama (n = 1 unaffected farm), Arizona (1 affected and 3 unaffected farms), California (8 affected and 3 unaffected farms), Colorado (2 unaffected farms), Florida (5 affected and 1 unaffected farms), Georgia (1 affected and 2 unaffected farms), Illinois (4 unaffected farms), Iowa (2 unaffected farms), Kansas (1 unaffected farm), Kentucky (6 affected and 1 unaffected farms), Louisiana (3 affected farms), Maine (3 unaffected farms), Maryland (1 affected and 5 unaffected farms), Michigan (1 affected and 2 unaffected farms), Minnesota (1 affected and 3 unaffected farms), Mississippi (1 unaffected farm), Missouri (1 affected and 4 unaffected farms), Nebraska (5 unaffected farms), Nevada (1 unaffected farm), New Jersey (5 affected and 2 unaffected farms), New Mexico (2 affected and 1 unaffected farms), New York (3 affected and 1 unaffected farms), North Carolina (2 unaffected farms), Ohio (3 unaffected farms), Oklahoma (2 affected and 2 unaffected farms), Pennsylvania (4 affected and 6 unaffected farms), South Carolina (2 unaffected farms), South Dakota (1 unaffected farm), Tennessee (1 affected and 2 unaffected farms), Texas (18 affected and 24 unaffected farms), Virginia (2 affected and 1 unaffected farms), Washington (2 unaffected farms), and Wyoming (4 unaffected farms).

Of the 162 farms, 24 control farms were excluded from analysis because they had a previous history of *R equi* pneumonia (21 farms) or history of previous *R equi* pneumonia was unknown (3 farms). The 138 farms that were included in the analyses housed 14,366 horses and foals (9,136 horses and 5,230 foals). Of these 5,230 foals, 530 of the 3,990 (13.3%) foals born at affected farms were reported to have developed *R equi* pneumonia during 2003. The reported mortality proportion was 8% (44/530).

Twenty-eight (43%) affected farms reported a diagnosis of *R equi* pneumonia on the basis of a combination of clinical signs of pneumonia and isolation of *R equi* by microbiologic culture of a TBA. The remaining 37 farms reported a diagnosis of *R equi* pneumonia on the basis of clinical signs of bronchopneumonia and at least 2 of the following findings: multifocal pulmonary opacities detected on thoracic radiographs, ultrasonographically visible pulmonary abscesses, cytologically visible gram-positive coccobacilli in TBA fluid specimens, a history of endemic *R equi* disease on the premises, or a positive response to treatment directed against *R equi* infection. The most common clinical signs reportedly used for diagnosing *R equi* pneumonia among foals at affected farms were fever (61/65 [94%]), cough (58/65 [89%]), clinical signs of bronchopneumonia (58/65 [89%]), abnormal lung sounds during thoracic auscultation (56/65 [86%]), increased abdominal effort during breathing (54/65 [83%]), respiratory distress (52/65 [80%]), and nasal discharge (33/65 [51%]). Excluding results of TBA, the most common ancillary diagnostic testing methods were ultrasonography (36/65 [55%]), necropsy (26/65 [40%]), and radiography (16/65 [25%]). Clinical response to treatment directed against *R equi* (53/65 [82%]), farm history of recurrent or endemic *R equi* pneumonia (41/65 [63%]), and other foals at the farm with confirmed *R equi* pneumonia (26/65 [40%]) were also used to determine a diagnosis of infection.

The number of years the farm was used for horses was generally longer for affected farms (median, 20 years; range, 1 to 90 years) than unaffected farms (median, 15 years; range, 1 to 40 years); this difference was significant when considered as a continuous variable but not when considered as a categorical variable (by use of the farm population median of 18 years; **Table 1**). Predominant breeds at farms included Quarter Horses (20 affected and 43 unaffected farms), Thoroughbreds (31 affected and 8 unaffected farms), Arabians (6 affected and 5 unaffected farms), and other breeds (8 affected and 17 unaffected farms). Relative to other breeds, Thoroughbred farms had significantly higher odds of being affected with *R equi* pneumonia. Region was significantly associated with the odds of a farm being affected by *R equi*. In particular, farms from the midwestern United States were significantly less likely to have been affected farms.

Affected farms were significantly larger than unaffected farms. The median number of acres used for horses at affected farms was 130 acres (range, 5 to 2,000 acres) and that at unaffected farms was 50 acres (range, 10 to 10,000 acres). The proportion of affected farms with ≥ 80 acres used for horses (the median value for all farms) was significantly greater for affected than unaffected farms. Affected farms also had significantly more horses and foals residing at the farm during 2003. The median number of horses and foals at affected farms was 88 horses (range, 15 to 900 horses) and that at unaffected farms was 40 horses (range, 8 to 375 horses). The median number of foals at affected farms was 30 (range, 5 to 550 foals) and that at unaffected farms was 11 (range, 5 to 165 foals). Affected farms were significantly more likely to have had ≥ 50 horses and foals and ≥ 15 foals than were unaffected farms. Density of horses (horses/acre) was similar and did not differ significantly for affected farms (median, 0.8 horses/acre; range < 0.1 to 7.5 horses/acre) and unaffected farms (median, 0.8 horses/acre; range, < 0.1 to 6.0 horses/acre). The density of foals (foals/acre) was similar and did not differ significantly between affected farms (median, 0.2 foals/acre; range, < 0.1 to 2.8 foals/acre) and unaffected farms (median, 0.2 foals/acre; range, < 0.1 to 1.8 foals/acre).

The number of resident mares was considerably greater for affected farms (median, 35 resident mares; range, 6 to 300 resident mares) than for unaffected farms (median, 15 resident mares; range, 2 to 140 resident mares), and the difference in distribution was significant. There was no significant difference between affected and unaffected farms in the number of transient mares at the farm, although affected farms tended to have more transient mares (median, 8 transient mares) than unaffected farms (median, 5 transient mares). Similarly, there was no significant difference in the proportion of affected farms (49/65 [75%]) and unaffected farms (51/73 [70%]) that had any transient mares at the farm (ie, ≥ 1 transient mare at the farm). There was no significant difference between affected and unaffected farms with respect to the ratio of resident to transient mares, when considered as either a continuous or dichotomous (by use of the median value as the cutoff value) variable. Although the proportion of mares that were shipped from the farm to foal elsewhere was greater among affected farms (14/65 [22%]) than unaffected farms (7/73 [10%]), the difference was not significant ($P = 0.06$).

Most foals at participating affected and unaffected farms were born in specially designated foaling

Table 1—Variables significantly associated with a horse farm being affected with *Rhodococcus equi* pneumonia during 2003 in a study of 138 farms (65 affected and 73 unaffected farms) in the United States.

Variable	No. (%) of affected farms	No (%) of unaffected farms	OR (95% CI)	*P* value
Thoroughbred farm	31 (48)	8 (11)	7.3 (3.2–17.0)	< 0.001
Farm used for horses ≥ 18 years	40 (62)	31 (42)	2.0 (< 1.0–4.2)	0.059
Region				
Midwest	3 (15)	17 (85)	1.0 (NA)	NA
Northeast	9 (41)	13 (59)	7.7 (1.8–33.4)	0.007
Southeast	11 (38)	18 (62)	8.8 (1.9–40.4)	0.006
Southwest	24 (51)	23 (49)	5.1 (1.3–20.1)	0.021
West	12 (60)	8 (40)	3.4 (0.7–16.8)	0.132
Midwest (vs all others)	3 (15)	17 (85)	0.2 (< 0.1–0.6)	0.007
≥ 80 acres used for horses	46 (71)	29 (40)	3.6 (1.7–7.3)	< 0.001
≥ 50 horses at farm during 2003	45 (69)	30 (41)	3.1 (1.6–6.4)	0.001
≥ 15 foals at farm during 2003	46 (71)	36 (37)	4.0 (2.0–8.1)	< 0.001
≥ 18 resident mares at farm	51 (78)	24 (33)	7.1 (3.3–15.2)	< 0.001
Foals born in pasture	10 (15)	30 (41)	0.3 (0.1–0.6)	0.002
Concrete flooring in foaling stalls	9 (14)	3 (4)	3.9 (1.1–14.2)	0.039
> 75% foalings observed/attended	51 (81)	38 (53)	3.8 (1.6–8.9)	0.002
Some foals from farm exposed to another farm during the first month of life	44 (68)	30 (41)	2.8 (1.4–5.4)	0.002
Some foals from farm exposed to another farm during the first 6 months of life	48 (74)	33 (46)	3.2 (1.5–6.5)	0.002
Foals tested for passive transfer of immunoglobulin	53 (85)	31 (44)	7.4 (3.1–17.6)	< 0.001
Administration of *R equi* immune plasma	36 (56)	2 (3)	72.2 (12.5–419.1)	< 0.001
Anthelmintic administered to mares at least every 8 weeks	49 (79)	24 (36)	7.4 (3.3–16.5)	< 0.001
Vaccination against *Streptococcus equi*	43 (68)	27 (38)	3.5 (1.6–7.3)	0.001
Program for removal of manure	54 (86)	49 (68)	2.6 (> 1.0–6.4)	0.044
Environment described as moderately to severely dusty	28 (43)	19 (26)	2.2 (> 1.0–4.8)	0.039

OR = Odds ratio derived using logistic regression with generalized estimating equations. CI = Confidence interval. NA = Not applicable.

stalls (53/65 [82%] and 52/73 [71%], respectively). However, foals at affected farms were significantly less likely to have foaled in a pasture (vs a stall or small paddock) than were foals from unaffected farms. Foaling stalls at affected farms were significantly more likely to have concrete flooring than were unaffected farms. There were no significant differences between the proportions of affected and unaffected farms having flooring in foaling stalls made of dirt, sand, rubber mats, or other material. The most common type of flooring for affected farms (27/65 [42%]) and unaffected farms (28/73 [38%]) was dirt flooring. There was no significant difference between affected and unaffected farms in the type of any bedding used in foaling stalls. All foals born on concrete floors were bedded with straw or hay.

Affected farms were significantly more likely to have had > 75% of foalings observed or attended than were unaffected farms. The proportion of foals that were initially exposed to pasture during the first 2 weeks of life was similar to the proportion of foals at affected (93%) and unaffected (95%) farms. Although the median age at which foals were no longer housed in stalls was greater at affected farms (median, 4 weeks) than unaffected farms (median, 2 weeks), this difference was not significant, whether considered as a continuous ($P = 0.821$) or dichotomous variable ($P = 0.063$). There was no significant difference in the proportion of farms that housed mare-foal pairs in separate paddocks. For affected farms, the proportions housing some or all foals in separate mare-foal units were 17% and 15%, respectively; the corresponding proportions for unaffected farms were 23% and 12%, respectively. For farms reporting that mare-foal pairs were not housed separately (ie, some or all mare-foal pairs housed in pairs > 1 pair), the median number of the reported mean number of mare-foal pairs in paddocks or pastures was similar for affected farms (5 mare-foal pairs) and unaffected farms (4 mare-foal pairs). Although the proportion of affected farms that weaned foals at > 5 months of age (37/65 [57%]) was greater than the proportion of unaffected farms (29/73 [40%]), the difference was not significant ($P = 0.07$). Although the proportion of affected farms that reported some transient mare-foal pairs at the farm (46/65 [71%]) was greater than the proportion of unaffected farms (45/73 [62%]), the difference was not significant. Affected farms were significantly more likely to report that some foals had exposure to other breeding farms during the first month of life.

Affected farms were significantly more likely to test foals for PTI than unaffected farms. Affected farms were significantly more likely to have administered *R equi* immune plasma to foals to prevent *R equi* pneumonia than unaffected farms. Twenty of 36 affected farms that administered *R equi* immune plasma administered the plasma 2 times to each foal; the remaining farms administered plasma once to each foal. All but 1 of 36 affected farms that administered plasma reported its administration by the foals' first week of life (1 farm administered plasma at 2 weeks of age). The second plasma administration was most frequently administered during the third week of life (n = 9 farms). Nearly all of the 36 affected farms that used plasma reported administration of a volume of 1 L/transfusion; 4 farms reported administration of < 1 L/transfusion (volumes ranged from 250 to 750 mL). The 2 unaffected farms that administered plasma used a single treatment of 1 L to foals.

Affected farms were significantly more likely to have administered an anthelmintic to mares at the farm at least every 8 weeks than were unaffected farms. Affected farms were significantly more likely to have vaccinated mares or foals against *S equi* infection than were unaffected farms. Having a program for removal of manure was significantly more common among affected than unaffected farms. The proportions of affected (24%) and unaffected (27%) farms that removed manure from paddocks or pastures were similar. The proportions of affected (33%) and unaffected (31%) farms reporting that manure was spread on pastures or paddocks to fertilize the soil were similar. Among farms in which foaling stalls were used, the proportion in which feces were removed from foaling stalls at least once daily was similar for affected farms (96%) and unaffected farms (91%). Among farms in which foaling stalls were used, affected farms (33/55 [60%]) were not significantly more likely to disinfect

Table 2—Multivariable model of variables significantly associated with a horse farm being affected with *R equi* pneumonia during 2003 in a study of 138 farms (65 affected and 73 unaffected farms) in the United States.

Variable	OR (95% CI)	*P* value
Significant associations		
Thoroughbred breed	4.7 (1.7–12.8)	0.003
≥ 15 foals at farm during 2003	2.8 (1.3–6.2)	0.009
Concrete flooring in foaling stalls	3.9 (1.3–11.8)	0.017
Foals tested for passive transfer of immunoglobulin	5.2 (1.8–14.4)	0.002
Significant associations including variable for exposure of some foals to other breeding farms during the first month of life		
Thoroughbred breed	4.3 (1.5–12.0)	0.006
≥ 15 foals at farm during 2003	2.4 (1.1–5.1)	0.023
Concrete flooring in foaling stalls	4.5 (1.4–14.3)	0.010
Foals tested for passive transfer of immunoglobulin	4.9 (1.7–13.8)	0.003
Exposure of some foals to another breeding farm during the first month of life	2.1 (0.9–5.0)	0.083
Significant associations including variables for region of the United States		
Thoroughbred breed	5.6 (1.9–16.8)	0.004
≥ 15 foals at farm during 2003	2.8 (1.2–6.5)	0.012
Concrete flooring in foaling stalls	5.1 (1.5–12.6)	0.014
Foals tested for passive transfer of immunoglobulin	5.2 (1.8–14.7)	0.003
Region (relative to midwest)		
Northeast	1.0 (0.2–7.1)	0.982
Southeast	1.9 (0.3–10.8)	0.451
Southwest	2.6 (0.5–13.5)	0.256
West	1.1 (0.2–7.0)	0.931
Significant associations including variable for exposure of some foals to other breeding farms during the first month of life and region of the United States		
Thoroughbred breed	4.7 (1.5–14.9)	0.008
≥ 15 foals at farm during 2003	2.4 (1.1–5.4)	0.035
Concrete flooring in foaling stalls	5.3 (1.7–17.1)	0.005
Foals tested for passive transfer of immunoglobulin	4.7 (1.6–13.4)	0.004
Exposure of some foals to another breeding farm during the first month of life	2.4 (0.9–6.4)	0.080
Region (relative to midwest)		
Northeast	1.1 (0.2–6.7)	0.942
Southeast	2.7 (0.4–18.6)	0.321
Southwest	2.8 (0.5–15.8)	0.248
West	1.3 (0.29.5)	0.764

Odds ratios were derived by use of logistic regression with generalized estimating equations. *See* Table 1 for key.

foaling stalls between occupants than unaffected farms (24/50 [48%]).

Affected farms were significantly more likely to report that the foal's environment would be considered moderately to severely dusty (vs mildly or not dusty) than unaffected farms. Affected farms (16/62 [26%]) were not significantly more likely than unaffected farms (12/72 [17%]) to use management practices other than grass management to reduce dust in the environment. Although affected farms (7/64 [11%]) were less likely than unaffected farms (13/73 [18%]) to have paddocks that were > 75% dirt (compared with grass), the difference was not significant. The proportion of affected farms that described the ventilation in foaling stalls as being poor (7/59 [12%]) was not significantly greater than the proportion of unaffected farms (5/58 [9%]).

Variables that were significantly associated with *R equi* pneumonia were included in a purposeful step-wise regression model, with the exception of the variable administration of *R equi* immune plasma to foals because it was considered to be an effect (rather than a possible cause) of the disease. The final multivariate model included the following variables: Thoroughbred breed, ≥ 15 foals at the farm, concrete flooring in foaling stalls, and whether farms tested foals for PTI **(Table 2)**. Because of clinical importance and its approximation of significance, a term for exposure of foals to another farm during the first month of life was included in a second multivariate model. To account for any bias from regional differences, we also included models with the regional indicator variables forced into the model. None of the interaction terms for any pair of main effects was significant. Each of the variables included in the final multivariate model remained significantly associated when the 24 unaffected farms with either an unknown history (n = 3 farms) or a previous history of *R equi* pneumonia (21) were included in analyses as affected farms; however, a history of *R equi* pneumonia also was significantly associated with *R equi* pneumonia and was the strongest predictor of a farm being affected by the disease.

Discussion

Results of this study indicated that pneumonia caused by *R equi* in foals appeared to be a disease of particular importance to larger breeding farms that use management practices determined to be desirable for improving health (ie, farms that are considered well managed). Several characteristics relating to farm size (number of acres) and farm population (number of horses, resident mares, and foals) were significantly associated with farms being affected by *R equi* pneumonia. Of these characteristics, only the number of foals remained in the final model, likely because each of these covariates pertaining to population numbers was significantly associated with the others. Terms for the number of acres, horses, or resident mares could be substituted for the number of foals in the final model without altering the significance, magnitude, or direction of any of the resultant ORs. The number of mares and foals at the farm might have reflected increased occurrence of transmission through increased opportunity for contact and environmental contamination.[1] The bacterium can replicate in the intestinal tract of foals,[9] and a larger population of foals may result in greater environmental contamination with *R equi*.[3,4] Alternatively, a greater number of horses or foals may have increased the probability that a farm had a foal that developed *R equi* pneumonia. Density of horses or foals (horses or foals/acre) was not significantly associated with increased risk of farms being affected by *R equi* pneumonia. This finding is in contrast to results of a previous study[5] performed in Texas. In that study, densities of horses (median, 1.0 horses/acre) and foals (0.25 foals/acre) were similar to those of farms participating in the study reported here (0.8 horses/acre and 0.2 foals/acre). Thus, the disparity of results between studies is not explained by differences between study farm populations in the densities of horses and foals. The observation that the odds of a farm being affected with *R equi* pneumonia were not associated with density is consistent with the fact that this infectious disease is not highly contagious.

Similar to results of a previous study,[6] a number of management practices determined to be desirable were significantly associated with increased risk of *R equi* pneumonia in our study. In the final multivariate model, *R equi* pneumonia was significantly associated with farms testing foals for PTI; however, other management practices determined to be desirable (eg, > 75% of foalings observed or attended or deworming mares at least every 8 weeks) and that were strongly associated with affected farms could have been substituted for testing foals for PTI in the final model. One possible explanation for these observed associations is that farms that were better managed tended to be more likely to diagnose *R equi* pneumonia, possibly because of closer monitoring of foals for signs of disease. We believe this explanation is unlikely, given the severe and progressive clinical course of *R equi* pneumonia.[2] Thus, results of the study reported here and a previous study[6] indicate that desirable management practices commonly used on affected farms do not appear to be effective or sufficient for controlling or preventing *R equi* pneumonia. Therefore, this study is important because it indicates that host (ie, foal) factors that predispose foals to *R equi* infection may be more important than management factors in preventing or controlling this disease. It is also possible that practices reflecting intensive management would increase the number of indirect animal contacts, such that failure to increase biosecurity concurrent with increased intensity of management could be an important factor predisposing to increased risk of infection. Although biosecurity measures may be expected to be more effective for more highly contagious infections than *R equi*, affected farms should give careful consideration to biosecurity measures.

Whether the association between *R equi* pneumonia and Thoroughbred breed was causal could not be determined. To the authors' knowledge, genetic susceptibility to *R equi* pneumonia has not been reported; however, such an explanation can not be excluded, and genetic susceptibility to other intracellular organisms has been reported in other species.[10-14] This finding should be interpreted with caution because results of a

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similar study[6] in Texas did not indicate that Thoroughbred farms were more likely to be affected with *R equi* pneumonia. The association may have been confounded by some other unmeasured factor or may have been attributable to a bias in selection of such farms by participants. Although Thoroughbred farms in this study tended to be larger in acreage and have more horses and foals than other farms, the association with Thoroughbred breed remained significant even after adjusting for the number of foals (or mares or acres used for horses) at the farm by use of multivariate modeling.

The association between concrete flooring in foaling stalls and farms being affected with *R equi* pneumonia also was difficult to interpret. We believe that this finding must be interpreted with caution until it is substantiated or refuted by results of other studies. Concrete flooring may have been a marker for some other peripartum management practice or exposure not measured in this study, or this factor may have been strongly opposite to another potentially protective factor, such as foaling in pasture. The proportion of farms reporting the use of foaling stalls with concrete floors was small (12/138 [9%]). Results of a previous study[6] indicate that there was moderate evidence that farms that used dirt floors in foaling stalls had increased odds of *R equi* pneumonia, compared with farms that used other types of flooring.

A second alternative multivariate model was presented that included a term for exposure of some foals to other farms during the first month of life. The rationale for considering this model was both statistical and clinical. Statistically, the adjusted OR for this term indicated an approximate doubling of the odds of a farm being affected when some foals had exposure to other farms; the *P* value for the term approached significance; and inclusion of this term did not alter the magnitude (by > 15%), direction, or significance of any of the estimated ORs in the original multivariate model. Clinically, it is not unusual for foals to be exposed to multiple farms during the first month of life. Because the age at which foals acquire infection with *R equi* is not definitively known, it can be difficult or impossible to determine at which farm a foal became infected when that foal was exposed to multiple farms early in life. Thus, it was noteworthy that the factors significantly associated with farms being affected by *R equi* pneumonia remained significantly associated after accounting for exposure of some foals to other breeding farms. Unfortunately, we did not query whether these other breeding farms had a history of *R equi* pneumonia and did not determine whether it was specifically the affected foals that were exposed to other farms.

A number of other factors significantly associated with *R equi* pneumonia in bivariate analysis merit discussion. Affected farms were significantly larger in area (acres) used for horses. This variable (whether considered as a continuous or categorical variable) was significantly associated with the number of horses and foals at farms. As previously mentioned, *R equi* pneumonia appears to be a disease of larger farms.

In our study, foaling in pasture was associated with decreased risk of farms being affected by *R equi* pneumonia. Although the finding was not significant, affected farms were less likely to have foals born in pasture than were control farms in another study.[6] The association between foaling at pasture and decreased risk of *R equi* pneumonia may be spurious. From the standpoint of controlling infectious diseases, foaling at pasture has been associated with decreased risk of diarrhea in foals.[15,16]

The associations among more frequent administration of anthelmintics to mares, being more likely to observe or attend foalings, and having a program for removal of manure with increased odds of farms being affected were considered attributable to overall practices determined to be better at affected farms, compared with control farms. Larger breeding farms may have been more likely to report such practices; however, we believe that the association between desirable management practices and increased odds of disease was more likely attributable to larger farms employing these practices and the finding that these practices did not appear to be effective for preventing *R equi* pneumonia. Vaccination of mares or foals against *S equi* also may have indicated use of good management practices at affected farms. Alternatively, larger farms with more horses also may have been more likely to experience disease associated with *S equi* infection because of greater opportunity for exposure to infected horses and more intensive management. It is also possible that such vaccination was implemented to reduce respiratory infection in foals at affected farms. Although not significant, vaccination against *S equi* of mares or foals was previously detected to be more common among affected than unaffected farms.[6]

Rhodococcus equi pneumonia was associated with an environment that was subjectively determined by participating veterinarians to be moderately to severely dusty. A dusty environment (dusty stables or housing foals on dusty, bare paddocks) has been putatively associated with disease caused by *R equi* infection.[2,17-22] Moreover, the number of airborne *R equi* has been reported to be greater on dry and windy days.[23] To our knowledge, this is the first controlled study documenting an association between a dusty environment and *R equi* pneumonia. However, this finding should be interpreted with caution for a number of reasons. First, the assessment was based solely on a subjective impression; more objective (and presumably more precise) quantification of the extent of dust in the environment would provide more convincing evidence. Second, a time scale was not incorporated in the evaluation of this outcome, and a number of temporal biases could have influenced the impression that the environment of foals was dusty. For example, a bias may have occurred if data were completed for control farms during cooler or wetter months than affected farms (many pneumonic foals may have been identified during the hot, dry months of summer). Finally, other indicators of a dusty environment for foals (eg, paddocks that were > 75% dirt) were not more prevalent among affected farms than among unaffected farms. Nevertheless, the association of dusty environment merits further consideration in light of previous descriptive reports[2,17-22] and results of this study; conceivably, efforts to reduce dust in the environment (such as reseeding and irrigating to promote growth of grass in paddocks and use of water sprinklers in paddocks to reduce aerosolization of dust particles that may be laden with *R equi*) might help decrease the incidence of disease attributed to *R equi* pneumonia.

The duration that the farm was used for raising horses was significantly greater for affected farms (median, 20 years) than for unaffected farms (median, 15 years) when considered as a continuous variable. This finding corroborates results of a previous study[21] of 5 horse farms in Ontario but contradicts results of a study[5] performed in Texas similar to the study reported here. In the former study, the authors quantified *R equi* in the environment of horses and foals and proposed that prolonged use of farms for breeding horses leads to a cumulative increase in environmental contamination with *R equi*, with consequent increased risk of exposure to the organism and of disease caused by *R equi*. In the latter study, affected farms tended to be used for raising horses for a longer duration (median, 13.5 years) than control farms (median, 10 years); although that difference was not significant, it was similar to the magnitude of difference between medians for the affected and unaffected farms in our study. The magnitude of these differences in duration was modest, and the study reported here likely had greater statistical power to detect differences than the study[5] performed in Texas to detect such a difference. The magnitude of this difference did not appear to offer much clinically useful information, but this may have been because the duration that a farm was used for raising horses was a crude measure of environmental contamination with *R equi*. The study reported here or our previous study[5] in Texas did not quantify the amount of *R equi* in the environment of mares and foals at breeding farms; such information could be useful for assessing risk of *R equi* pneumonia at farms. Results of 1 study[24] indicate that simply determining whether there are *R equi* (or virulent *R equi*) in the soil does not reliably differentiate affected from unaffected farms; thus, studies quantifying *R equi* in the environment are needed. Whether increased environmental contamination with the organism is a cause or effect of *R equi* pneumonia has not been determined. Rather than being a reflection of environmental contamination, it is possible that duration that a farm was used for horses merely indicated a higher cumulative probability of exposure and therefore risk of having *R equi* pneumonia among foals at a farm.

Administration of *R equi* immune plasma was considered to be a result of the disease rather than a cause of *R equi* pneumonia. Although the practice was more common among affected farms, efficacy of plasma transfusion could not be assessed from this study. Other studies[25-29] have yielded conflicting results regarding efficacy of plasma transfusion; however, most evidence indicates that plasma transfusion decreases the incidence of disease and death from *R equi*. Efficacy of plasma transfusion for prophylaxis of *R equi* pneumonia is likely < 100%, and other control measures are needed, as indicated by the findings of this study.

A number of control farms had previous history of *R equi* pneumonia (n = 21 farms) or unknown history (3). We chose to exclude these farms from analysis because we believed that comparison of affected farms with farms that had no history of *R equi* pneumonia would be more meaningful than comparisons including these farms. To assess the affect of this decision, we also performed the same analyses (bivariate through multivariate modeling), including data from these 24 control farms. Results of these analyses were similar with respect to results of bivariate and multivariate analyses presented herein (ie, the significance, magnitude, and direction of associations were essentially unchanged), except that the strongest predictor of being an affected farm was a history of *R equi* pneumonia.

There were other limitations to the study reported here in addition to those that have already been described. A selection bias may have occurred because of regional variation among farms with respect to the odds of being an affected farm. Control farms were overrepresented among farms from the midwestern United States and Texas. A selection bias based on region did not appear to confound our results; region did not affect our results, whether it was considered as indicator variables for categories of region, a dichotomous variable for midwestern states, or a dichotomous variable for Texas (vs other states). Another potential source of selection bias was the way in which veterinarians selected farms to contribute to the study. Because veterinarians received no specific instructions on systematically selecting farms (eg, random sampling of the affected and unaffected farms in their practice), it is possible that farms were biased by the way in which they were selected. For example, veterinarians may have selected only the most severely affected farms. Although we think this is unlikely on the basis of reported proportions of affected foals and affected foals that died, compared with what has been reported previously,[2,4-6] it is not possible to examine the extent or affect of this bias. Future studies should, if possible, be designed to account for this potential source of bias.

In the study reported here, the definition of a foal affected with *R equi* pneumonia included a variety of diagnostic procedures and techniques. The most widely accepted method for definitive antemortem diagnosis of *R equi* pneumonia is a combination of clinical signs of pneumonia and isolation of *R equi* by microbial culture of a TBA, preferably considered in light of cytologic findings of the aspirate. Fewer than half of affected farms reported a diagnosis of *R equi* on the basis of these criteria. The remaining 37 farms made diagnoses on the basis of clinical signs of bronchopneumonia and at least 2 of the following findings: multifocal pulmonary opacities on thoracic radiographs, ultrasonographically visible pulmonary abscesses, cytologically visible gram-positive coccobacilli in TBA specimens, a history of endemic *R equi* disease on the premises, or a positive response to treatment directed against *R equi* infection. The diagnostic criteria for a case definition in this study were selected to facilitate comparison of results of this nationwide study with our previous, similar studies[5,6] from Texas and to incorporate the varying diagnostic preferences, equipment, and levels of expe-

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rience and expertise among participating veterinarians and farm managers or owners. Clearly, it is possible that some foals were misclassified with respect to disease; the affect of this misclassification is unknown.

Misclassification of farms was also a possible limitation of this study. Affected farms were defined on the basis of history of disease during 2003, whereas control farms had to have been free of disease during all previous years. Had the study been performed during a preceding year, any affected farms that did not have disease during that year could have been classified as control farms. We believe that the potential for this misclassification was small because most affected farms had a history of *R equi* pneumonia and would not have been classified as control farms, as defined for analysis in this study. Moreover, analyses were repeated that included control farms with a history of *R equi* pneumonia as affected farms, and there was no change in the significance or direction of any of the significant associations observed in bivariate or multivariate analyses. The purpose of this study was to compare farms affected by *R equi* pneumonia with farms without current or previous history of the problem; we believe that farms included in this study were accurately classified.

We depended on participating veterinarians to accurately report data from farms. It is our hope and belief that participants responded accurately. Although we did not attempt to validate reported observations from a sample of submitted forms, it was the experience of 2 of the authors (NDC and MSO), on the basis of follow-up conversations with some participating veterinarians about discrepant or unusual values, that participating veterinarians strived to be precise and accurate in their reporting.

The response rate of veterinarians for participation in this study was low. Fewer than 10% of those veterinarians contacted chose to respond. Moreover, only 24% of those that initially indicated willingness to participate contributed eligible farms. Lack of participation may have been attributable to the length of the study questionnaire, confusion about requirements for participation (eg, some participants did not realize that data from unaffected farms was as important as data from affected farms), the need to complete the forms later in 2003 despite initial contact earlier in the year, and the busy schedules of practicing veterinarians.

The principal reason for performing this study was to substantiate whether previous findings from similar studies[5,6] in Texas could be generalized to other regions of the country; however, participation in this study was heavily influenced by contributions from veterinarians in Texas; 39 of 138 (28%) of farms were contributed by veterinarians from Texas. This may have been because *R equi* pneumonia is a greater problem in Texas; more likely, it indicated that participants were familiar with the investigators from, or were loyal to, Texas A&M University. The affect of these potential response biases is unknown. The fact that this study of data from farms in 33 states (including 72% of farms from states other than Texas) was similar to findings from the previous studies[5,6] indicates that these biases either were not important or were replicated in both studies.

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Selected abstract for *JAVMA* readers from the *American Journal of Veterinary Research*

Laboratory measures of hemostasis and fibrinolysis after intravenous administration of ε-aminocaproic acid in clinically normal horses and ponies

Peter Heidmann et al

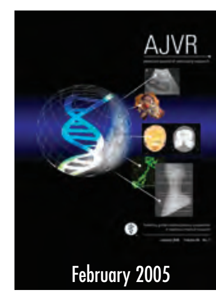
Objective—To determine whether ε-aminocaproic acid (EACA) administered IV affects hemostasis and fibrinolysis in clinically normal horses and ponies.

Animals—20 clinically normal adult horses and ponies.

Procedures—Blood samples were collected 24 hours before (baseline) and 1 and 5 hours after IV administration of a low dose (30 mg/kg) or high dose (100 mg/kg) of EACA. Platelet count, fibrinogen concentration, prothrombin time, partial thromboplastin time (PTT), D-dimer concentration, α_2-antiplasmin activity, and thrombin-antithrombin complex concentration were measured. Values at 1 and 5 hours were compared with baseline values.

Results—1 hour after administration of a low dose of EACA, mean fibrinogen concentration was significantly lower than baseline concentration. Mean PTT was significantly shorter than the baseline value 5 hours after administration of a low dose of EACA. One hour after administration of 100 mg of EACA/kg, mean α_2-antiplasmin activity was significantly higher than baseline activity. Mean fibrinogen concentration was significantly lower than baseline concentration 1 and 5 hours after administration of a high dose of EACA. Mean PTT was significantly shorter than the baseline value 5 hours after administration of a high dose of EACA.

Conclusions and Clinical Relevance—IV administration of 30 mg of EACA/kg to clinically normal horses significantly modified some laboratory measures of hemostasis, consistent with its known antifibrinolytic effects. Although enhanced clot maintenance and diminished bleeding were not directly assessed, the clinical use of EACA may benefit some patients. (*Am J Vet Res* 2005;66:313–318)



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