Analysis of risk factors for recurrent airway obstruction in North American horses: 1,444 cases (1990–1999)

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Objective—To identify risk factors for recurrent airway obstruction (RAO) among horses examined at veterinary teaching hospitals in North America.

Design—Retrospective case-control study.

Animals—1,444 horses with RAO and 1,444 control horses examined for other reasons.

Procedure—The Veterinary Medical Database was searched for records of horses in which RAO was diagnosed. A control group was identified by randomly selecting a horse with a diagnosis other than RAO that matched the institution and year of admission for each of the horses with RAO. Information obtained included hospital, admission year and month, age, sex, breed, and discharge status. The association between risk factors and diagnosis of RAO was estimated with logistic regression models.

Results—The risk of RAO increased significantly with age, with horses ≥ 7 years old being 6 to 7 times as likely to have RAO as were horses ≤ 4 years old. Thoroughbreds were 3 times as likely to have RAO as were ponies. Horses were 1.6 and 1.5 times as likely to be examined because of RAO during winter and spring, respectively, than they were during summer.

Conclusions and Clinical Relevance—Results suggest that RAO was more likely to be diagnosed in females, horses ≥ 4 years old, and Thoroughbreds and that RAO has a seasonal distribution. (*J Am Vet Med Assoc* 2003;223:1645–1650)

Recurrent airway obstruction (RAO), also known as heaves, is a chronic respiratory tract disease of horses characterized by coughing, mucopurulent airway exudate, increased respiratory efforts, and exercise intolerance.[1] In the literature, RAO is commonly referred to as chronic obstructive pulmonary disease, but participants at a workshop on equine chronic airway disease in 2001 recommended that chronic obstructive pulmonary disease be referred to as RAO or heaves.[2] Clinical signs of RAO are usually triggered by exposure to high concentrations of organic molds, such as when horses are housed indoors and fed hay.[3,4] Clinical signs of the disease usually resolve within a few days after horses are placed on pasture or the housing environment is improved to reduce the amount of dust and increase ventilation in the horse stalls.[3,5,6] Recurrent airway obstruction is believed to be an allergy to inhaled molds and is similar to certain forms of asthma in humans.[7-9]

Horses with RAO tend to be mature (> 7 years old) or older. There is no apparent breed or sex predilection, although RAO has been observed to be more common in ponies.[10-13] However, data supporting these observations come from case series or retrospective reviews of records from a particular hospital that involve small numbers of horses. Most studies published thus far have not incorporated a reference population for comparison, making generalizations to other horse populations unreliable. In 1 study,[13] the hospital population was compared with the National Army horse population and not to a random control population.

The incidence of RAO appears to be related to traditional horse management factors, such as stall housing, the feeding of hay, and the use of straw bedding, that expose them to high dust concentrations.[14-19] A 1998 epidemiologic study[20] that included 28 states representing more than 78% of the United States equine population showed that 34% of owners confined horses indoors during the summer and 43% confined horses indoors during the winter. Therefore, we would expect the prevalence of RAO to be substantially higher during the winter, which clinical experience suggests. However, this hypothesis has not yet been tested on large equine populations.

Identifying host or environmental factors that may increase or decrease the risk of RAO would be useful in the prevention and management of the disease. Currently, there are no published epidemiologic studies that were designed to determine risk factors for RAO in horses. The purpose of the study reported here was to identify risk factors for RAO among horses examined at veterinary teaching hospitals in North America. A secondary objective was to generate new hypotheses concerning the etiology and pathogenesis of the disease.

Criteria for Selection of Cases

The **Veterinary Medical Database (VMDB)** was used to identify records of horses examined at veterinary teaching hospitals in the United States and Canada between January 1, 1990, and December 31, 1999. The VMDB is a computerized database established in 1964 by the National Cancer Institute to gather clinical information concerning all animals admitted to the 24 participating hospitals. A standardized

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abstract describing each animal's examination is reported to the VMDB. This study included records of horses examined at 17 veterinary teaching hospitals[a] during the study period. Information collected included name of the veterinary teaching hospital where the horse was examined, date of admission, breed, age at admission (< 2 weeks, 2 weeks to 2 months, 2 to 6 months, 6 to 12 months, 1 to 2 years, 2 to 4 years, 4 to 7 years, 7 to 10 years, 10 to 15 years, > 15 years, unknown), sex (female, sexually intact male, gelding), and discharge status (alive, died, euthanatized). Horses were categorized as 1 of the following breeds: American Paint Horse, American Saddle Horse, Appaloosa, Arab, Belgian, Donkey, Hackney, Hanover, Holstein, Morgan, Palomino, Pony, American Quarter Horse, American Trotter (Standardbred, American Pacer), Tennessee Walking Horse, Thoroughbred, Foreign Warmblood, mixed breed, and other.

Horses in which RAO was diagnosed were identified by searching for the diagnosis code 362061900 (chronic obstructive pulmonary disease) in the VMDB. Horses in which pulmonary emphysema or bronchitis had been diagnosed were excluded. Only data from the first date of diagnosis were included in analyses. A control group was identified by randomly selecting a horse with a diagnosis other than RAO that matched the institution and year of admission for each of the horses with RAO. The population of horses at risk for developing RAO was estimated as the total number of horses examined at each institution that reported to the VMDB during the study period.

Procedures

Statistical analyses—Associations (**odds ratio [OR]** and 95% **confidence limits [CL]**) between a diagnosis of RAO and age, sex, breed, and discharge status were calculated by means of logistic regression[b] with control horses as the comparison group. Because RAO is a rare disease in the general horse population, calculated ORs were considered good approximations of relative risks, and ORs were therefore interpreted as the increase (or decrease) in risk of RAO associated with each exposure factor.

In these analyses, RAO status (case vs control) was used as the dependent variable, and age, sex, breed, discharge status, and date of diagnosis (month and season) were used as independent variables. Age was treated as a categorical variable. Bivariate logistic regression models were individually fitted to the data. Fit of each model was assessed by use of the Pearson χ^2 test. An all-possible-subsets regression procedure was used to determine whether age, sex, and breed in combination better explained the risk of RAO. Interactions between independent variables in the final multiple logistic regression model were assessed for association with the risk of RAO. In all analyses, values of $P < 0.05$ were considered significant. Fit of the final model was assessed by calculating the Hosmer-Lemeshow statistic.[21] If the model fit was inadequate, diagnostic procedures (standardized residual, leverage, distance, and outlier statistics) were used to identify reasons for lack of fit.[c] In each bivariate model, records were excluded if information on age, sex, or breed group was missing. In multivariate models, records were excluded if information was missing on any of the variables included in the model.

Results

The study population consisted of 1,444 horses with RAO (cases) and 1,444 horses examined for other reasons (controls; **Table 1**). Mean and median hospital prevalences of RAO were 0.92% and 0.86%, respectively. Nine of the veterinary teaching hospitals provided information to the VMDB during all 10 years of the study period; the remaining 8 provided data for 2 to 8 years. Median age group of horses included in the study was 10 to 15 years (interquartile range, 7 to 10 years to > 15 years).

Table 1—Prevalence of recurrent airway obstruction (RAO) among horses examined at 17 veterinary teaching hospitals in North America between January 1, 1990, and December 31, 1999

Veterinary teaching hospital	Reporting period	No. of horses with RAO	No. of horses admitted	Prevalence of RAO (%)
University of Michigan	1990–1999	167	14,554	1.15
University of Missouri	1990–1999	55	6,815	0.81
University of Minnesota	1990–1999	30	6,774	0.44
Iowa State University	1990–1999	133	14,985	0.89
Cornell University	1990–1991	18	2,330	0.77
University of Guelph	1990–1991	24	2,572	0.93
Purdue University	1990–1999	102	10,470	0.97
University of Georgia	1990–1999	75	10,402	0.72
Kansas State University	1990–1993	23	4,006	0.57
University of Illinois	1990–1999	76	12,826	0.59
Colorado State University	1990–1999	258	16,926	1.52
Texas A&M University	1990–1999	157	29,189	0.54
University of Tennessee	1990–1996	121	6,300	1.92
Louisiana State University	1990–1994	46	4,469	1.03
Virginia-Maryland Regional College of Veterinary Medicine	1990–1994	17	1,050	1.62
University of Wisconsin	1990–1997	81	5,170	1.57
University of Florida	1990–1995	61	8,953	0.68
Total	**NA**	**1,444**	**157,791**	**0.92**

NA = Not applicable.

Analysis of risk factors for RAO—Age, sex, breed, and discharge status were significantly associated with the risk that a horse would be identified with RAO during the study period (**Table 2**). The risk of RAO increased with age. Older horses (≥ 7 years old) were approximately 5 times as likely to have RAO as were horses ≤ 4 years old ($P < 0.001$). The risk of RAO in females was 1.4 times the risk in sexually intact males ($P = 0.004$). Thoroughbred horses had a significantly ($P = 0.001$) greater risk (OR, 2.5), compared with ponies. Other breeds were not at an increased risk, compared with ponies. Horses with RAO were not at an increased risk of dying during hospitalization; however, they were more likely to be euthanatized than were control horses ($P < 0.001$).

Multiple regression analyses were performed to adjust for age, sex, and breed effects (**Table 3**), and results confirmed findings obtained from bivariate analyses. Horses ≥ 4 years old were 5 to 7 times as likely to have RAO as were horses < 4 years old, after adjusting for breed and sex effects ($P < 0.001$). Females had a greater risk of RAO than did sexually intact males, after adjusting for age and breed ($P = 0.08$). Thoroughbreds had a higher risk of RAO ($P < 0.001$), compared with ponies. Arabs, Morgans, American Trotters (Standardbred, American Pacer), mixed breeds, and other breeds were also found to be at a higher risk ($P < 0.05$), after adjusting for age and sex effects.

Temporal distribution of RAO—Bivariate logistic regression analyses revealed that horses were more likely to be examined because of RAO between January and June than in July ($P < 0.01$; **Table 4**). The risk between August and December was neither significantly increased nor decreased, compared with July. Analyses were repeated to compare the risk among seasons, with summer as the comparison group. Horses were 1.6 and 1.5 times as likely to be examined because of RAO during winter and spring, respectively ($P < 0.001$), than they were during summer. Horses were significantly ($P < 0.001$) less likely (OR = 0.64) to be examined because

Table 3—Results of multivariate logistic regression analysis, adjusting for age, sex, and breed, of potential risk factors for RAO among horses examined at veterinary teaching hospitals in North America between 1990 and 1999

Variable	Category	Odds ratio	95% CL	*P* value
Age (y)				< 0.001*
	< 4	1.0	NA	NA
	4 to 7	4.9	3.1, 7.6	< 0.001
	7 to 10	6.6	4.3, 10.1	< 0.001
	10 to 15	6.6	4.3, 10.0	< 0.001
	> 15	6.2	4.1, 10.0	< 0.001
Sex				< 0.001*
	Sexually intact male	1.0	NA	NA
	Gelding	0.9	0.7, 1.2	0.53
	Female	1.3	1.0, 1.6	0.08
Breed				< 0.001*
	Pony	1.0	NA	NA
	American Paint	1.3	0.6, 2.4	0.51
	American Saddle	1.9	0.9, 3.7	0.07
	Appaloosa	1.5	0.8, 2.7	0.19
	Arab	1.9	1.1, 3.2	0.03
	Morgan	2.1	1.1, 4.0	0.03
	Quarter Horse	1.4	0.8, 2.4	0.20
	American Trotter	2.3	1.2, 4.3	0.01
	Tennessee Walking	0.8	0.4, 1.6	0.57
	Thoroughbred	3.0	1.7, 5.3	< 0.001
	Mixed	1.8	1.0, 3.3	0.04
	Other	2.1	1.2, 3.6	0.01

*Wald statistic *P* value.

Table 2—Results of bivariate logistic regression analysis of potential risk factors for RAO among horses examined at veterinary teaching hospitals in North America between 1990 and 1999

Variable	Category	No. of controls	No. of cases	Odds ratio*	95% CL*	*P* value
Age (y)						< 0.001
	< 4	149	33	1.0	NA	NA
	4 to 7	195	172	4.0	2.7, 6.4	< 0.001
	7 to 10	253	291	5.2	3.6, 8.3	< 0.001
	10 to 15	468	533	5.1	3.7, 8.3	< 0.001
	> 15	367	392	4.8	3.4, 7.8	< 0.001
Sex						< 0.001
	Sexually intact male	183	152	1.0	NA	NA
	Gelding	707	636	1.1	0.9, 1.4	0.46
	Female	550	645	1.4	1.1, 1.8	0.004
Breed						< 0.001
	Pony	38	25	1.0	NA	NA
	American Paint	55	37	1.0	0.5, 2.0	0.98
	American Saddle	33	42	1.9	1.0, 3.8	0.06
	Appaloosa	84	78	1.4	0.8, 2.5	0.27
	Arab	144	164	1.7	1.0, 3.0	0.06
	Morgan	42	48	1.7	0.9, 3.3	0.10
	Quarter Horse	552	469	1.3	0.8, 2.2	0.36
	American Trotter	72	64	1.4	0.7, 2.5	0.34
	Tennessee Walking	66	36	0.8	0.4, 1.6	0.55
	Thoroughbred	127	212	2.5	1.5, 4.4	0.001
	Mixed	93	105	1.7	1.0, 3.0	0.07
	Other	138	164	1.8	1.0, 3.1	0.04
Discharge status						0.002
	Alive	1,382	1,338	1.0	NA	NA
	Died	6	8	1.4	0.4, 4.1	0.53
	Euthanatized	56	98	1.8	1.3, 2.6	< 0.001

*Unadjusted odds ratio and 95% confidence limits (CL).

Table 4—Results of bivariate logistic regression analysis of month of admission as a risk factor for RAO among horses examined at veterinary teaching hospitals in North America between 1990 and 1999

Month of admission	No. of controls	No. of cases	Odds ratio	95% CL	*P* value
July	162	113	1.0	NA	NA
August	166	131	1.1	0.8, 1.6	0.48
September	145	98	1.0	0.7, 1.4	0.85
October	162	85	0.8	0.5, 1.1	0.10
November	111	62	0.8	0.5, 1.2	0.25
December	63	42	1.0	0.6, 1.5	0.81
January	76	141	2.7	1.9, 4.0	< 0.001
February	71	118	2.4	1.7, 3.6	< 0.001
March	98	140	2.1	1.5, 3.0	< 0.001
April	145	156	1.5	1.1, 2.2	0.006
May	109	182	2.4	1.8, 3.5	< 0.001
June	136	176	1.9	1.4, 2.6	< 0.001

of RAO during the fall. Institutional prevalences of RAO ranged from 0.44% (University of Minnesota) to 1.92% (University of Tennessee). There was a significant difference among institutions in regard to prevalence of RAO ($P < 0.001$).

Discussion

In the present study, RAO was more likely to be diagnosed in females, horses ≥ 4 years old, and Thoroughbreds. Between 1990 and 1999, horses were more commonly examined because of RAO between January and June than at other times of the year.

Our results indicated that in horses, the risk of RAO increased with age. Horses ≥ 7 years old were between 6 and 7 times as likely to be examined because of RAO as were horses < 4 years old, and the median age for horses with RAO was between 10 and 15 years. These findings are in agreement with results of previous reports,[10,13] in which the mean age for horses with RAO was 9 years and horses with RAO were significantly older than horses examined for other reasons. Adjusting for breed and sex did not change our interpretation, although the risk associated with age increased, indicating that horses with RAO tend to be older, regardless of breed or sex. Horses may require prolonged (months to years) exposure to sufficient amounts of organic dust to develop clinical signs of RAO.[22] Traditional management practices, including stall confinement and hay feeding, provide such exposure, making RAO an occupational disease of horses.[23] The immune mechanisms responsible for the development of this allergic condition need to be further investigated.

In the present study, females were more likely to be examined for RAO than were sexually intact males, after adjusting for breed and age. However, because the *P* value for this association in the multivariate analysis ($P = 0.08$) was not less than our cutoff for significance, the association between female sex and RAO identified in bivariate analyses may have been an artifact. Previous studies[10,24] have not identified sex differences related to susceptibility to RAO; however, these studies may have been biased because control populations were not selected at random. Also, χ^2 analysis of sex data from a previous study[13] revealed that the proportion of mares in the RAO group was significantly higher than the proportion of mares in the National Army control group. The biological explanation for this difference is unclear, but it is possible that some of the genetic traits predisposing horses to RAO are sex-linked or that environmental exposures of females (eg, broodmares) are different from environmental exposures for males.

An interesting finding in the present study was that Thoroughbreds were 3 times as likely to be examined because of RAO, compared with ponies. Previous studies[10,13,24] involving Thoroughbreds did not find any breed susceptibility for RAO. However, a study[25] involving Lipizaners and German and Swiss Warmbloods showed that horses were 3.2 times as likely to develop RAO if 1 parent was affected and 4.6 times as likely if both parents were affected. The authors also found that prevalence of RAO was higher among German Warmbloods than among Lipizaners, despite similar environmental conditions, and pointed out that German Warmbloods originated from cross breeding of Thoroughbreds and a local breed. Thus, susceptibility to RAO among Thoroughbreds may have contributed to their findings. This said, hypotheses concerning breed predisposition to RAO are only speculative, and further studies are needed to address issues related to confounding (eg, effects of feeding practices and stall environment). However, interactions between genetic factors and environmental exposure may play a role in RAO.[26] There is a high degree of genetic similarity among Thoroughbreds, in that 78% of alleles in the breed can be traced back to 30 founder horses (27 stallions and 3 mares),[27] and the heritability of susceptibility to particular diseases is expected to be high in breeds in which genetic variation is low. In addition, most Thoroughbreds are bred for racing and are usually sent to training centers at an early age where for their entire racing careers, they will spend at least 23 hours a day confined to a stall and be exposed to high concentrations of organic dust. Thus, a combination of genetic susceptibility and environmental risk factors may explain the high incidence of RAO in Thoroughbreds.

Most American Trotters are also destined to become racehorses and subjected to environmental

conditions similar to those for Thoroughbreds, which may help explain the significantly increased risk of RAO among American Trotters in the present study. The increased risk of RAO in Arabs, Morgans, and mixed-breed horses in the present study requires further investigation.

Horses with advanced RAO have markedly increased respiratory efforts and, as a result, decreased food consumption. Affected horses tend to be thin or cachectic if the condition is left untreated for prolonged periods. Often, owners of horses with RAO are discouraged by the chronicity and recurrent nature of the disease, the expense associated with management and treatment, and the lack of response to commonly used treatments. In this context, the observed increased risk of euthanasia among horses with RAO in the present study is understandable.

The risk that RAO would be diagnosed was significantly increased during the winter and spring, with the highest risk during January. These results are consistent with our current understanding of the pathogenesis of RAO.[28] The National Animal Health Monitoring System study[20] conducted in 1998 confirmed that in the United States, the percentage of horses confined indoors more than doubles during the winter, compared with the summer. Traditional equine housing and feeding practices have been shown to increase exposure to airborne dust and endotoxins,[15,17] and exposure of RAO-susceptible horses to high concentrations of organic dust and endotoxin results in clinical signs of the disease within hours to days.[6,29-31] Therefore, RAO is more likely to be diagnosed during the winter. The risk of RAO was still significantly elevated between April and June in the present study, when weather conditions in North America are milder and horses tend to be turned out on pasture. Clinical signs of RAO usually resolve after a few days in a low-dust environment, such as pasture. Persistence of the increased risk for RAO during the spring may be explained by several factors. Practitioners in private practice refer most horses with RAO examined at veterinary teaching hospitals. Usually, these field veterinarians have implemented environmental control strategies and provided medical treatment, but elect to refer horses for further examination because of a lack of response.[10] Thus, weeks to months may pass between the time clinical signs develop in the field and the time RAO is diagnosed at the veterinary teaching hospital. Also, more than a third of horses spend most of their time stabled, even if they have increased access to pastures or paddocks during spring, summer, and fall.[20] Considering that 99% of US equine operations feed hay,[32] exposure to allergens continues into the spring, even if it is less than during the winter. As a result, resolution of clinical signs would be expected to be delayed.

Results of the present study could have been biased by inclusion of horses with summer pasture-associated obstructive pulmonary disease, rather than RAO, because the VMDB coding system does not allow a distinction between these 2 diagnoses. Summer pasture-associated obstructive pulmonary disease is clinically indistinguishable from RAO, except that affected animals have recurrences while kept on pasture during the summer months and improve clinically during the winter or when horses are housed indoors.[33,34] However, such bias would have lead to an underestimation of the seasonal risk of RAO.

Data used in this study were based on information provided by participating institutions to the VMDB. Thus, caution must be used when trying to extrapolate our findings to the general equine population. Horses with RAO examined at veterinary teaching hospitals represent only a fraction of all affected animals and may not accurately reflect the characteristics of the general population. In a previous study[35] of 166 horses selected at random at a slaughterhouse, RAO incidence was 12% on the basis of results of histologic examination of lung tissue. Mean prevalence of RAO in the present study was substantially lower (0.9%); however, it was comparable to the 1.6% prevalence observed by 1 of the authors (LLC) in the general population of horses in Indiana during 2001 (unpublished observations). Also, making a diagnosis on the basis of histologic findings would likely include horses with subclinical RAO and horses with inflammatory airway disease, leading to a higher prevalence estimate. Data analysis was limited to variables recorded in the VMDB in the present study, and it is possible that associations between age, sex, breed, and RAO detected in this study were confounded by other variables that were not measured and therefore not included. Nevertheless, age, breed, and seasonal associations with RAO are consistent with findings from previous research. The criteria used by clinicians to make a diagnosis of RAO were not included in the analyses, and a variety of respiratory tract diseases, including infectious, parasitic, and miscellaneous conditions, may have been falsely diagnosed as RAO. Data collected at the veterinary teaching hospitals included historical information and results of physical examination. In addition, diagnostic tests such as hematologic testing, radiography, collection of tracheal wash fluid, and bronchoalveolar lavage were performed in 46%, 52%, 40%, and 5% of horses with RAO, respectively. Thus, we believe that the diagnosis was accurate for most horses with RAO in the present study. Results of the present study could also have been biased by inclusion in the control group of horses with RAO that were examined during a period of disease remission. However, the number of horses with RAO that might have been included as controls would be expected to be low, given the low prevalence of RAO in the general population.

In conclusion, the present study confirmed previous clinical observations regarding risk factors for RAO in horses. In particular, we found that the risk of disease increased with age and that RAO was more commonly diagnosed during winter and spring. Additional research is needed to confirm or refute other findings, including the increased susceptibility among Thoroughbreds and females. Results from this study are consistent with the suggestion that environmental and genetic factors contribute to the development of RAO. The seasonal and, possibly, age effects support the role of the environment. Breed and sex factors support environmental and genetic effects. Future studies should examine the relative contributions of these fac-

tors to the development of RAO. In particular, identifying gene polymorphism and understanding how genes interact with environmental factors to induce RAO may prove invaluable to the understanding of disease pathophysiology and, ultimately, the prevention and treatment of RAO.[36]

[a]Colorado State University, University of Florida, University of Georgia, University of Illinois, Iowa State University, Kansas State University, Louisiana State University, Michigan State University, University of Minnesota, University of Missouri, Cornell University, University of Guelph, Purdue University, University of Tennessee, Texas A&M University, Virginia-Maryland Regional College of Veterinary Medicine, and University of Wisconsin.
[b]SPSS for Windows, version 10.1.0, SPSS Inc, Chicago, Ill.
[c]Statistix, version 7, Analytical Software, Tallahassee, Fla.

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