

Risk factors associated with nasopharyngeal cicatrix syndrome in horses

Tracy E. Norman, VMD, DACVIM; M. Keith Chaffin, DVM, MS, DACVIM;
Wesley T. Bissett, DVM, PhD; James A. Thompson, DVM, DVSc, DACT, DACVPM

Objective—To determine risk factors associated with the development of nasopharyngeal cicatrix syndrome (NCS) in horses.

Design—Retrospective case-control study.

Animals—242 horses referred for endoscopic evaluation of the upper portion of the respiratory tract (121 horses with NCS and 121 control horses).

Procedures—Medical records of horses that had an endoscopic evaluation of the upper airway performed between January 2003 and December 2008 were reviewed. Signalment, housing management, and season of evaluation were recorded and reviewed for each horse. The associations between clinical signs and endoscopic findings were evaluated by the use of a prospective logistic model that included a Bayesian method for inference.

Results—Breed and sex had no significant effect on the risk of having NCS. The risk that a horse had NCS increased significantly with age. Exclusive housing in a stall was protective against the development of NCS. In addition, the amount of pasture turnout had a dose-related effect, with exclusive pasture turnout positively correlated with increased risk of developing NCS, compared with a mixture of pasture turnout and stall confinement. Horses were significantly more likely to be evaluated because of clinical signs of the syndrome during the warm months of the year.

Conclusions and Clinical Relevance—The risk factors for NCS identified in this study may support chronic environmental exposure to an irritant or infectious agent as the cause of NCS. Information gained from this study should be useful for investigating the cause of NCS. (*J Am Vet Med Assoc* 2013;242:1267–1270)

Nasopharyngeal cicatrix syndrome has been reported for horses living in central and southeastern Texas.^{1–3} This syndrome was first reported in 1987, and within that report¹ were descriptions of horses with the syndrome as early as 1972. More recently, NCS was noted to be the most common condition in horses seen at Texas A&M University's Large Animal Teaching Hospital from 1995 to 2005 for which permanent tracheostomy was required,² and it was the most common disorder of the upper portion of the respiratory tract seen at that hospital during that period.^{1–3} Clinical features of NCS include catarrhal inflammation of the nasopharynx, larynx, or both during the acute phase of the syndrome, which is replaced with web-like scarring during the chronic phase of the syndrome. Common endoscopic findings of NCS include scarring of the nasopharynx, circumferential or localized to the soft palate just rostral to the epiglottis; epiglottic deformation; bilateral arytenoid chondropathy; thickening of the vocal cords; and scarring of the salpingopharyngeal openings. Ulceration and scar formation of the mucosa of the nasal cavities and proximal aspect of the trachea are also observed in some cases. Severity of the syndrome

ABBREVIATIONS

MCMC	Markov chain Monte Carlo
NCS	Nasopharyngeal cicatrix syndrome

ranges from abnormalities that are detected as incidental findings at the time of endoscopic examination of the upper portion of the respiratory tract to obstruction of the upper respiratory tract so severe that the horse requires permanent tracheostomy for survival.² A recent study⁴ on a subset of the population of horses evaluated in the study reported here identified nasal discharge, exercise intolerance, respiratory stridor, and respiratory distress as clinical signs associated with endoscopic findings of NCS.

Despite long-standing awareness of this condition and its anecdotally high morbidity rate in some geographic regions, risk factors for the condition have received little investigation. The purpose of the study reported here was to determine risk factors associated with the development of NCS in horses.

Materials and Methods

Case selection—The medical records of horses admitted to the Texas A&M University Large Animal Teaching Hospital for endoscopic examination of the upper portion of the respiratory tract for any reason from January 2003 to December 2008 were searched by use of the computerized Veterinary Medical Information System. Horses were included for analysis as NCS

From the Department of Large Animal Clinical Sciences, College of Veterinary Medicine and Biological Sciences, Texas A&M University, College Station, TX 77843.

The authors thank Dr. James Schumacher for his assistance in reviewing the manuscript and Kim Hensarling for assistance with medical records.

Address correspondence to Dr. Norman (tnorman@cvm.tamu.edu).

affected if they met the following criteria: the medical record was available (complete information regarding clinical signs was not required), endoscopic images (still images or video) of the nasopharynx and larynx were available for examination, and endoscopic images revealed changes to the respiratory tract consistent with those associated with NCS. Information obtained from the records included signalment, housing management (maintained at pasture exclusively, maintained partially at pasture and partially in a stall, or stalled exclusively), and season during which the horse was referred. For the NCS-affected horses, the chronicity of lesions (acute with active inflammation or scar tissue without inflammation) was also recorded.

A control population of horses was also identified. The control group was chosen from the remaining list of horses that met the study inclusion criteria but for which there were no endoscopic findings consistent with NCS. To minimize selection bias and potential bias associated with the date of admission to the veterinary teaching hospital, every third horse was selected from the list. The list underwent 1.5 iterations to attain a number of control horses equal to the number of case horses.

Medical records review—Age, sex, and breed were recorded for all case and control horses. Age was classified into < 4 years old, 4 to 10 years old, 11 to 16 years old, and > 16 years old to represent growing, young, middle-aged, and aged horses, respectively. Housing management, occupation (use) of horse, and the season in which the horse was referred for evaluation were also recorded. Endoscopic images were evaluated to confirm the presence (case) or absence (control) of NCS-associated changes.

Statistical analysis—A logistic regression approach was used. The modeling used Bayesian inference, with vague or flexible prior beliefs and an MCMC implementation. The MCMC implementation was performed with commercial software.^{3,a} The initial 5,000 iterations were discarded to allow for convergence, and every 50th of the following 250,000 iterations was sampled for the posterior distribution. Observing convergence of 2 chains with widely divergent initial values checked convergence to the posterior distribution. This interval is referred to as a Bayesian credibility interval or a Bayesian confidence interval. The term confidence interval was used throughout this report. The results were reported as the median of the posterior distribution, and the 2.5th and 97.5th percentiles were taken directly from the posterior distribution. The OR was considered to be significant ($P < 0.05$) if the 95% confidence interval excluded the value 1. Missing data points were considered to be missing at random.

Results

Horses—During the study period, 1,236 horses underwent endoscopic evaluation of the upper portion of the respiratory tract. Endoscopic findings consistent with NCS were recorded for 121 horses that met the inclusion criteria for cases. Changes consistent with NCS were absent in 1,115 endoscopically evaluated horses;

121 horses that met the inclusion criteria were selected as control horses.

Horses with NCS ranged in age from 4 to 28 years (median, 16 years; mean, 14.2 years). There were 0 NCS-affected horses < 4 years old, 36 from 4 to 10 years old, 44 from 11 to 16 years old, and 41 horses > 16 years old. Control horses ranged in age from 0 to 29 years (median, 14.6 years; mean, 8.7 years). There were 27 control horses < 4 years old, 54 from 4 to 10 years old, 27 from 11 to 16 years old, and 13 horses > 16 years old. One hundred fourteen horses were geldings, 110 were mares, and 18 were stallions. The American Quarter Horse was the most common breed (79/121 [65.2%] affected horses and 62/121 [51.2%] control horses), followed by mixed-breed horses, Thoroughbreds, American Paint Horses, Arabians, and other breeds. Horses in the case and control groups were used for barrel racing, roping, ranch work, breeding, racing, hunter-jumper showing, pleasure, dressage, eventing, polo, polocross, cutting, and therapeutic riding. Occupation (use) was not recorded in the record of 19 of the NCS-affected horses or in the record of 21 of the control horses.

Assessment of risk factors—Signalment, housing management, and season of referral of affected horses were compared with those of control horses to determine risk factors associated with NCS.

SIGNALMENT

There was a significant association of age with the occurrence of NCS (Table 1). Nasopharyngeal cicatrix syndrome-affected horses were significantly more likely to be > 11 and > 16 years old than were control horses. No significant differences in sex or breed were identified between NCS-affected horses and controls.

HOUSING MANAGEMENT

Data regarding housing management were available for 113 NCS-affected horses and 105 control

Table 1—Odds ratios for NCS on the basis of age, housing, and season as determined retrospectively from 242 horses referred for endoscopic evaluation of the upper portion of the respiratory tract (121 horses with NCS and 121 control horses).

Variable*	OR (95% CI)	
	All phases of NCS	Acute inflammatory phase of NCS
Age		
4–10 y	22.1 (2.8–638)	ND
11–16 y	92.4 (11.4–2,427)†	ND
> 16 y	89.0 (10.7–2,528)†	ND
Housing		
Exclusively stalled	0 (0.0–0.0)‡	ND
Exclusively turned out to pasture	4.52 (2.1–9.9)†	ND
Season		
Summer	3.8 (1.5–10.4)†	5.1 (2.2–10.6)†
Fall	1.9 (0.7–4.8)	3.4 (1.4–7.4)†
Spring	1.4 (0.5–4.1)	3.2 (1.2–7.0)†

*Baseline values for comparisons were < 4 years old, combination of stall and pasture housing, and winter for the variables of age, housing, and season, respectively. †The OR was considered to be significantly ($P < 0.05$) different from 1 if the 95% CI excluded the value 1. ‡The OR was nearly completely protective; the value was approximately 0.
CI = Confidence interval. ND = Not determined.

horses. Nasopharyngeal cicatrix syndrome-affected horses were maintained either exclusively at pasture (86/113 [76%]) or in stalls with some time at pasture (27/113 [24%]). No NCS-affected horses were stalled exclusively. Control horses were maintained in all 3 conditions, with the majority maintained in stalls with pasture turnout (44/105 [42%]). Others were exclusively turned out to pasture (40/105 [38%]) or exclusively confined to a stall (21/105 [20%]). Horses with access to pasture had a significantly increased risk of developing NCS (Table 1).

SEASON

Data regarding the season of referral were available for all 242 horses included in the study. Horses with NCS were significantly more likely to be referred for evaluation in the summer than were control horses. Horses in the acute inflammatory phase of NCS were significantly more likely to be referred for evaluation during the spring, summer, and autumn, with the highest risk occurring in the summer months (Table 1).

Discussion

Identifying risk factors for a disease process is an important step toward identifying preventative strategies and etiologies of idiopathic disease. Possible risk factors for NCS have not been investigated since Schumacher and Hanselka¹ described 47 horses with the syndrome in 1987. That study evaluated the signalment, clinical history, and endoscopic and radiographic findings of horses with NCS and compared information pertaining to 24 of those cases with information about the general hospital population at that time. The purpose of the study reported here was to further evaluate the questions raised by Schumacher and Hanselka and to evaluate signalment, housing management, and season of referral as potential risk factors for the development of NCS. To prevent underestimation of possible risk factors, only horses that had undergone endoscopic evaluation of the upper respiratory tract were eligible to act as controls; this prevented selection of horses with subclinical NCS as controls.

Horses with NCS were similar to controls with regard to breed and sex. Schumacher and Hanselka¹ reported a higher proportion of affected females in their study population, compared with the proportion of females in the general hospital population, whereas the present study found no difference between the proportion of females in the study group and the proportion of females in the control group. This variability between studies may be because the present study examined a larger group of affected horses or because of temporal differences in the types of horses (eg, broodmares) within the referral area for the present study.

Both the present study and that of Schumacher and Hanselka¹ found that NCS was more likely to be identified in horses older than those in the general population. In addition, the results of the present study suggested that the risk of NCS progressively increases with age. This finding indicated that NCS is a chronic, progressive disease, either the result of prolonged infection or as a syndrome of multiple exposures over time

to an irritant or infectious agent leading to cycles of inflammation and fibrous remodeling of the equine upper airway.

One other notable difference between the present study and that of Schumacher and Hanselka¹ is the number of horses identified with NCS during the period of each study. Schumacher and Hanselka¹ identified 47 horses with NCS in a span of 13 years, whereas 121 horses with NCS were identified in only 5 years in the present study. This difference can be explained by the change in the total number of horses referred to the veterinary teaching hospital yearly; the total number of horses seen at the veterinary teaching hospital during the period of Schumacher's study (13 years) was 7,396, compared with 19,309 in the 5 years of the present study. Other reasons for the higher number of horses with NCS in the present study could include increased use of endoscopic examination of the upper portion of the equine respiratory tract during the period of study and increased recognition of NCS. It seems unlikely that the prevalence of NCS is increasing, however, given that the proportions of NCS-affected horses seen by the veterinary teaching hospital during the periods of the 2 studies are similar (0.64% [Schumacher and Hanselka¹] vs 0.63% [present study]).

In the present study, associations between clinical signs and endoscopic findings were evaluated by the use of a prospective logistic model that used a Bayesian method for inference. There has been a growing interest in evidence-based medicine and, along with it, an increased use of Bayesian statistics in medical applications. For the present study, the Bayesian approach was selected and performed because of advantages it offers over a frequentist approach. First, Bayesian results can apply to patients, whereas results from a frequentist approach have only a population-based inference. Second, Bayesian results can identify a specific probability for every parameter value, whereas results of a frequentist approach address acceptance or rejection of the null hypothesis. For example, when a frequentist approach states that a *P* value is < 0.05, the frequentist approach will (usually) reject the initial or fixed parameter value, but the analysis does not support any other parameter value. Third, Bayesian estimates are influenced by both prior beliefs and information from the data collected from the evaluation of prognostic factors. Prior beliefs are said to be informative if they are known relatively precisely and thus are allowed to influence the posterior likelihood (the evaluation of prognostic factors). When the priors are said to be vague or uninformative, the results are primarily influenced by the data. Fourth, Bayesian inference, as implemented by MCMC, can produce full posterior distributions even for very small samples without fear of violating assumptions like small sample normality. These considerations identify considerable utility for Bayesian statistics when evaluating prognostic factors in small samples of hospital patients.

Housing management of horses significantly affected the risk of developing NCS. Exclusive housing in a stall was nearly infinitely protective against the development of NCS. In addition, the amount of pasture turnout had a dose-related effect, with exclusive

pasture turnout positively correlated with increased risk of developing NCS, compared with a mixture of pasture turnout and stall confinement. This finding offered strong evidence that exposure to the etiologic agent likely occurs when horses are grazing at pasture. The etiologic agent is likely not airborne because most barns in Texas are exposed to environmental air. Nasopharyngeal cicatrix syndrome is unlikely to be caused by a pathogen spread thorough aerosolization of respiratory secretions because confinement in air spaces shared with infected horses should enhance, rather than decrease, the risk of developing NCS.⁶

Referral of horses for evaluation because of NCS differed significantly by season. Horses with NCS were significantly more likely than control horses to be referred for evaluation during the summer. Horses with NCS characterized by acute nasopharyngeal inflammation⁴ were more likely to be referred in spring, summer, or autumn than in winter for endoscopic evaluation of the upper portion of the respiratory tract. This may reflect an effect of higher ambient temperatures on the possible aerosolization of the etiologic agent of NCS from pasture grass or from the ground. The effect of season may also be due to the seasonality of the production of an irritant, such as a pollen or algal toxin. Acute inflammation associated with NCS has been shown to be associated with nasal discharge and the onset of respiratory distress⁴; the increased proportion of horses with NCS referred during the warmer months may reflect greater recognition of clinical signs associated with this inflammation. Higher ambient temperatures may also cause horses to increase their respiratory frequency or pressures, which may increase the exposure of the upper airway to a noxious substance or infectious agent and make chronic narrowing of the airway from NCS more apparent.

This study had a number of limitations. As a retrospective study, the available information was limited to that which was entered into the medical records. More specific information about the environment in which horses were housed, herd size, and cohabitation with other livestock species was lacking in most records. A prospective study would have the advantage of gathering more specific information to more precisely characterize risk factors and the length of time required for horses exposed to those risks to develop clinical or endoscopic signs of disease. Assessment of occupation of horses as a risk factor could not be determined in this study because of limited numbers of records in which these data were recorded and the confounding effect of use on housing management.

Another potential limitation was that some cases of NCS may have been missed because of errors in coding of medical records, lack of endoscopic images, or both. The study and control groups were strictly defined in this study, but because images were required for review, a sizeable number of cases may have been missed. The fact that NCS is a common disorder in our geographic region may have also affected the results of this study, a limitation that may not apply in areas where NCS occurs less commonly.

It would have been informative to analyze the effect of geographic location, and duration at those locations, of horses on their risk for NCS. Unfortunately, that information was not accessible for the present retrospective study. The physical location of the horses and the billing address of clients are often different, and it was determined that these data from the records would be unreliable. Prospective work evaluating geographic location and animal movement as risk factors for NCS would provide important information about the likely etiology of the syndrome.

This study identified increasing age, access to pasture, and warm environmental conditions as risk factors for NCS in horses. These factors support the notion that repeated exposure to an environmental agent causing cycles of inflammation is a likely etiology of NCS, but other possibilities, such as chronic infection or hypersensitivity reaction, exist. Work is needed to determine the etiology and progression of this disorder, to discover whether other livestock species are involved or affected, and to define the geographic boundaries where the syndrome occurs.

a. WinBUGS, version 3.1.1, MRC Biostatistics Unit, Cambridge, England.

References

1. Schumacher J, Hanselka DV. Nasopharyngeal cicatrices in horses: 47 cases (1972–1985). *J Am Vet Med Assoc* 1987;191:239–242.
2. Chesen AB, Rakestraw PC. Indications for and short- and long-term outcome of permanent tracheostomy performed in standing horses: 82 cases (1995–2005). *J Am Vet Med Assoc* 2008;232:1352–1356.
3. Dean PW, Cohen ND. Arytenoidectomy for advanced unilateral chondropathy with accompanying lesions. *Vet Surg* 1990;19:364–370.
4. Norman TE, Chaffin MK, Bisset WT, et al. Association of clinical signs with endoscopic findings in horses with nasopharyngeal cicatrix syndrome: 118 cases (2003–2008). *J Am Vet Med Assoc* 2012;240:734–739.
5. Lunn D, Spiegelhalter D, Thomas A, et al. The BUGS project: evolution, critique and future directions. *Stat Med* 2009;28:3049–3067.
6. Gildea S, Arkins S, Cullinane A. Management and environmental factors involved in equine influenza outbreaks in Ireland 2007–2010. *Equine Vet J* 2011;43:608–617.