Effect of topical anesthesia of the laryngeal mucosa on upper airway mechanics in exercising horses

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Objective—To determine the effect of desensitization of the laryngeal mucosal mechanoreceptors on upper airway mechanics in exercising horses.

Animals—6 Standardbreds.

Procedure—In study 1, videoendoscopic examinations were performed while horses ran on a treadmill with and without topical anesthesia of the laryngeal mucosa. In study 2, peak tracheal and nasopharyngeal pressures and airflows were obtained from horses during incremental treadmill exercise tests, with and without topical anesthesia of the laryngeal mucosa. A nasal occlusion test was performed on each horse while standing during an endoscopic examination for both trials.

Results—In study 1, horses had nasopharyngeal collapse while running on the treadmill when the laryngeal mucosa was anesthetized. In study 2, inspiratory upper airway and nasopharyngeal impedance were significantly higher, and peak tracheal inspiratory pressure, respiratory frequency, and minute ventilation were significantly lower in horses when the laryngeal mucosa was anesthetized, compared with values obtained when horses exercised without topical anesthesia. Peak inspiratory and expiratory airflows were lower in horses when the laryngeal mucosa was anesthetized, although differences did not quite reach significance ($P = 0.06$ and 0.09, respectively). During a nasal occlusion test, horses had episodes of nasopharyngeal collapse and dorsal displacement of the soft palate when the laryngeal mucosa was anesthetized. Upper airway function was normal in these horses without laryngeal mucosal anesthesia.

Conclusions and Clinical Relevance—Receptors within the laryngeal mucosa may be important in maintaining upper airway patency in exercising horses. (*Am J Vet Res* 2001;62:1706–1710)

Collapse of the rostral, dorsal, and lateral portions of the nasopharynx are clinically recognized causes of upper airway obstruction in horses during exercise.[1] These forms of nasopharyngeal obstruction can cause exercise intolerance and are diagnostic challenges[1]; dorsal displacement of the soft palate is a more commonly diagnosed form of nasopharyngeal collapse. Unfortunately, the cause of any of these obstructive syndromes is unknown.

Contraction of upper respiratory tract muscles is principally responsible for dilation and stabilization of the nasopharynx.[2] Activation of these muscles during augmented breathing, which occurs during intense exercise, is stimulated by chemical drive and mechanical and sensory afferent input from the upper airways in cats, dogs, and humans.[3-9] The laryngeal mucosa has an abundant supply of sensory receptors that control a complex pattern of respiratory reflexes that influence the patency of the upper airway and the pattern of breathing.[10] Most of these receptors are concentrated within the laryngeal mucosa and receive afferent innervation from superior laryngeal branches of the vagus nerve.[10-12] Negative pressure receptors are the most abundant type of receptors in the laryngeal mucosa and are stimulated during upper airway obstruction when large collapsing pressures are produced in the upper airway. Specifically, these mechanoreceptors provide afferent information to the CNS, signaling the contraction of upper airway muscles that ultimately leads to dilation and stabilization of the upper airway.[10] These reflexes are markedly reduced or abolished by sectioning the superior laryngeal nerve or by topical anesthesia of the laryngeal mucosal, indicating that the superior laryngeal nerve afferents are primary mediators of these reflex responses in dogs and humans.[13,14]

Laryngeal mucosal pressure receptors and the associated reflex motor activity have not been studied in horses, but we infer from work in other species that these receptors and associated reflexes may exist in horses. Contraction of upper airway muscles is especially important in upper airway stability and dilation in obligate nasal breathers such as horses. The upper airway must be able to resist collapse as driving pressures become more negative in order to maintain high airflows during intense exercise.[15] Therefore, we hypothesized that desensitization of the laryngeal mucosa would cause nasopharyngeal dysfunction during exercise and during upper airway occlusion. This would occur because the reflex signaling of nasopharyngeal dilator muscle contraction would be abolished. The purpose of the study reported here was to determine the effect of desensitization of the laryngeal mucosal mechanoreceptors on upper airway mechanics in exercising horses.

Materials and Methods

Horses—Six Standardbreds (3 geldings and 3 mares) 3 to 12 years old and weighing between 487 and 548 kg were used in the experiment, which was approved by the All-University Committee for Animal Use and Care at Michigan State University. All horses were vaccinated against tetanus, equine influenza, rhinopneumonitis, and eastern and western equine encephalitis. Physical examinations of the horses

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and endoscopic examinations of the larynx and nasopharynx at rest and during high-speed treadmill exercise failed to reveal any abnormalities. All horses were trained to run on a treadmill prior to the experiment. Maximum heart rate (HR_{max}) was determined by use of a telemetry system[a] and an incremental exercise test.[16] Speeds corresponding to 50% (HR_{max50}) and 75% (HR_{max75}) of maximum heart rate were interpolated from these data.

Topical anesthesia of the laryngeal mucosal—The endoscope was passed through the left naris, and the tip of the endoscope was positioned just rostral to the epiglottis. Polyethylene tubing (internal diameter, 1.19 mm; external diameter, 1.7 mm)[b] was placed through the biopsy portal of the endoscope such that the tip of the tubing projected 3 to 7 cm from the endoscope tip. Approximately 20 ml of mepivicaine hydrochloride (2%)[c] was sprayed over the mucosa of the larynx, including the epiglottis and the piriform recesses. As the larynx was bathed in anesthetic, some of the anesthetic was swallowed or ran out the horse's nose. Ten minutes after application of the anesthetic, the endoscope was passed into the nasopharynx, and the biopsy instrument was inserted through the portal to test the tactile response of the laryngeal mucosa. The piriform recesses, epiglottis, corniculate processes of the arytenoid cartilages, and vocal folds were stimulated with the biopsy instrument. If the horse made any attempt to gag or swallow, more local anesthetic was applied to the laryngeal mucosa. This occurred in 4 of the 6 horses, and between 10 and 20 ml of 2% mepivicaine hydrochloride was used. We considered the laryngeal mucosa anesthetized when the horse did not respond to tactile stimulation. Duration from the time the laryngeal mucosa was anesthetized to the end of the protocol was approximately 15 minutes.

Experiment 1—Six horses performed an incremental treadmill exercise test with the videoendoscope placed in the right naris so nasopharyngeal conformation could be observed. Each horse performed the exercise trial twice, 7 to 10 days apart, once without topical anesthesia and once with topical laryngeal mucosal anesthesia. The experiment was randomized such that 3 horses performed the trial first with the laryngeal mucosa anesthetized, and 3 horses performed the trial first without mucosal anesthesia. The endoscopic examination during each trial was recorded.

Flow mechanics measurements—Horses were instrumented to measure tracheal and nasopharyngeal pressures and airflow while running on a treadmill. Two catheters were made with 150 cm of polyethylene tubing (internal diameter, 2.15cm; external diameter, 3.25cm)[b] with 6 side holes beginning a distance of 8 catheter diameters from the sealed tip. Catheters were phase-matched up to 10 Hz.[17] Tracheal and pharyngeal pressures were measured by use of differential pressure transducers[d] and were recorded on a computer with software designed to measure respiratory function variables.[e] One catheter was passed through the right nostril and then through the laryngeal opening into the trachea, with endoscopic guidance. The tip of the catheter was placed approximately at the junction of the proximal and middle thirds of the cervical tracheal. The second catheter was passed through the right naris. The tip of the catheter was positioned at the level of the right auditory diverticulum (guttural pouch) opening in the nasopharynx. The positioning of the catheter was confirmed by use of endoscopy. The differential pressure transducers were calibrated with a water manometer before and after each experiment.

Airflow was measured by use of a 15.2-cm diameter pneumotachograph laminar flow element[f] mounted on an airtight facemask. The fiberglass facemask covered the mouth and nostrils and was fitted on the horse's head and sealed with a rubber shroud and adhesive tape. The mask fit the horse's head in such a way as to allow unimpeded nostril dilation. The pneumotachograph was mounted on the end of the facemask with a protective wire screen positioned between the horse's muzzle and the pneumotachograph. The resistance of the pneumotachograph was 0.04 cm H_2O/L per second measured up to an airflow of 90 L/s. The combined resistance of the mask-pneumotachograph system was 0.05 cm of H_2O/L per second at 90 L/s. Pressure changes across the pneumotachograph were measured by use of a differential pressure transducer.[d] Before each protocol, the pneumotachograph was calibrated by use of a rotameter flow meter[g] capable of measuring airflow up to 90 L/s.

Pressure signals were passed through an amplifier and then into the computer. Peak inspiratory and expiratory tracheal and nasopharyngeal pressures and peak inspiratory and expiratory airflow were obtained from the tracings on the computer screen. Because inertia and airway deformation result in complex upper airway pressure and flow relationships at high respiratory flow rates,[18] pressure and flow signals generated during exercise were not in phase (ie, have the same wave form but do not occur at the same time). Peak inspiratory and expiratory pressures as well as inspiratory and expiratory flows were measured for a given breath.[18] Upper airway impedance was calculated as the ratio of peak tracheal pressure divided by peak airflow. Nasopharyngeal impedance was calculated by dividing peak nasopharyngeal pressure by peak airflow. Translaryngeal impedance was calculated by subtracting nasopharyngeal impedance from translaryngeal impedance to determine the change in impedance across the larynx. Tidal volume was obtained by digitally integrating the flow signal with respect to time by use of an algorithm in the computer. Respiratory frequency was determined from the physiograph tracings on the computer screen. Minute ventilation was calculated as the product of tidal volume and respiratory frequency. The mean of values obtained from 10 consecutive breaths was used for each data point.

Experiment 2—A lip twitch was applied to the horse's nose for restraint, and the endoscope was passed through the left naris and positioned in the nasopharyx. The tracheal and nasopharyngeal catheters were passed through the right naris and positioned as described. A 60-second nasal occlusion test was performed while nasopharyngeal and tracheal pressures were measured. The examination was recorded on a videotape machine. The endoscope was withdrawn, and a facemask was placed over the horse's muzzle and secured. The horses were exercised on a treadmill for 3 minutes at 4 m/s. Horses then exercised at the speeds corresponding to HR_{max50}, HR_{max75}, and HR_{max} for 1 minute at each speed. Catheters were flushed with air during the experiment to avoid fluid accumulation and dampening of pressure values. Horses performed the exercise trial 2 times, once with topical laryngeal mucosal anesthesia and once without topical anesthesia. The sequence of exercise trials was randomized so that 3 horses performed the trial with topical anesthesia first, and 3 horses performed the trial first without topical anesthesia. Trials for each horse were separated by 7 to 10 days.

Data analysis—Data points were collected during the last 30 seconds at each speed. Data were analyzed by use of repeated-measures ANOVA with speed and treatment (laryngeal mucosal anesthesia or no anesthesia) as main factors. Post-hoc comparisons, if applicable, were made by use of the Student-Newman-Keuls test. A significance level of $P < 0.05$ was chosen.

Results

All horses tolerated the topical laryngeal mucosal anesthesia well. We were able to obtain mucosal anes-

thesia in every horse such that none of the horses reacted to tactile stimulation of the larynx or piriform region by gagging or swallowing. Mepivicaine hydrochloride solution ran out of the nose or was swallowed by some horses, and portions of nasal and nasopharyngeal mucosa were potentially desensitized. None of the horses coughed or had trouble swallowing after the topical anesthesia.

Study 1—When horses were exercised without anesthesia of the laryngeal mucosa, videoendoscopy failed to reveal any abnormalities. In contrast, various degrees of nasopharygeal collapse were observed in all horses during exercise when the laryngeal mucosa was anesthetized. Some horses had severe dorsal pharyngeal collapse, and 2 horses had complete collapse of the nasopharynx such that the nasopharynx formed a sphincter. Dorsal displacement of the soft palate was not observed. Laryngeal function was judged to be normal on the basis of results of endoscopic examination.

Study 2—Horses had episodes of nasopharyngeal collapse during nasal occlusion when the laryngeal mucosa was anesthetized, whereas no dysfunction was observed in horses without topical anesthesia of the laryngeal mucosa. When the laryngeal mucosa was anesthetized, 2 horses had dorsal displacement of the soft palate, and 3 horses had complete collapse of the nasopharynx such that the nasopharynx formed a tight sphincter during nasal occlusion (**Fig 1**). In the absence of topical anesthesia of the laryngeal mucosa, none of these horses had any signs of soft palate dysfunction or nasopharyngeal instability during nasal occlusion. Peak tracheal and nasopharyngeal pressures achieved during nasal occlusion were not significantly different with or without topical laryngeal mucosal anesthesia. Airway pressures during nasal occlusion tests were (mean ± SEM [cm H_2O]): peak tracheal inspiratory pressure, –27.2 ± 1.35; peak nasopharyngeal inspiratory pressure, –27.3 ± 1.38; peak tracheal expiratory pressure, 29.3 ± 3.95; and peak nasopharyngeal expiratory pressure, 29.3 ± 4.0.

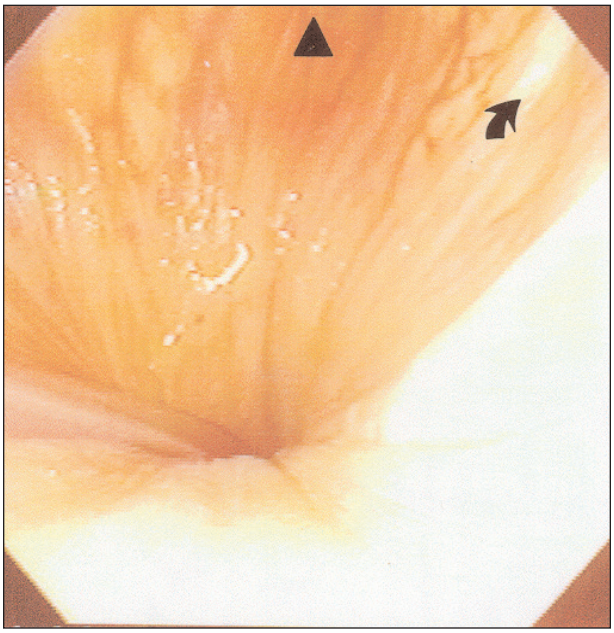

Figure 1—Endoscopic view of the nasopharynx of a horse with anesthesia of the laryngeal mucosa during nasal occlusion. Notice that the nasopharynx is completely collapsed, forming a sphincter. Arrowhead = Dorsal pharyngeal recess. Curved arrow = Caudal aspect of the pharyngeal opening of the left auditory tube diverticulum (guttural pouch).

Table 1—Measurements (mean [SEM]) of upper airway mechanics in 6 horses with (Anesth) and without (Control) topical anesthesia of the laryngeal mucosal, measured during treadmill exercise at 4 m/s and at speeds corresponding to 50, 75, and 100% of maximum heart rate

Speed	TIP	TEP	PIP	PEP	IF	EF	Z_{IU}	Z_{EU}	Z_{INP}	Z_{ENP}	Z_{ITL}	RF	V_T	VE
4 m/s														
Anesth	–21.9*	14.3	–13.1	12.7	30.7	32.7	0.63*	0.46	0.43*	0.41	0.20	60*	10.7	675.1
	(–2.7)	(2.8)	(–1.6)	(2.3)	(2.9)	(2.6)	(0.04)	(0.12)	(0.4)	(0.10)	(0.04)	(5.8)	(0.52)	(69)
Control	–14.2	9.4	–10.6	7.6	35.2	36.4	0.40	0.27	0.31	0.22	0.10	67	11.0	707.1
	(–1.0)	(0.8)	(–0.9)	(0.6)	(2.8)	(2.8)	(0.02)	(0.02)	(0.3)	(0.2)	(0.02)	(5.0)	(0.90)	(52.9)
50%														
Anesth	–22.1*	16.7	–17.3	14.4	35.5	38.5	0.64*	0.49	0.49*	0.42	0.16	67*	12.4	829.8*
	(52.9)	(4.8)	(–2.4)	(4.8)	(2.7)	(3.0)	(0.07)	(0.19)	(0.6)	(0.18)	(0.04)	(3.6)	(1.2)	(102.5)
Control	–20.3	14.3	–14.2	12.6	41.8	42.6	0.49	0.3	0.34	0.25	0.15	72	13.1	943.1
	(–1.6)	(0.7)	(–1.6)	(4.8)	(3.3)	(3.1)	(0.03)	(0.03)	(0.03)	(0.03)	(0.01)	(3.8)	(0.94)	(74.4)
75%														
Anesth	–29.8	20.1	–19.2	18.4	49.9	49.4	0.62*	0.43	0.40*	0.39	0.21	66*	15.4	1,005.8*
	(–1.8)	(5.3)	(–1.6)	(4.8)	(4.9)	(3.1)	(0.04)	(0.18)	(0.04)	(0.18)	(0.03)	(2.7)	(1.37)	(73.3)
Control	–28.1	14.3	–16.8	11.3	53.3	52.8	0.55	0.23	0.31	0.21	0.22	75	16.7	1,282.0
	(–2.7)	(1.5)	(–1.7)	(1.1)	(3.2)	(4.2)	(0.03)	(0.03)	(0.02)	(0.02)	(0.02)	(3.0)	(1.32)	(116.2)
100%														
Anesth	–40.8*	22.0	–20.3	18.1	54.2	55.6	0.73*	0.46	0.38*	0.38	0.35	76*	16.8	1,159.4*
	(–4.4)	(6.6)	(–1.1)	(6.0)	(4.0)	(4.1)	(0.02)	(0.19)	(0.03)	(0.17)	(0.06)	(4.0)	–	(94.1)
Control	–34.4	15.7	–18.1	13.1	61.6	59.2	0.57	0.25	0.30	0.21	0.27	81	18	1,510.0
	(–2.4)	(2.0)	(–1.7)	(1.2)	(4.1)	(3.4)	(0.01)	(0.03)	(0.03)	(0.02)	(0.02)	(5.5)	(1.2)	(137.4)

TIP = Peak tracheal inspiratory pressure (cm H_2O). TEP = Peak tracheal expiratory pressure (cm H_2O). PIP = Peak pharyngeal inspiratory pressure (cm H_2O). PEP = Peak pharyngeal expiratory pressure (cm H_2O). IF = Peak inspiratory flow (L/s). EF = Peak expiratory flow (L/s). Z_{IU} = Upper airway inspiratory impedance (cm H_2O/L per second). Z_{EU} = Upper airway expiratory impedance (cm H_2O/L per second). Z_{INP} = Nasopharyngeal inspiratory impedance (cm H_2O/L per second). Z_{ENP} = Nasopharyngeal expiratory impedance (cm H_2O/L per second). Z_{ITL} = Translaryngeal inspiratory impedance. RF = Respiratory frequency (breaths/min). V_T = Tidal volume (L). VE = Minute ventilation (L/min).

*Significantly ($P < 0.05$) different from value obtained when the laryngeal mucosa was anesthetized.

Flow mechanics measurements—All horses were able to complete the incremental exercise treadmill protocol (**Table 1**). Treadmill speed had a significant effect on peak tracheal and nasopharyngeal inspiratory and expiratory pressures, inspiratory upper airway and nasopharyngeal impedances, respiratory frequency, tidal volume, and minute ventilation such that these values increased as treadmill speed increased. Peak tracheal inspiratory pressure was significantly more negative and upper airway and nasopharyngeal inspiratory impedance were significantly higher in horses with topical anesthesia of the laryngeal mucosal, compared with control values. We were unable to detect a significant difference in translaryngeal impedance when the laryngeal mucosa was anesthetized, compared with values obtained when the laryngeal mucosa was not anesthetized, suggesting that the main decrease in airway cross-sectional area occurred in the nasopharynx. Minute ventilation and respiratory frequency were significantly lower in horses with topical anesthesia of the laryngeal mucosal, compared with values obtained when the mucosa was not anesthetized. Peak inspiratory flow (P = 0.06) and peak expiratory flow (P = 0.09) were lower in horses with topical anesthesia of the laryngeal mucosal, although differences did not quite reach significance.

Discussion

Dynamic upper respiratory tract obstructive diseases are common in equine athletes, and many of these disorders are attributed to dysfunction of skeletal muscles that control airway caliber. Results of the study reported here indicate that disrupting the sensory component of the local reflex that controls contraction of upper airway muscles can also cause dynamic upper respiratory obstruction. After local anesthesia of the laryngeal mucosa, horses had dorsal displacement of the soft palate and nasopharyngeal collapse, which resulted in measurable obstruction of the upper airway. This suggests that upper airway sensory reflexes may be involved in clinical disorders such as nasopharyngeal collapse and dorsal displacement of the soft palate.

Topical anesthesia of the laryngeal mucosa resulted in increased inspiratory upper airway and nasopharyngeal impedances and decreased respiratory frequency and minute ventilation. These data suggest that topical anesthesia of the laryngeal mucosa caused dynamic obstruction of the upper airway. The dynamic obstruction was likely caused by collapse of the nasopharynx because of decreased skeletal muscle support. Observations from our study and data from other species support this conclusion.[2,3,6,8] During our first study, nasopharyngeal collapse in exercising horses occurred only when the laryngeal mucosa was anesthetized. Similarly, during nasal occlusion, nasopharyngeal collapse and dorsal displacement of the soft palate occurred when the laryngeal mucosa was anesthetized. Results of studies[14,19] in other species indicate that topical anesthesia of the laryngeal mucosa, local anesthesia of the superior laryngeal nerves, or transection of these nerves abolishes the electromyographic response to negative pressure in muscles that dilate the upper airway.

During our study, we attempted to determine the site of airway obstruction by partitioning the change in pressure along the upper airway. We measured tracheal and nasopharyngeal pressures and airflows and calculated the impedance of the entire upper airway between the nares and the trachea and the impedance between the nares and the nasopharynx. Translaryngeal inspiratory impedance was calculated by subtracting the nasopharyngeal inspiratory impedance from the upper airway inspiratory impedance to determine if alterations in the shape of the laryngeal opening contributed to the increased upper airway impedance in horses with anesthesia of the laryngeal mucosa. Indeed, although upper airway and nasopharyngeal inspiratory impedance was higher when the laryngeal mucosa was anesthetized, translaryngeal impedance was not different, suggesting that the increased impedance was caused by nasopharyngeal collapse and not by obstruction at the laryngeal opening. Despite the fact that some local anesthetic ran out of the horse's nose and may have anesthetized mucosa in the ventral meatus, it is unlikely that this was responsible for the observations in this study. Mucosal mechanoreceptors in the nasal passages are innervated by branches of the trigeminal nerve.[12] These mechanoreceptors have little effect on nasopharyngeal or laryngeal muscle activity but do mediate the increased activity of the alae nasi muscles, the principal dilating muscle of the nares, in response to negative pressure.[20] Results of a recent study[21] indicate that receptor mechanisms in the nasal passages in humans have minimal impact on the neural drive to the nasal dilator muscles during exercise.[21] Therefore, on the basis of this information, and because only a portion of the nasal mucosa was exposed to the local anesthetic, it is unlikely that the small amount of local anesthetic that contacted the nasal mucosa affected the contraction of the nasal dilator muscles.

Although the laryngeal mucosa was anesthetized, it is important to note that the local anesthetic did not paralyze muscle function. All horses were able to swallow, vocalize, and had normal tongue movement. Therefore, although the afferent limb of a local reflex was temporarily abolished, motor function was normal and could be demonstrated by having the horses perform other tasks that used the upper airway muscles that are involved in the maintenance of nasopharyngeal patency.

The degree of nasopharyngeal collapse caused by topical anesthesia of the laryngeal mucosa was more severe during nasal occlusion than during exercise, based on the videoendoscopic examinations and the impedance values obtained during exercise. During nasal occlusion, the negative pressures produced in the upper airway were similar to those during intense exercise, yet the degree of nasopharyngeal collapse was more severe. Abolishing the afferent pathway that mediated nasopharyngeal dilator muscle activation likely caused the severe nasopharyngeal collapse that occurred during the nasal occlusion test. By contrast, during intense exercise, multiple stimuli trigger contraction of upper airway-dilating muscles. In addition to the local negative pressure stimulus, which was

abolished by local anesthesia in this experiment, chemical stimuli such as hypercapnia, limb movement, and input from deeper mechanoreceptors stimulate increased activity of upper airway-dilating muscles.[22] Perhaps more importantly, central motor command is present during exercise, resulting in an enhanced excitability of upper airway motor neurons such that the effect of afferent inputs from the respiratory centers and other sources is amplified by the locomotor-linked cortical influences.[21,22] These other stimuli, present during exercise, prevented some of the nasopharyngeal collapse that was observed during nasal occlusion.

The increased upper airway impedance likely caused the decrease in respiratory frequency and minute ventilation by altering the breathing strategy of the horses. In the face of increased resistance, the work of breathing can be reduced by decreasing respiratory frequency and increasing tidal volume.[23] In our study, when the laryngeal mucosa was anesthetized and the upper airway became obstructed, horses decreased their respiratory frequency but did not increase their tidal volume. Perhaps the increased resistance to breathing imposed by the dynamic upper airway obstruction limited inspiratory time such that increasing tidal volume was not possible, despite decreased respiratory frequency. Alterations in breathing strategy may also have been limited by the coupling of respiratory frequency to stride frequency in running horses.[24]

Topical anesthesia of the laryngeal mucosa caused dynamic nasopharyngeal obstruction in exercising horses. This observation suggests that dysfunction of the mucosal mechanoreceptors and the branches of the superior laryngeal nerve may be involved in dynamic obstructions of the upper airway of the horse.

[a]Digital VHF telemetry system, MI403A, Hewlett Packard, Palo Alto, Calif.
[b]Baxter Scientific Products, McGraw Park, Ill.
[c]The UpJohn Co, Kalamazoo, Mich.
[d]DP-45-22, Validyne Engineering Sales, Northridge, Calif.
[e]LabVIEW 5.0, National Instruments Software, Austin, Tex.
[f]Laminar flow straightener element, Meriam Instruments, Grand Rapids, Mich.
[g]Model FP-2-37-P-10/77, Fisher & Porter Co, Warminister, Penn.

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