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SUBTOTAL ARYTENOIDECTOMY FAILS
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BY INDUCED LARYNGEAL HEMIPLEGIA

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SUBTOTAL ARYTENOIDECTOMY FAILS TO IMPROVE FLOW MECHANICS IMPAIRED BY INDUCED LARYNGEAL HEMIPLEGIA

By

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ABSTRACT

SUBTOTAL ARYTENOIDECTOMY FAILS TO IMPROVE UPPER AIRWAY AIRFLOW MECHANICS IN EXERCISING HORSES WITH INDUCED LARYNGEAL HEMIPLEGIA

By

James Kennedy Belknap

Upper airway airflow mechanics and arterial blood gas measurements were used to assess the efficacy of subtotal arytenoidectomy in the treatment of induced equine laryngeal hemiplegia. Measurements were collected with the horses on a treadmill (6.38 degree incline) standing, and trotting or pacing at 4.2 and 7.0 meters/second (m/s). Experimental protocols were performed after right common carotid artery exteriorization (baseline), after left recurrent laryngeal nerve transection, and after left subtotal arytenoidectomy.

At baseline, increasing treadmill speed progressively increased peak inspiratory and expiratory flow ($\dot{V}_I$max and $\dot{V}_E$max), peak inspiratory and expiratory pressure (Pu_I and Pu_E), respiratory frequency (f), tidal volume (V_T), minute volume ($\dot{V}_E$) , and heart rate. Arterial oxygen tension (PaO_2) decreased with increased treadmill speed; inspiratory and expiratory impedance (Z_I and Z_E) did not change. When the horses were exercised after left recurrent laryngeal neurectomy (LRLN), inspiratory flow, respiratory frequency and PaO_2 were significantly ($P < 0.05$) less than the baseline measurement at the identical treadmill speeds. Inspiratory transupper airway pressure and inspiratory impedance were significantly increased.

Left recurrent laryngeal neurectomy had no effect on expiratory air flow, expiratory transupper airway pressure, expiratory impedance, heart rate, arterial carbon dioxide tension ($PaCO_2$), or tidal volume.

Subtotal arytenoidectomy did not improve upper airway airflow mechanics or blood gas measurements impaired by laryngeal hemiplegia.

This work is dedicated to my mother and father, Barbara and Jon Belknap, for their faith in my abilities, for their continuous support and encouragement during times of disappointment and frustration, and for their excessive pride during times of accomplishment. But I especially want to dedicate this thesis to my wife, Ellen, who has given me so much support and happiness, and who helps me keep the priorities in life in perspective.

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I. INTRODUCTION

Upper respiratory abnormalities in the equine athlete have been recognized as an important cause of exercise intolerance for the past 3 centuries.[1,2] The most commonly described anomaly in the earlier literature is laryngeal hemiplegia. The basic pathologic changes involved in the disease were discovered in the early 1800's,[1] but the underlying cause of idiopathic laryngeal hemiplegia is still under investigation. Many other causes of upper airway obstruction of laryngeal origin have been described in the recent equine literature, but idiopathic laryngeal hemiplegia remains the most common disease of the upper airway.[3]

Upper respiratory surgery in the horse has progressed from the initial invasive ventriculectomy and arytenoidectomy techniques of Gunther,[4] which warranted a poor prognosis for survival,[4] to the modern prosthetic laryngoplasty. Although, compared to earlier techniques, improved success rates are reported using the laryngoplasty procedure for treatment of laryngeal hemiplegia, many surgical failures are still reported.[4-9] Recently, arytenoidectomy has resurfaced as a treatment for equine laryngeal hemiplegia. Two types of arytenoidectomy, the partial and subtotal techniques, have been reported to be successful in the treatment of the disease.[10,11] However, the postoperative assessment of the various surgical techniques for the correction of equine laryngeal hemiplegia in numerous reports

is commonly based on subjective criteria such as the owner's assessment of noise production and exercise tolerance.

At Michigan State University, objective methods using measurement of airway airflow mechanics have been developed for assessment of the efficacy of the various surgeries in the treatment of laryngeal hemiplegia.[12,13] In the following chapters, I will describe the anatomy of the structures associated with the arytenoid cartilage, laryngeal involvement in respiration, airflow mechanics, and blood gas measurements in the exercising subject. I will then discuss the pathology of the arytenoid cartilage, and the surgical treatments which have been used to treat abnormalities of the arytenoid cartilage. In subsequent sections, I will describe the results of assessment of the subtotal arytenoidectomy in the treatment of induced laryngeal hemiplegia.

II. ANATOMY

The larynx consists of six cartilages, three of which are paired (Figure 1).[14] The cricoid, thyroid and epiglottic cartilages are unpaired, whereas the arytenoid, cuneiform and corniculate cartilages are paired. The cricoid, thyroid and arytenoid cartilages consist of hyaline cartilage; the corniculate, epiglottis, and cuneiform cartilages are made of elastic cartilage.

The arytenoid cartilages are located rostral to the cricoid cartilage, and medial to the laminae of the thyroid cartilage. Each arytenoid cartilage consists of a base and an apex. The muscular process, vocal process, and facet for articulation with

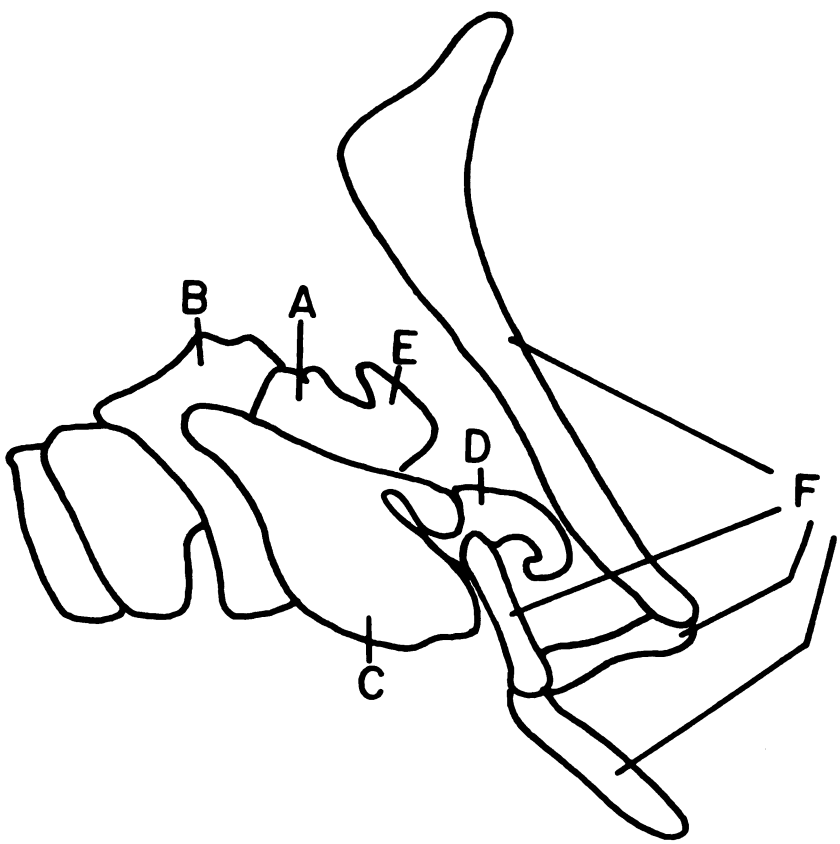

Figure 1. Lateral view of the right side of the laryngeal cartilages and hyoid apparatus (F) showing the arytenoid cartilage (A), cricoid cartilage (B), thyroid cartilage (C), epiglottis (D), and corniculate process (E).

the cricoid cartilage adjoin the base of the arytenoid cartilage. The apex is attached to the base of the corniculate cartilage. Whereas the cricoarytenoid articulation is diarthrodial in nature, the arytenoid-corniculate attachment is classified as a cartilaginous joint.[14]

The intrinsic muscles of the larynx which insert on the muscular process of the arytenoid cartilage include the cricoarytenoideus dorsalis, cricoarytenoideus lateralis, cricoarytenoideus transversus, arytenoideus transversus, and thyroarytenoideus. The majority of these muscles are adductors; only the cricoarytenoideus dorsalis causes abduction of the arytenoid cartilage.

The motor neurons of both recurrent laryngeal nerves originate from the nucleus ambiguus in the medulla oblongata.[15] The neurons of the right and left recurrent laryngeal nerves travel down the neck within the respective vagus nerve. The right and left recurrent laryngeal nerves branch from the vagus nerve at different locations. The right nerve is given off at the level of the second rib, travels around the right subclavian artery or costocervical trunk, and runs craniad to ascend the neck on the dorsolateral aspect of the trachea.[16] The left nerve originates from the vagus at the aortic arch, passes around the aortic arch, and ascends the neck on the left side in a similar path as the right. The left and right nerves pass over the respective cricoarytenoideus dorsalis muscles giving off branches to these and arytenoideus transversus muscle, and then pass on the medial aspect of each thyroid lamina to terminate as the caudal laryngeal nerves which innervate the majority of the intrinsic laryngeal muscles.[14,17] The left and right

recurrent laryngeal nerves innervate all of the intrinsic laryngeal muscles except for the cricothyroideus.[16]

Motor innervation of the cricothyroideus muscle occurs by the external branch of the cranial laryngeal nerve.[16] The external branch arises from the esophageal division of the pharyngeal branch of the vagus, and travels caudally to innervate cricothyroid, thyropharyngeal, and cricopharyngeal muscles. The internal branch of the cranial laryngeal nerve arises from the vagus caudal to the pharyngeal branch, continues ventrocaudally, and passes through the thyroid foramen to supply sensory innervation to the mucosa of the aditus laryngis, arytenoid cartilage, aryepiglottic fold, and lateral ventricle.[16]

The motor innervation to the equine larynx, unlike the dog and man, does not cross over midline to supply innervation to the contralateral laryngeal musculature.[16] This was demonstrated by transection of the motor innervation to the right laryngeal intrinsic muscles, and using electromyography to reveal no changes in electric activity of the intrinsic laryngeal musculature 6 weeks after nerve transection when compared to that measured initially after denervation of the intrinsic muscles.

III. LARYNGEAL INVOLVEMENT IN RESPIRATION

Respiration is an organized sequence of neural and muscular events that is regulated by the brainstem respiratory centers, but is influenced by a vast amount of afferent nervous input and numerous reflexes involving the entire respiratory

tract. Laryngeal movements during normal respiration consist of abduction of the corniculate cartilages and vocal folds during inspiration and relative adduction during expiration.[18,19] The vocal folds begin to abduct before the onset of inspiration, remain in full abduction for the initial 75% of inspiration, but then move towards midline to maintain a narrowed glottis through 95% of expiration.[19] These observations correlate well with the majority of reports on upper airway flow mechanics in humans and laboratory animals which state that expiratory upper airway pressure and resistance are increased during expiration relative to the inspiratory parameters.[18-21] It has been suggested that the relative expiratory adduction of the vocal folds acts as a "braking mechanism" slowing expiratory airflow.[19] This "braking mechanism" will influence the duration of the expiratory phase of the respiratory cycle and subsequently the respiratory frequency.[19-21]

The activity of the recurrent laryngeal nerves and laryngeal musculature during the respiratory cycle have been reported to correlate well with the observations of laryngeal movement and the airflow mechanics measurements mentioned above.[20,22] The recurrent laryngeal nerve has a low grade tonic activity throughout the expiratory phase, but there is an "inspiratory burst" that starts as a gradual rise in activity late in expiratory phase and peaks quickly on inspiration.[23] After the peak, the nerve's activity remains fairly constant until the end of the inspiratory phase when there is a gradual decrease in neural activity towards the tonic activity of expiration.[23]

Activity of the cricoarytenoideus dorsalis muscle (posterior cricoarytenoid muscle) closely follows the activity of the recurrent laryngeal nerve. The muscle activity peaks in early inspiration, and then reaches a plateau or decreases slowly throughout inspiration.[24] Because of the relative adduction of the vocal folds during expiration, it was stated in an earlier study that there was "adductor tone" during expiration.[22] More recent studies have found no activity of the thyroarytenoideus, a prominent adductor muscle of the larynx, during inspiration or expiration.[20,25] Although other adductor muscles are present in the larynx, these results indicate that the expiratory closure of the vocal folds is from decreased tone in the cricoarytenoideus dorsalis muscle (CAD) rather than active adduction of other laryngeal muscles.[20]

The neuromuscular activity of the larynx is intimately coordinated with activity of the phrenic nerve and diaphragm, but the pattern of activity differs greatly between the two neuromuscular units. The onset of phrenic nerve activity coincides with the peak in recurrent laryngeal nerve activity, and the activity rises steadily through inspiration before declining abruptly at the end of inspiration.[23,24,26] The activity of the diaphragm muscle follows that of the phrenic nerve closely.[24] This time-related sequence of activity between the laryngeal and diaphragmatic muscles allows full abduction of the larynx before inspiration begins, and the augmenting activity of the diaphragm (versus the plateau activity of the CAD) allows for gradual expansion of the lungs.

Investigations into the differences in neuromuscular activity of the larynx and diaphragm have led to the determination of some of the factors governing laryngeal activity. Studies of volume-related feedback (Hering-Breuer reflex) to the laryngeal and diaphragm neuromuscular units have shown a more prominent vagal effect on the larynx than the diaphragm.[24] Occlusion of the trachea at minimal lung volume causes an immediate increase in recurrent laryngeal nerve activity which then increases further through the inspiratory phase.[23] This differs from the initial peak and following plateau seen during unoccluded inspiration. The inspiratory phase of recurrent laryngeal nerve activity is also lengthened by approximately 60% with tracheal occlusion at minimum lung volume.[23]

With the same minimum lung volume, electrical activity of the CAD also steadily increases through the inspiratory phase and peaks late in inspiration, mimicking the changes seen in recurrent laryngeal nerve activity.[23] The normal augmentation of phrenic nerve activity on inspiration was not changed by airway occlusion at minimum lung volume, although the inspiratory phase was lengthened.[23] Airway occlusion at maximal lung volume causes a lengthening of duration of decreased nervous activity in the expiratory phase of both the recurrent laryngeal and phrenic nerves. An increase in discharge of both nerves occurred after release of the tracheal occlusion.

Bilateral vagotomy distal to the level of recurrent laryngeal nerves abolished the lung volume-related responses described above for the recurrent laryngeal and phrenic nerves.[23,24] These results indicate that lung expansion has a vagally

mediated inhibitory effect on the laryngeal innervation and musculature which may be attributed to pulmonary stretch receptors. Although this inhibitory effect is present in both the larynx and diaphragm, the cricoarytenoideus dorsalis is inhibited to a greater extent and for a longer time period than the diaphragm.[24]

Hypoxia has been reported to increase activity of the recurrent laryngeal nerve[27] and cricoarytenoideus dorsalis[25] and therefore decrease inspiratory and expiratory laryngeal resistance in laboratory animals with intact vagi.[20,25,28] However, after vagotomy, expiratory CAD activity has been reported to decrease,[25] and expiratory laryngeal resistance has been reported to increase.[25,28]

It was suggested that the carotid peripheral chemoreceptor may be responsible for the increased expiratory laryngeal constriction seen with hypoxia after vagotomy.[25,28] This theory is supported by experimental stimulation of the carotid chemoreceptor with a cyanide salt and simultaneous measurement of increased expiratory laryngeal resistance and observation of expiratory constriction of the glottis.[25,28] This expiratory glottic closure response to cyanide injection is stronger after bilateral vagotomy.[28] Carotid sinus resection abolishes the increased expiratory laryngeal resistance observed in hypoxic animals after vagotomy,[25] further confirming the involvement of the carotid sinus in the laryngeal response to hypoxia. Therefore, both central and peripheral chemoreceptors appear to be involved in the laryngeal response to hypoxia, but the vagally mediated response normally overrides that of the carotid sinus.

Hypercapnia has been reported to increase cricoarytenoideus dorsalis activity and increase both inspiratory and expiratory abduction of the vocal folds in humans[21,29] and laboratory animals.[18,20,25] The expiratory laryngeal resistance decreases to a greater extent than inspiratory resistance.[18,20,25] In a study using anesthetized cats, hypercapnia caused a significant decrease in laryngeal resistance both before and after bilateral vagotomy, indicating that the afferent response is from peripheral chemoreceptors.[25] Hypocapnia was found to raise expiratory laryngeal resistance in anesthetized cats.[20]

Both exercise and hyperpnea are reported to increase expiratory abduction of the vocal folds in humans.[21,29] A significant positive relationship (rank correlation test) was found between the extent of vocal fold abduction and decrease in time of expiration in one study.[21] Because previous reports on the importance of expiratory vocal fold adduction in controlling expiratory time concur with the results of the paper mentioned above,[18,19] increased abduction during expiration may function to decrease expiratory time and therefore increase respiratory frequency and overall ventilation during exercise.[21]

A study of the action of pulmonary irritant receptors and J receptors on the laryngeal diameter was performed using intravenous phenyl diguanide, and intravenous and aerosolized histamine in anesthetized cats and rabbits.[22] Phenyl diguanide, which stimulates J receptors, caused increased expiratory laryngeal resistance in both cats and rabbits; intrathoracic vagotomy abolished these changes. Intravenous and aerosolized histamine, which is reported to stimulate lung irritant

receptors (and J receptors to a lesser extent)[22] also caused expiratory constriction of the glottis and increased expiratory resistance. Vagotomy decreased the expiratory laryngeal resistance by approximately 50%. Therefore, although pulmonary receptor stimulation contributes to histamine's laryngeal effects, other systemic factors may also be involved. Both drugs caused increased expiratory activity of the recurrent laryngeal nerve; it is therefore possible that the increased expiratory laryngeal resistance is from activation of adductor muscles versus the inhibition of the cricoarytenoideus dorsalis muscle.

Experimental asphyxia, which caused a hypercapnic hypoxemia,[27,28] decreased both inspiratory and expiratory laryngeal resistance.[28] With vagotomy, inspiratory resistance decreased slightly, but expiratory resistance increased. The carotid chemoreceptors are likely to be involved in this response.

Laryngeal afferent receptors are also responsible for the caliber of the glottis, and respond to a wide variety of stimuli. The majority of the afferent nerve fibers from the larynx are located in the superior laryngeal nerve (cranial laryngeal nerve).[30,31] A study in anesthetized cats with bilateral intrathoracic vagotomies reported an increase in expiratory laryngeal resistance when a noxious stimulus, ammonia vapor, was exposed to the laryngeal lumen.[30] The response of expiratory resistance was abolished when the superior laryngeal nerve was transected. The lack of vagal influence and response to superior laryngeal nerve transection indicate that the laryngeal response to the noxious stimulus originated from the larynx itself.

Three different types of receptors in the laryngeal mucosa which respond mainly to pressure, flow, or upper airway muscle activity are reported to exist following a study which measured the activity of individual nerve fibers from the superior laryngeal nerve in response to the three stimuli.[31] All 3 types of receptors are reported to be most active during inspiration, and their activity markedly increases during upper airway obstruction. The fact that 65% of the receptors were found to be active on inspiration during eupnea prompted the investigator to suggest that these receptors play an important role in the control of respiration.[31]

A great deal of chemical specificity appears to be present in the laryngeal receptors. The presence of "crib death" in human infants and the finding that water in the larynx of neonates can cause apnea has stimulated the investigation of the effects of fluids of different properties applied to the laryngeal lumen.[32] It was found that solutions containing relatively large anions induce apnea on contact of the laryngeal mucosa, whereas solutions containing small anions do not induce apnea.[32] The principal stimulus for the apneic reflex appeared to be a low concentration of chloride in the solution.

IV. AIRFLOW MECHANICS

The character of air flow down an airway may be either laminar or turbulent depending on the characteristics of the gas, the geometry of the airway, and the velocity of air flow.[33,34] According to the Reynold's equation:

$$N_R = V \times 2r \times d / \eta$$

where N_R is the Reynold's number, V is the velocity of air flow, r is the radius, d is density, and η is absolute viscosity. The critical Reynold's number for the establishment of laminar flow is approximately 2300.[35] Above this number, the airflow will be transitional until a value of 3000, at which fully developed turbulence exists. For laminar air flow, the flow rate ($\dot{V}$) is directly proportional to the pressure gradient down the airway and is proportional to the radius to the 4th power. Air flow is inversely proportional to airway length and viscosity.[33] This is summarized in Poiseuille's Law for laminar air flow:

$$V = \pi \times \Delta P \times r^4 / 8 \times L \times \eta$$

where n is the coefficient of viscosity and ΔP is the pressure difference between the two ends of the tube.[33] This equation is only applicable if the Reynolds number is less than 2,000.

When fluid enters a tube, the length required to obtain a constant velocity profile is called the entrance length.[35,36] In the case of laminar flow, this is the airway length until a parabolic velocity profile develops.[35] When fluid enters a tube, the fluid in contact with the sides of the tube is at rest. The laminae of air flowing adjacent to the walls of the airway will have a high shearing force and will decelerate to decrease the shear. Proceeding towards the center of the tube, the shearing force will be less and therefore the central air laminae still accelerate until there is an optimal distribution of shearing force.[36] This gradual acceleration towards the center of the tube will establish the parabolic velocity profile seen with laminar flow. The boundary layer is the region adjacent to the wall in which

the velocity increases from zero to its average velocity throughout the core.[35] The boundary layer will increase with increased shearing forces (ie. with increased gas viscosity), and increases as the fluid progresses down the tube approaching laminar flow.

In human airways, and most likely most animals, the geometry of the airways and airflow velocities used (particularly with exercise) favor turbulent airflow through the central airways. In human respiration during "heavy breathing", the entrance length for development of laminar flow exceeds the length of the trachea and therefore laminar flow never develops.[35] With turbulent flow, a mean velocity becomes established more rapidly (shorter entrance length) than with laminar flow.[36] However, the mean core velocity is much lower with turbulent flow versus laminar flow.[35]

An airway pressure gradient is needed to maintain airflow and to overcome the following forces: the friction between gas and airway walls, resistance represented by airway irregularities, and shearing forces within flowing fluid.[36] The viscosity of the gas inspired will affect the shearing forces. The driving pressure necessary to maintain airflow increases linearly with increasing flow rate with laminar flow, but the driving pressure increases as the square of the flow rate when turbulent airflow exists. The pressure gradient to maintain flow increases linearly with the length of the airway, but increases in a non-linear fashion with changes in diameter.[35] With a constriction in the airway, air velocity must increase to maintain the same airflow. According to Bernoulli's theorem, a change in cross-sectional

area between points 1 and 2 will cause changes in airway pressure and air velocity according to the equation:

$$P_1 + \frac{1}{2} \rho \bar{u}_1^2 = P_2 + \frac{1}{2} \rho \bar{u}_2^2$$

where $\bar{u}$ is mean velocity, P is driving pressure, and ρ is gas density.[35] According to this equation, driving pressure must decrease with increasing velocity to maintain a favorable pressure gradient across a narrowing in the airway. This can lead to airway collapse if the walls of the airway are unsupported. In the majority of the upper airways, the walls are rigid being supported by bone or cartilage. The nares and arytenoid cartilages are the only collapsible structures of the upper airway, and therefore must be actively abducted by muscle contraction. If paresis or paralysis of these respiratory muscles occur, the negative pressure present in the airways on inspiration will cause partial collapse of the arytenoid cartilage. According to the Bernoulli principle, the increased velocity necessary to maintain the airflow through the partial obstruction caused by the collapsed arytenoid cartilage will result in a further decrease in intraluminal pressure, and therefore exacerbate the collapse of the unsupported arytenoid cartilage.

Fluid resistance of a straight cylinder is equal to the ratio of pressure change and change in flow rate across the pipe.[37] In the straight pipe, the only source of energy dissipation present is frictional in nature. In the human or animal airway, energy is not only lost by frictional/viscous forces, but may also be stored in compliant airway walls (elastance), and inertia of airflow also plays an important role in energy uptake during the respiratory cycle.[37] Respiratory system impedance

is calculated as the ratio of airway pressure to airway flow at a specific respiratory frequency.[37] The calculation of impedance is similar to resistance, but the term impedance includes not only the frictional element of air flow, but also the elastic effects of the airways, and inertial effects of the respiratory cycle on air flow.[37]

V. EFFECT OF EXERCISE AND UPPER AIRWAY OBSTRUCTION ON BLOOD GASES

The efficacy of pulmonary gas exchange is essential to the human or equine athlete; the most critical factor determining gas exchange is the matching of alveolar ventilation and perfusion.[38] The effectiveness of gas exchange is usually assessed by measuring PO_2 and PCO_2 in arterial blood (PaO_2 and $PaCO_2$, respectively). Both the PaO_2 and $PaCO_2$ have been measured in the normal exercising human and equine athlete,[39-45] and have also been measured in the horse with upper airway obstruction.[13,46,47] Blood gas measurements have been used to assess the efficacy of upper airway surgeries in the treatment of laryngeal hemiplegia in the exercising horse,[13,48] and in the resting dog.[49]

The human athlete is most commonly reported to develop a normocapneic or hypocapnic hypoxemia with strenuous exercise.[39] Hypoxemia is also reported in exercising horses;[13,40,45] hypocapnia[44] and hypercapnia[41,43] have been reported to exist with the hypoxemia. Arterial hypoxemia can be caused by: reduction in inspired PO_2, alveolar hypoventilation, a right-to-left pulmonary or cardiac shunt,

a diffusion abnormality at the alveolus/capillary interface, or a ventilation-perfusion imbalance.[38]

Alveolar hypoventilation is not a likely cause of hypoxia in exercising humans because a consistent hypercapnea has not been reported. Because hypercapnic hypoxemia is reported in the horse, it has been suggested that hypoventilation may play a part of exercise-induced hypoxemia in the horse.[43,50] The horse's respiratory frequency is coupled to its stride frequency at the canter and gallop; it has been stated that this respiratory/stride coupling may limit tidal volume at faster speeds and therefore cause alveolar hypoventilation.[44,50]

A right-to-left shunt has been ruled out as the cause of exercise-induced hypoxemia in both man and the horse. If blood is being shunted away from the alveoli, an increase in P_IO_2 (partial pressure of O_2 in inspired air) will increase the P_AO_2 (partial pressure of O_2 in the alveolus), but not significantly change the PaO_2 because the shunted blood is not exposed to the alveoli. When exercising humans[39] or horses[43] were exposed to hyperoxic conditions, the hypoxemia was abolished indicating that shunting does not play an important role in exercise-induced hypoxemia. A reduction in inspired PO_2 is not likely to play a role in exercised-induced hypoxia except at high altitudes.

Ventilation/perfusion ($\dot{V}/\dot{Q}$) inequalities have been proposed to not be a likely cause of hypoxia in the exercising human because the increased cardiac output in the exercising subject recruits previously closed capillaries in the upper lung fields

which are well ventilated, and also increases pulmonary capillary blood volume.[38] However, $\dot{V}/\dot{Q}$ inequalities have been reported in the human lung during exercise. These inequalities are most likely from intraregional $\dot{V}/\dot{Q}$ mismatch and not from $\dot{V}/\dot{Q}$ mismatches between vertical regions of the lung.[51,52] Ventilation/perfusion inequalities have been proposed to exist in the exercising horse,[43] but a recent study found only mild $\dot{V}/\dot{Q}$ inequalities in the exercising horse with the major mechanism for exercise-induced hypoxemia being a diffusion limitation.[53]

It has been suggested that there may be a diffusion limitation secondary to the short red cell transit times in the pulmonary capillaries from the increased cardiac output in the exercising human[54] and horse.[42,44] Therefore, there may be an alveolar to end capillary disequilibrium from inadequate oxygen binding to hemoglobin molecules.[42]

Blood gas values in exercising horses may be complicated by the presence of a mask for airway mechanics measurements in some studies. The wearing of a mask (and the use of gas collection systems) has been reported to exacerbate the hypoxemia seen with exercise.[41] An increase in $PaCO_2$ has also been reported with the use of masks in the exercising horse[41] and pony.[55]

Blood gas measurements in horses with laryngeal hemiplegia have resulted in greatly varying results. Both hypercapneic and normocapneic hypoxemia have been reported in exercising horses and ponies with laryngeal hemiplegia.[46,47] In another study, experimentally induced laryngeal hemiplegia caused no significant hypoxemia when compared to controls, but did cause a significant hypercapnea.[13] The great

discrepancies in the above data may have resulted from different methods of data collection and measurement. Face masks, as mentioned above, can greatly alter blood gas values; one of the above studies used a face mask.[13] Correction of blood gas measurements for arterial blood temperature was only performed in one of the above studies; it has been reported that arterial blood temperature rises more rapidly than rectal temperature in the exercising horse, and is therefore a more accurate measurement for blood gas correction.[13]

VI. PATHOLOGY OF THE ARYTENOID CARTILAGE

Diseases that involve the arytenoid cartilage in the horse include arytenoid chondritis, ossification of the arytenoid cartilages, arytenoid chondroma, and laryngeal hemiplegia. The pathogenesis of arytenoid chondritis is unknown.[56] Most reports describe the disease as a chronic, progressive septic condition of the arytenoid cartilage[56-59] which may be likened to chronic osteomyelitis.[56,58] On gross and microscopic examination, sinus tracts and inflammatory foci are present in the arytenoid cartilage.[56,58] Fibrous connective tissue laminates the cartilage causing severe thickening.[56] The septic process may invade the surrounding laryngeal musculature and involve the cricoarytenoid joint.[59] The resulting distortion of the arytenoid cartilage causes airway obstruction by intraluminal projection and reduced abduction from interference of the enlarged cartilage against the thyroid lamina.[59] Involvement of the cricoarytenoid joint may also reduce abduction of the cartilage.[59]

Calcification and ossification of the laryngeal cartilages are normal events in the mature horse[60] and human.[61] On postmortem examination, ninety percent of human cadavers were found have calcification or ossification of the arytenoid cartilages.[61] The same data is not available in horses. Although the ossification process may be a normal aging process in the equine larynx, hypertrophic ossification of the arytenoid cartilages causing upper airway obstruction has been reported in the horse.[62]

Chondromas, slow-growing benign cartilaginous tumors, have been reported to involve the arytenoid cartilage.[63,64] In both reports, the horses presented with signs of respiratory obstruction. The neoplasia was adequately localized to allow successful resection in both cases.

A. Laryngeal Hemiplegia

Laryngeal hemiplegia is the most common upper airway abnormality in the horse. In one study of 479 equine athletes, the prevalence of laryngeal hemiplegia was 3.3%.[3] The disease most commonly affects the left hemilarynx,[3,65,66] although right and bilateral laryngeal paralysis also occur.[65,66]

There are many known causes of equine laryngeal hemiplegia; however, the cause in the majority of cases is unknown. The disease is therefore commonly called idiopathic laryngeal hemiplegia. The pathogenesis of the disease has been the topic of a moderate amount of research for the past two centuries. The relationship of "roaring" to paralysis of the recurrent laryngeal nerve was first

suggested by Dupuy in 1807.[2] In 1834, Gunther reported that "roaring" was caused by atrophy of the left laryngeal musculature secondary to loss of function of the left recurrent laryngeal nerve.[1] He confirmed his findings by transecting the left recurrent laryngeal nerve and observing the changes in respiratory sound, and later the post mortem changes in the larynx.

Controversy has existed since the mid 1800's over the cause of the neurologic deficit in laryngeal hemiplegia. Biomechanical causes of laryngeal hemiplegia have been commonly suggested.[66-69] It has been proposed that the left recurrent laryngeal nerve is functionally shorter than the neck of the horse,[67-69] and that the nerve is fixed in position at the larynx and aortic arch.[69] Using the above assumption, it has been stated that excessive tension on the nerve may occur by simple extension of the neck, or by neck extension occurring simultaneously with backward movement of the heart during exercise.[66,68,69] The reported high incidence of laryngeal hemiplegia in tall, long-necked horses[69-73] has been used to support the biomechanical theory, stating that horses with longer necks are prone to have more tension on the left recurrent laryngeal nerve.[69]

Heritability of the disease in the horse has been suggested by many authors, but has not been proven. In one study of 85 test matings, it was stated that laryngeal hemiplegia may be autosomal recessive in nature.[74] However, only one out of two progeny from the mating of 2 "roarers" was affected with laryngeal hemiplegia; both horses should be affected if the trait were autosomal recessive. In an earlier study in South Africa, attempts to prove inheritance of laryngeal

hemiplegia were incomplete.[70] In a recent study of the progeny of a thoroughbred stallion with laryngeal hemiplegia, there was a significantly larger incidence of laryngeal hemiplegia in the stallion's offspring (11/47) when compared to a control group (1/50).[73] It was stated that a dominant gene may be responsible for laryngeal hemiplegia, but that the disease may be a phenocopy as well as having a genetic basis.[73] Cook has stated that there may be a hereditary component to physical characteristics which may predispose the animal to laryngeal hemiplegia.[74]

In depth studies on the pathology of the laryngeal innervation and musculature did not occur until the mid-1900's. In 1946, Cole reported severe peripheral degeneration of the left recurrent laryngeal nerve, with disappearance of myelin sheaths and fibrosis of the distal aspect of the nerve.[75] He found that the degree of degeneration decreased in a central direction, and that few pathologic changes were present in the left nerve at the level of the thoracic inlet. Further studies have confirmed Cole's findings, but have also found degenerative changes in the distal aspect of other long peripheral nerves including the right recurrent laryngeal nerve [68,76-78] and the peroneal nerve of the hindlimb.[76-78] The disease is now being classified as a peripheral neuropathy consisting of a primary distal axonopathy.[72,76-78]

Pathologic changes in the laryngeal musculature are characteristic of neurogenic atrophy. One of the most common changes seen is fiber-type grouping of the muscle fibers,[68,79,80] which indicates denervation and reinnervation by separate nerve fibers.[80] Other changes consistent with neurogenic atrophy include the

presence of atrophic and hypertrophic muscle fibers,[68] variation in muscle fiber size,[72] and degenerate muscle fascicles being replaced by connective tissue.[75] Atrophy occurs in the cricoarytenoideus lateralis, an adductor of the arytenoid cartilage, before the cricoarytenoideus dorsalis is affected.[68,72,80] The proposed reason for this is that the large diameter fibers of the recurrent laryngeal nerve are those most severely affected in laryngeal hemiplegia, and it has been confirmed that the larger fibers innervate the cricoarytenoideus lateralis.[76,80] The other possibility is that the nerve endings innervating the cricoarytenoideus lateralis are more distal than those innervating the cricoarytenoideus dorsalis. Neurogenic atrophy is also present in the right laryngeal intrinsic musculature[75,80,81] and the extensor digitorum longus[80] in horses with laryngeal hemiplegia supporting the present view that the disease is a generalized peripheral neuropathy. The left recurrent laryngeal nerve is most severely affected because it is the longest peripheral nerve.

Although most cases of laryngeal hemiplegia are idiopathic, the cause is known in some instances. Known causes include perivascular injections (jugular vein) of irritating substances,[6,65,72] organophosphate toxicity,[82,83] lead toxicity,[84] and paralaryngeal abscessation with Staphylococcus aureus infection.[85] Other suggested causes include various viral and bacterial respiratory tract infections,[81] plant toxicity including Lathyrus and alfalfa,[72] and thiamine deficiency.[86,87]

VII. UPPER RESPIRATORY SURGERY

The larynx has the smallest cross-sectional area of any part of the upper airway in humans, and is reported to contribute approximately 50% of the total upper airway resistance.[35] Although it has been stated that the equine larynx does not create as great a resistance during respiration because of the marked abduction of the arytenoid cartilages at rest and during hyperpnea,[88] this has not been confirmed in the live horse. As described previously in this review, the Bernoulli principle dictates that the increase in velocity of the airflow through the narrowed rima glottis of the hemiplegic equine larynx will cause a decrease in laryngeal luminal pressure, therefore causing further axial displacement of the affected corniculate process thus further narrowing the rima glottis. Whether it is the normal human larynx or the hemiplegic equine larynx, the narrowing of the rima glottis will cause flow separation with a turbulent jet of air forming from the center of the airway, and recirculating eddies forming at the sides of the jet posterior to the airway constriction. The resulting flow separation causes great energy loss and a subsequent decrease in driving pressure in the distal airways.[35] This section describes the various surgical techniques used to decrease the upper airway obstruction caused by laryngeal hemiplegia.

The majority of the earlier literature on equine upper respiratory surgery concentrated on laryngeal hemiplegia. The first surgical technique reported for the disease was total arytenoidectomy by Gunther Jr. in 1866.[10] He reported severe complications including dysphagia and aspiration pneumonia.[4,10] The technique was

still recommended for "roaring" in the early 1900's,[89] but then fell into disuse and was replaced by ventriculectomy and later a combination of laryngoplasty and ventriculectomy.

Although Gunther Jr. described a technique for ventriculectomy in the mid 1800's,[4] the technique was not commonly used until reintroduced by Williams in 1907,[89] and later popularized by Hobday in 1936.[90] In the ventriculectomy procedure, the mucosal lining of the lateral ventricle is removed to produce scar tissue formation between the thyroid and arytenoid cartilages. It is proposed that this will cause abduction and fixation of the involved arytenoid cartilage in the horse with laryngeal hemiplegia, thus reducing its axial displacement during inspiration.[59] Reduction of filling of the lateral ventricle of the involved hemilarynx on inspiration may also occur postoperatively. Using subjective criteria such as owner's appraisal of exercise tolerance and noise reduction to assess postoperative performance of the horse, good to excellent results were reported with ventriculectomy.[66,70,90,91] Recently, more conservative success rates have been reported.[5,6] Objective assessment of the ventriculectomy procedure at Michigan State University has demonstrated that the technique does not significantly improve upper airway airflow mechanics impaired by laryngeal hemiplegia.[12]

The combined laryngoplasty/ventriculectomy was introduced by Marks in 1970.[7] In this procedure, a nonabsorbable suture prosthesis is inserted through the cricoid cartilage and muscular process of the arytenoid cartilage to apply similar tension on the arytenoid cartilage as that of the cricoarytenoideus dorsalis muscle.[7]

Marks performed a unilateral ventriculectomy on the involved side of the larynx with the laryngoplasty procedure. Although modifications have been reported, the same basic technique has become the principal surgery for laryngeal hemiplegia.[92] Subjective assessment of laryngoplasty has resulted in reported success rates of 44% to 90%.[6,7,11] Objective laboratory data confirm the above reports, demonstrating that laryngoplasty (without ventriculectomy) significantly improves upper airway flow mechanics adversely affected by laryngeal hemiplegia.[12,13]

Although successful treatment of laryngeal hemiplegia is possible with laryngoplasty, numerous complications have been reported. Coughing and dysphagia, the most common complications, can occur when excessive abduction of the corniculate cartilage results in obliteration of the pyriform recess on the ipsilateral side, and thus allows food to enter the larynx.[4,5] However, a sham laryngoplasty procedure with no placement of a suture prosthesis also causes dysphagia, indicating that surgical trauma to the laryngeal muscles and nerves may be responsible for the laryngeal dysfunction.[8] Other complications include suture prosthesis failure, septic suture sinus formation,[4,6] esophageal obstruction,[4,6] intralaryngeal granuloma formation from penetration of the laryngeal lumen by prosthesis, ossification of the arytenoid cartilage,[4] and arytenoid chondritis.[4]

Because of the complications with the combined laryngoplasty/ventriculectomy procedure, arytenoidectomy has recently been reintroduced for treatment of laryngeal hemiplegia.[10,11] Although complications still occur with modern arytenoidectomy procedures, current surgery facilities and techniques allow the

surgery to be performed with less dissection and therefore less trauma. Three types of arytenoidectomy, the total, partial and subtotal techniques, are reported in the equine veterinary literature.[4] The total arytenoidectomy consists of removal of the entire corniculate and arytenoid cartilages. Partial arytenoidectomy is similar to the total procedure, except the muscular process of the arytenoid cartilage is not resected (Figure 2). In the subtotal arytenoidectomy, the muscular process and the corniculate cartilage are retained (Figure 2).

Arytenoidectomy procedures in the horse are most commonly used for the treatment of arytenoid chondritis and failed laryngoplasty.[9,11,56] Arytenoidectomy has also been used for treatment of ossification of the arytenoid cartilage,[9] laryngeal chondroma,[54,64] and as a primary procedure for correction of laryngeal hemiplegia.[10,11] The partial and subtotal techniques are more frequently used than the total arytenoidectomy.

Conflicting reports on the success rate of partial arytenoidectomy are present in the literature. In one clinical study, all four horses recovered with no serious complications, and two of the horses returned to their original athletic use.[9] Two of the horses continued to produce an inspiratory noise during exercise. Another study reported normal exercise tolerance in 78% (14/18) of the racehorses, but the long term incidence of coughing and dysphagia was 36%.[10] A recent clinical study reported that approximately 50% (19/36) of the Thoroughbred racehorses that returned to racing after unilateral partial arytenoidectomy raced successfully, whereas only 20% (2/10) of Standardbreds were able to race.[93] There was a low

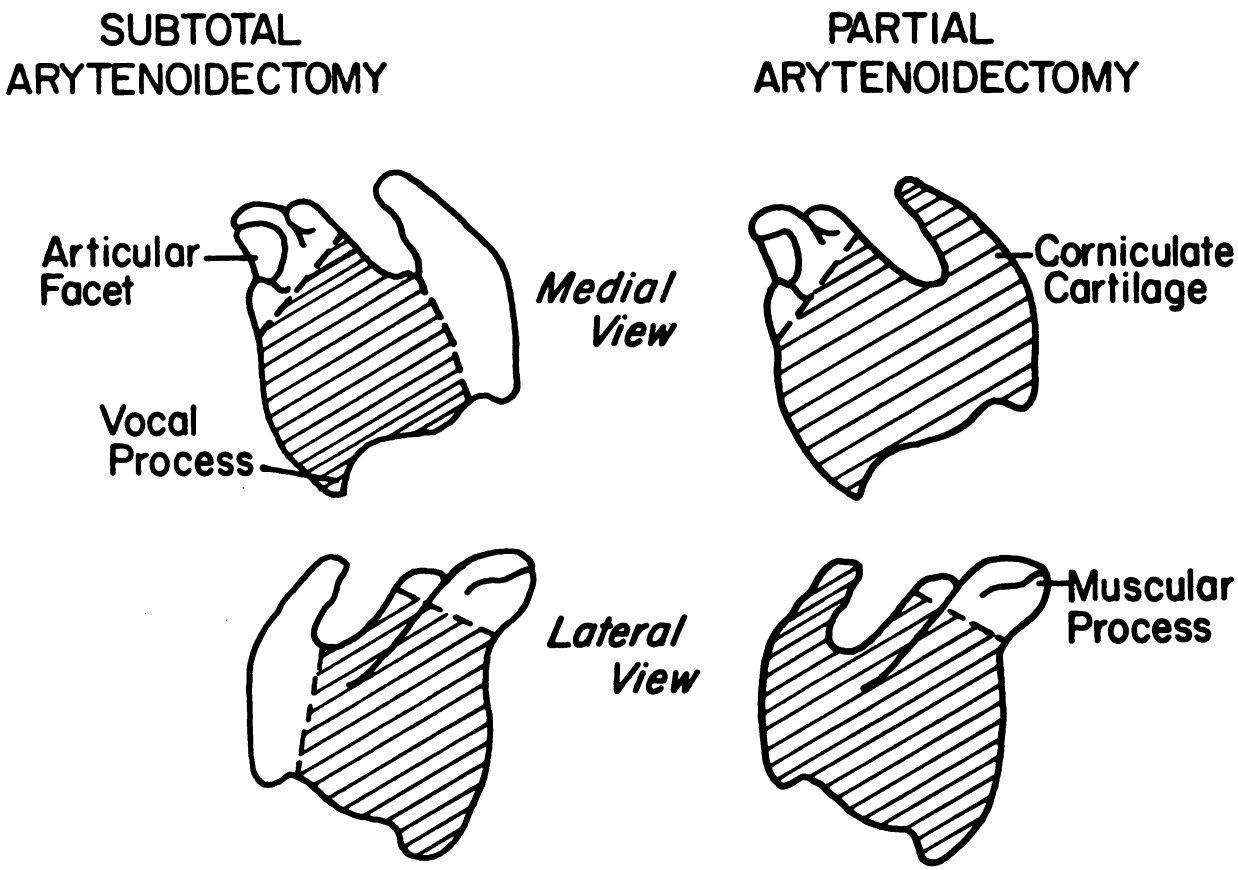

Figure 2. Schematic representation of arytenoid cartilage, and the components which are resected with the subtotal and partial arytenoidectomy. The shaded area is the portion of the arytenoid cartilage that is resected.

incidence of complications in this report. Two preliminary studies have reported minimal complications performing the partial technique without mucosal closure[94] and using an Nd:Yag (neodymium:yttrium-aluminum-Garnet) laser to perform the surgery,[95] but exercise tolerance was not assessed in the horses in these 2 studies.

Subtotal arytenoidectomy has been reported to be successful in the majority of horses treated for laryngeal obstruction from arytenoid chondritis and laryngeal hemiplegia.[15,52] Using owners' assessment of exercise tolerance and noise production as criteria for postoperative success, 83% (5/6) horses with laryngeal hemiplegia and 50% (7/14) horses with arytenoid chondritis had excellent outcomes.[11] Because of these results, it was suggested that subtotal arytenoidectomy may replace prosthetic laryngoplasty as the preferred technique for laryngeal hemiplegia. Eleven percent (3/27) of the horses in the same study did have signs of dysphagia, and 40% (8/20) produced respiratory noise with concurrent reduced exercise capacity.

Total arytenoidectomy is still reported to be unacceptable in the horse because of the same severe sequelae reported 100 years ago.[4] However, the technique is used in humans for treatment of laryngeal paralysis. Both an extralaryngeal[96] and intralaryngeal[97] approach are used. Intralaryngeal arytenoidectomy using lasers has been reported to be successful in humans.[97,98] However, success in the human literature is judged by the production of an adequate airway to allow decannulation of the trachea, with no testing of exercise tolerance.

Surgical reinnervation of the paralyzed larynx has been performed successfully in man for the past decade,[99-102] and has also been reported successful in experimentally induced laryngeal hemiplegia in dogs.[103] The surgical procedure consists of the creation of a neuromuscular pedicle graft which is most commonly inserted into the cricoarytenoideus dorsalis muscle for improved abduction of the arytenoid cartilage and vocal fold. In man, the pedicle is typically created from the ansa cervicalis and the omohyoideus muscle.[99-101]

Although the technique is reported successful in a large number of human patients, the criteria for success includes improved phonation and ability to breathe at rest without a tracheal cannula. Assessment of exercise tolerance is not mentioned in most studies. In dogs, successful treatment was based on visual evaluation of arytenoid abduction postoperatively.[103] Preliminary work on neuromuscular pedicle grafts in ponies with experimental laryngeal hemiplegia has shown little improvement in arytenoid abduction postoperatively.[104]

Although the prosthetic laryngoplasty has been shown to improve upper airway airflow mechanics in exercising horses using objective methods,[12,13] many clinical complications are still reported. Encouraging results have been reported using the nerve-muscle pedicle graft for treatment of laryngeal paralysis in the dog and man, but the technique has not been successful in the treatment of laryngeal hemiplegia in the horse. Both the subtotal and partial arytenoidectomy have been reported to improve exercise tolerance in the horse with laryngeal hemiplegia, but no objective assessments of these two techniques have been performed.

Additionally, the partial arytenoidectomy has been reported to have a high prevalence of postoperative complications. In this thesis, I therefore chose to objectively assess the efficacy of subtotal arytenoidectomy in the treatment of equine laryngeal hemiplegia.

Blood gas and upper airway flow mechanics measurements were performed in the normal horse, and in the horse with left laryngeal hemiplegia. These measurements are then used to assess the efficacy of subtotal arytenoidectomy in the treatment of equine laryngeal hemiplegia.

VIII. MATERIALS AND METHODS

Six Standardbred horses (body weight 409 ± 11 kg ($\bar{X}$ ± SE), age 5.8 ± 1.7 years) were used in this study. The horses were vaccinated against influenza, tetanus, and eastern and western equine encephalitis. Upper airway endoscopy failed to reveal any abnormalities in the experimental horses. Horses were trained to trot or pace on a treadmill[a] (6.38 degree incline) while wearing a fiberglass face mask. Once trained, a right common carotid artery exteriorization was performed under general anesthesia as previously described.[12]

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[a] Jetline, Desales Inc. Sand Lake, Mich.

A. Measurement Techniques

The upper airway flow mechanics measurement techniques used in this study have been previously described.[12,13] A fiberglass mask and pneumotachograph[b] (14 cm. diameter) were mounted over the face; a wire mesh[c] was inserted between the pneumotachograph and the horse's nostrils. The mask was constructed to fit tightly to the horse's face, but to allow for excursion of the nostrils. A rubber shroud was used to seal the mask against the face. The pressure difference across the pneumotachograph was measured using a differential pressure transducer[d] which gave a signal proportional to airflow. This signal was integrated to produce tidal volume. All signals were recorded on a physiograph.[e]

The pneumotachograph was calibrated before each experiment using a Rotameter flow meter.[f] Peak flows were reported in this study. Respiratory rate and times were calculated from the physiograph recordings. Minute volume was calculated as the product of respiratory rate and tidal volume.

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[b] Marian 6" Laminar Flow Straightener Element, Meriam Instruments, Grand Rapids, Mich.

[c] Mesh SS screen, McMaster-Carr, Chicago Ill.

[d] Model DP 45-22, Validyne Sales, Northridge, Calif.

[e] Model 8188, Gould Inc., Madison Hts, Mich.

[f] Model FP-2-37-P-10/77, Fisher and Porter Co., Werminster, Pa.

A polyethylene catheter was inserted percutaneously into the upper cervical trachea for measurement of lateral tracheal pressure.[13] Transupper airway pressure was defined as the difference between barometric pressure and lateral tracheal pressure. Pressure measurements were made using a differential pressure transducer[d] which was calibrated before each experiment using a water manometer. Inspiratory and expiratory impedance were calculated as the ratio of peak transupper airway pressure and airflow on inhalation and exhalation respectively. These measurements were averaged over 12 breaths. Pressure and flow catheter systems were evaluated for phase differences as previously described.[105] No phase differences were detected up to a frequency of 10 Hz.

A polyethylene catheter was inserted into the right common carotid artery for collection of arterial blood. Arterial blood gas tensions and pH were measured using a blood gas analyzer.[g] In order to correct PaO_2, $PaCO_2$, and pH for temperature, right common carotid artery temperature was measured using a thermistor[h] and telethermometer.[i] The heart rate was measured using a base apex lead system and a heart rate computer.[j]

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[g] Model ALB-3, Radiometer, Copenhagen, Denmark

[h] YSI Tissue Implantation temperature probe Model 520, Yellow Springs Instrument Co., Yellow Springs, Ohio

[i] YSI Telethermometer Model 43TF, Yellow Springs Instruments Co., Yellow Springs, Ohio

[j] Equistat, Equine Biomechanics and Exercise, Unionville, Pa.

B. Experimental Protocol

Measurements were made with the horses at rest, and exercising at a speed of 4.2 m/s and 7.0 m/s on a treadmill (6.38 degree incline). At each level of exercise, treadmill speed was maintained for 2 minutes; the data were collected during the last minute of each measurement period. The horses were rested for 2 minutes between the two exercise periods. Measurements were taken before left recurrent laryngeal neurectomy (baseline), 14 days after left recurrent laryngeal nerve neurectomy (LRLN), and 60 days after left subtotal arytenoidectomy (STA). The horses were kept at pasture between protocols.

The subtotal arytenoidectomy was performed as described by Jennings,[11,59] except that neither the thyroid nor the cricoid cartilages were incised to enlarge the laryngotomy in any of the horses. Anesthesia was induced with glycerol guiacolate[k] and thiamylal[l] and maintained with halothane[m]; the animals were intubated via a midcervical tracheotomy. A laryngotomy was performed through the cricothyroid membrane with the horse in dorsal recumbency. A fiberoptic retractor[n] was used to illuminate the larynx. An incision was made over the ventral and caudal aspect of the body of the arytenoid cartilage. The laryngeal mucosa was elevated off of

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[k] Glycerol Guiacolate, Guaiacol Glyceryl Ether USP, Aceto Chemical Co., Flushing, NY

[l] Biotal, Bioceutic Division, Boehringer Ingelheim Animal Health Inc., St. Joseph, Mo.

[m] Fluothane, Ayerst Laboratories, Inc. New York, NY

[n] Shea Fiberoptic retractor, Stryker Corp., Kalamazoo, Mich.

the axial side of the arytenoid cartilage, and the lateral aspect of the body of the arytenoid cartilage was then dissected from the laryngeal musculature. The body was then transected from the corniculate cartilage, after which the body was transected from the muscular process of the arytenoid cartilage. The body of the arytenoid cartilage was then removed, and the laryngeal mucosa was sutured with 2-0 polydioxanone suture[o] in a simple continuous pattern. A ventriculectomy was also performed on the ipsilateral side of the larynx, and was closed with 2-0 polydioxanone suture[o] in a simple continuous pattern. Tracheotomy tubes[p] were maintained through the midcervical tracheotomy site for 72 hours postoperatively. Laryngotomy and tracheotomy sites were left to close by second intention; both sites were cleansed daily with a dilute antiseptic solution until second intention healing occurred. The horses were treated perioperatively with procaine penicillin[q] (20,000 IU/kg IM BID for 2 days), and were also given phenylbutazone paste[r] (3 mg/kg PO BID for 3 days). Endoscopic examination was performed 2, 4, 6, and 60 days postoperatively.

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[o] PDS, Ethicon, Inc., Somerville, NJ

[p] Dyson self retaining tracheal tubes, Cooper Animal Health, Mishawaka, Indiana

[q] Procaine Penicillin G, Pfizer Inc., New York, NY

[r] Butazolidin Paste, Coopers Animal Health Inc., Kansas City, Mo.

C. Statistical Analysis

Data were analyzed using a two-way analysis of variance; log transformation was performed on the impedance (Z_I and Z_E) data. When the F value was significant ($P < 0.05$), the Tukey omega procedure[106] was used to evaluate the differences between the means.

IX. RESULTS

Increasing the treadmill speed significantly increased ($P < 0.05$) the following variables at the baseline measurement period: minute ventilation ($\dot{V}_E$), tidal volume (V_T), $PaCO_2$, inspiratory and expiratory flow ($\dot{V}_I max$ and $\dot{V}_E max$), inspiratory and expiratory transupper airway pressure (Pu_I and Pu_E),respiratory frequency (f), and heart rate (HR). Significant decreases were present in arterial oxygen tension (PaO_2), pH, and inspiratory and expiratory times (T_I and T_E). There were no significant changes in inspiratory and expiratory impedance (Z_I and Z_E). These data are present in Table 1.

After left recurrent laryngeal neurectomy, $\dot{V}_I max$ was significantly decreased from baseline measurements at 4.2 and 7.0 m/s (Figure 3), whereas Pu_I was significantly increased at 7.0 m/s (Figure 4). There was no significant change in $\dot{V}_E max$ or Pu_E. The Z_I, the ratio of Pu_I and $\dot{V}_I max$, showed a significant increase from baseline at both 4.2 and 7.0m/s (Figure 5). There was no significant change in Z_E. There was a significant decrease in f at 7.0 m/s (Figure 6). Inspiratory time

Table 1. Effects of exercise on upper airway airflow mechanics values, blood gas tensions, and acid base variables in six horses before left recurrent laryngeal neurectomy (baseline).

	EXERCISE		
Value	At Rest	4.2 m/s	7.0m/s
HR(min^{-1})	30.8±1.1	175.5±5.1[a]	209.7±3.1[a,b]
f(min^{-1})	27±4.2	79±3.8[a]	84.5±3.9[a]
$\dot{V}_I$max(L/s)	7.2±0.8	56.3±1.0[a]	80.4±4.2[a,b]
$\dot{V}_E$max(L/s)	7.9±1.1	47.5±4.2[a]	66.6±4.3[a,b]
Pu_I(cm H_2O)	2.6±0.2	22.1±2.4[a]	42.9±2.8[a,b]
Pu_E(cm H_2O)	1.5±0.2	7.3±0.5[a]	9.2±3.8[a]
Z_I(cm H_2O/L/s)	0.38±0.04	0.40±0.16	0.53±0.02
Z_E(cm H_2O/L/s)	0.20±0.03	0.16±0.02	0.14±0.06
V_T (L)	5.7±0.4	16.0±0.9[a]	22.2±1.6[a,b]
$\dot{V}_E$(L/min)	147±6	1256±63[a]	1858±109[a,b]
PaO_2(torr)	101.3±2.0	82.1±1.7[a]	71.7±1.6[a,b]
$PaCO_2$ (torr)	44.3±0.9	48.2±1.1	54.7±1.9[a,b]
pH	7.40±0.01	7.36±0.01	7.27±0.01[a,b]
CA Temp °C	37.8±.1	38.4±0.2[a]	39.9±0.2[a,b]
T_I	0.74±0.08	0.38±0.02[a]	0.36±0.01[a]
T_E	0.92±0.01	0.39±0.02[a]	0.33±0.02[a]

a = Data significantly different ($P < 0.05$) from same measurement made in standing horses. b = Data significantly different ($P < 0.05$) from same measurement made in horses at 4.2 m/s.

HR = heart rate; *f* = respiratory frequency; $\dot{V}_I$max and $\dot{V}_E$max = inspiratory and expiratory airflow, respectively; Pu_I and Pu_E = inspiratory and expiratory transupper airway pressures, respectively; Z_I and Z_E = inspiratory and expiratory impedances, respectively; V_T = tidal volume; $\dot{V}_E$ = minute ventilation; CA Temp °C = Carotid artery blood temperature, degrees Celsius.

(T_I) significantly increased after left recurrent laryngeal neurectomy at both 4.2 and 7.0 m/s (Figure 7). Although $\dot{V}_E$ at 7.0 m/s decreased from 1858 ± 109 liters/min at baseline to 1372 ± 99 liters/min post-LRLN (Figure 6), this decrease was not significant. There was no significant change in tidal volume (Figure 6) following left recurrent laryngeal neurectomy. PaO_2 decreased significantly at 7.0 m/s after left recurrent laryngeal neurectomy when compared to baseline measurements (Figure 8). There were no significant differences in other blood gas values. Heart rate did not change significantly after left recurrent laryngeal neurectomy (Figure 9).

Left subtotal arytenoidectomy did not significantly change any of the parameters which were increased or decreased from baseline by left recurrent laryngeal neurectomy. Compared to baseline measurements, there was a significant decrease in f at all exercise periods (Figure 6). Heart rate was significantly increased at the standing measurement after subtotal arytenoidectomy compared to baseline (Figure 9).

There were no postoperative complications, except one case of transient laryngeal swelling after left subtotal arytenoidectomy. Endoscopic examination 60 days postoperatively showed that all 6 horses had complete mucosal healing.

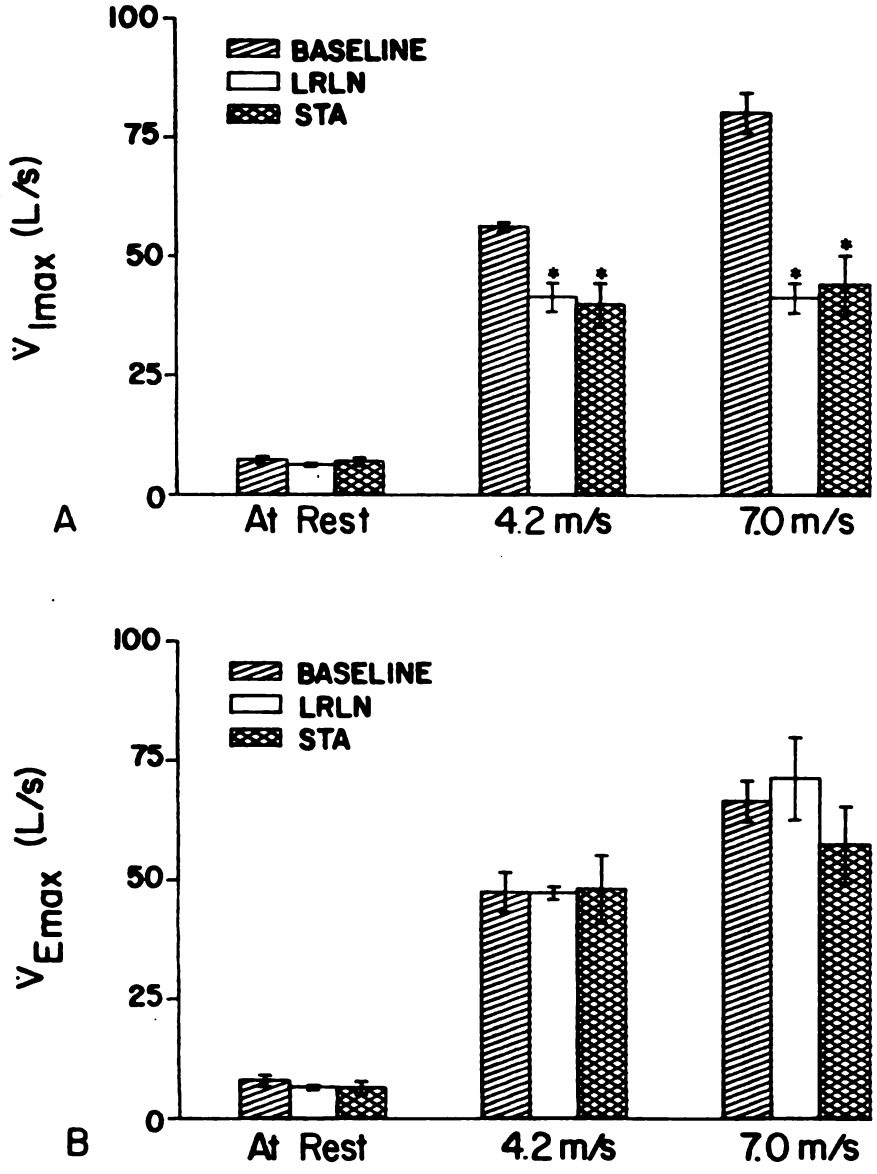

Figure 3. Maximal inspiratory ($\dot{V}_I$max) (A) and expiratory ($\dot{V}_E$max) (B) flow at 3 levels of exercise measured prior to left recurrent laryngeal neurectomy (baseline), after left recurrent laryngeal neurectomy (LRLN), and after left subtotal arytenoidectomy (STA). * = value is significantly different ($P < 0.05$) from base line measurement at the same treadmill speed.

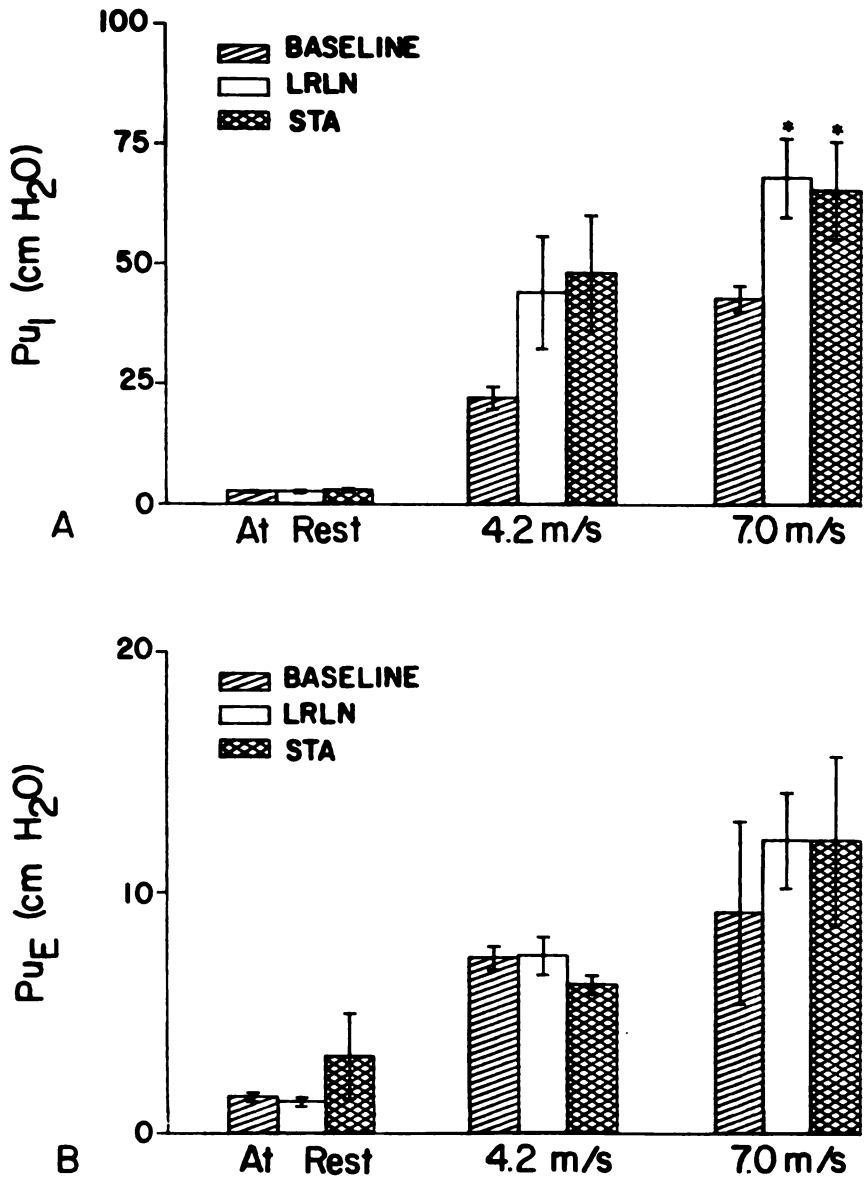

Figure 4. Peak transupper airway inspiratory (Pu_I) (A) and expiratory (Pu_E) (B) pressure at 3 levels of exercise measured prior to left recurrent laryngeal neurectomy (baseline), after left recurrent laryngeal neurectomy (LRLN), and after left subtotal arytenoidectomy (STA). * = value is significantly different ($P < 0.05$) from base line measurement at the same treadmill speed.

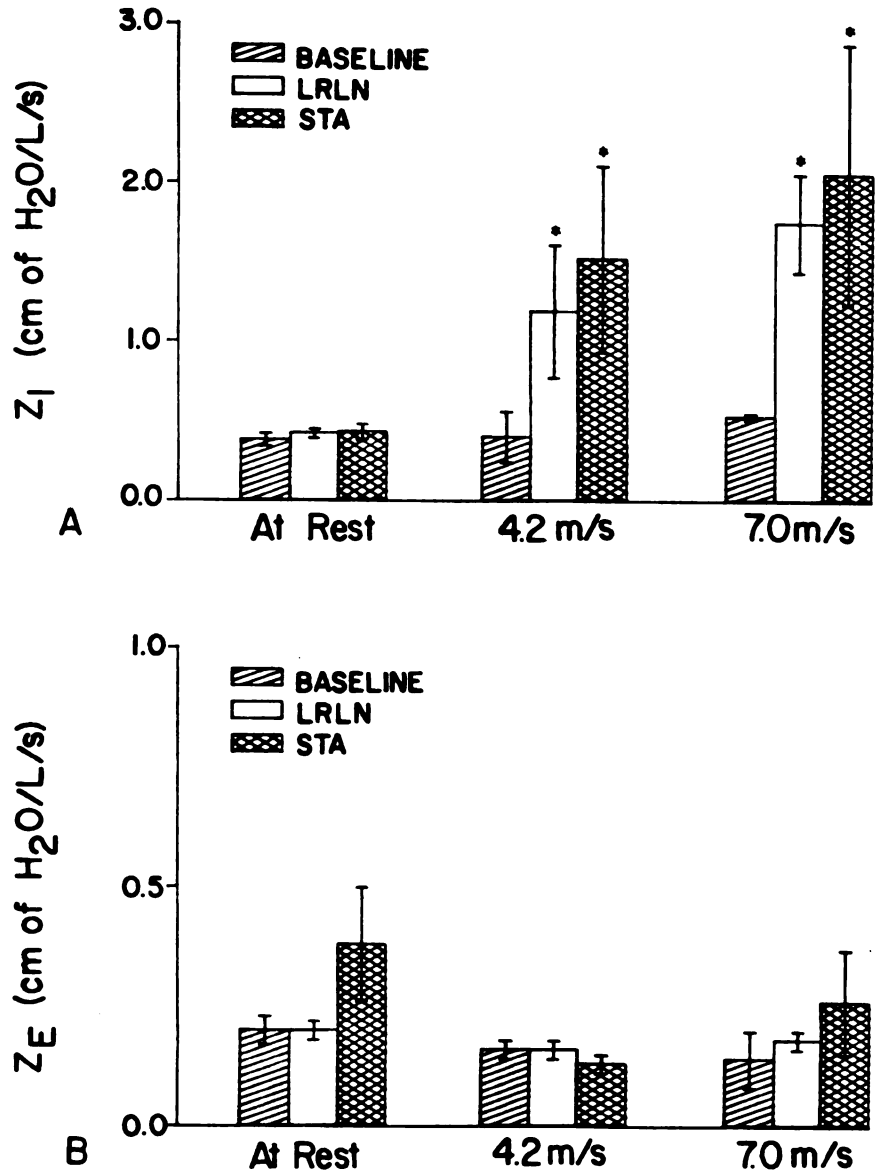

Figure 5. Inspiratory (Z_I) (A) and expiratory (Z_E) (B) impedance at 3 levels of exercise measured prior to left recurrent laryngeal neurectomy (baseline), after left recurrent laryngeal neurectomy (LRLN), and after left subtotal arytenoidectomy (STA). * = value is significantly different ($P < 0.05$) from base line measurement at the same treadmill speed.

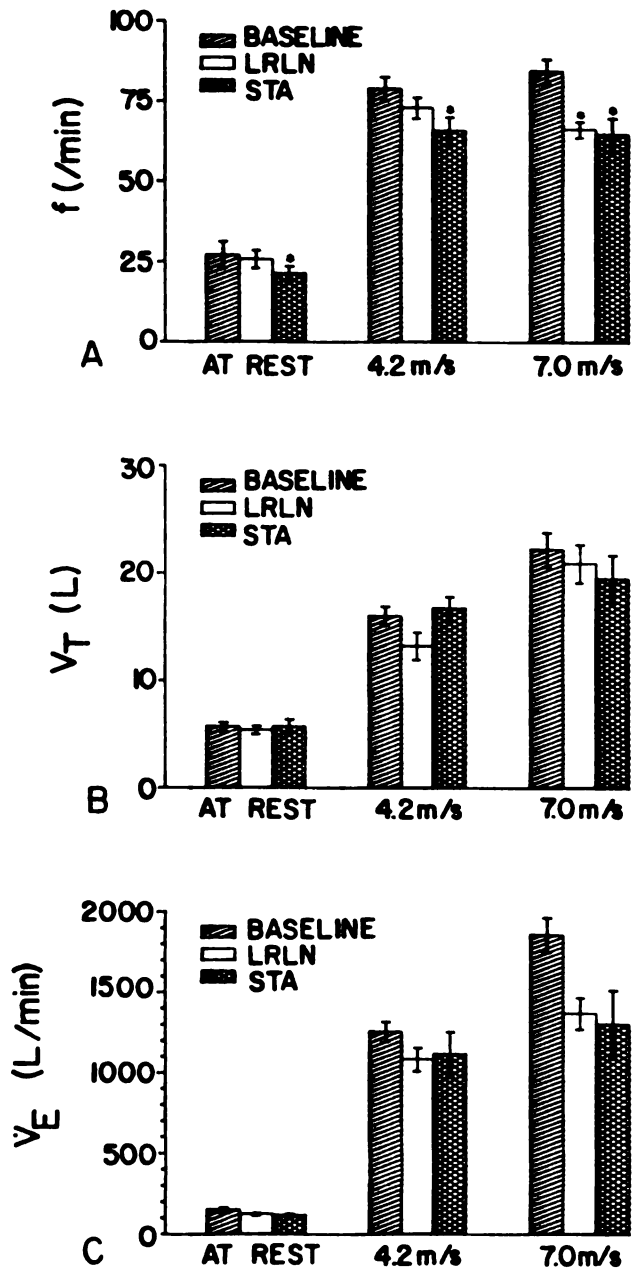

Figure 6. Respiratory frequency (f) (A), tidal volume (V_T) (B), and minute ventilation ($\dot{V}_E$) (C) at 3 levels of exercise measured prior to left recurrent laryngeal neurectomy (baseline), after left recurrent laryngeal neurectomy (LRLN), and after left subtotal arytenoidectomy (STA). * = value is significantly different ($P < 0.05$) from baseline measurement at the same treadmill speed.

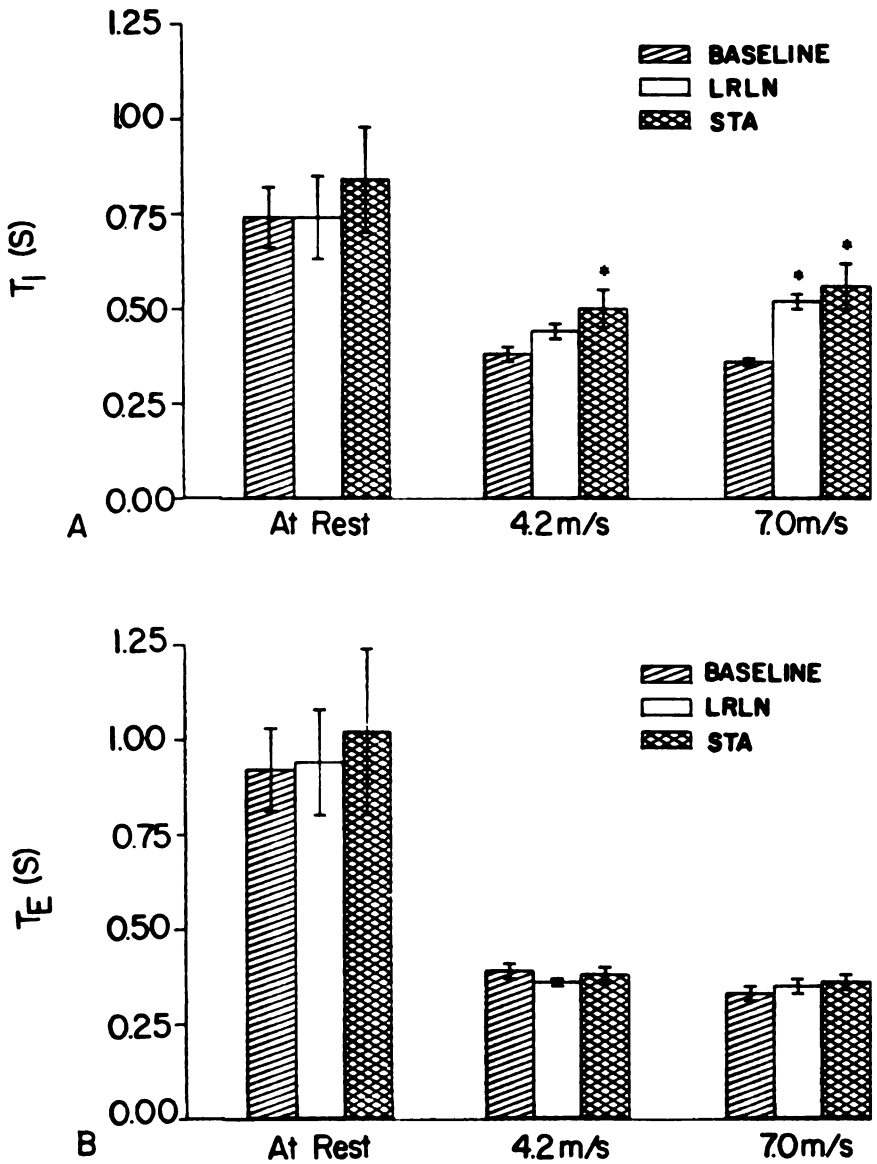

Figure 7. Inspiratory (T_I) (A) and expiratory (T_E) (B) times at three levels of exercise measured prior to left recurrent laryngeal neurectomy (baseline), after left recurrent laryngeal neurectomy (LRLN), and after left subtotal arytenoidectomy (STA). * = value is significantly different ($P < 0.05$) from baseline measurement at the same treadmill speed.

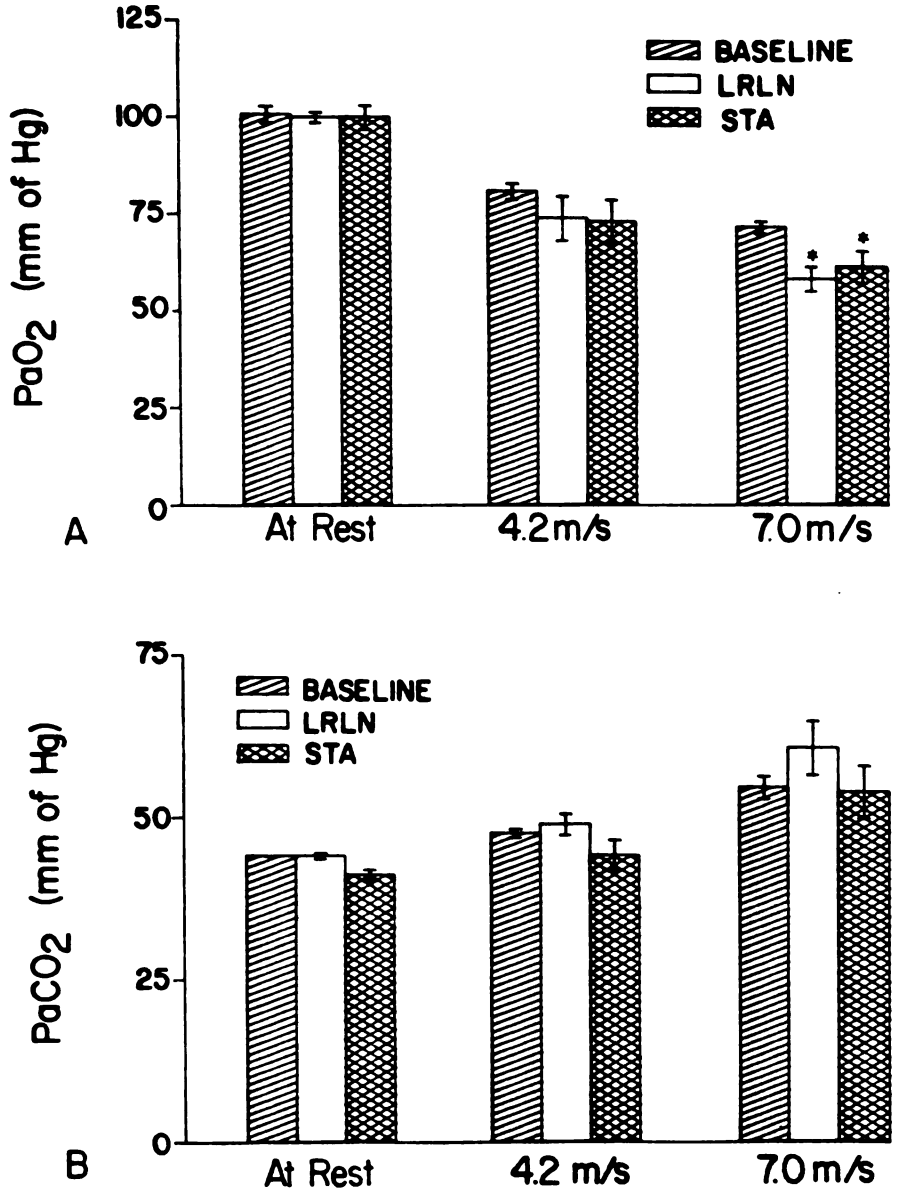

Figure 8. Arterial partial pressure of oxygen (PaO_2) (A) and arterial partial pressure of carbon dioxide ($PaCO_2$) (B) at 3 levels of exercise measured prior to left recurrent laryngeal neurectomy (baseline), after left recurrent laryngeal neurectomy (LRLN), and after left subtotal arytenoidectomy (STA) * = value is significantly different ($P < 0.05$) from base line measurement at the same treadmill speed.

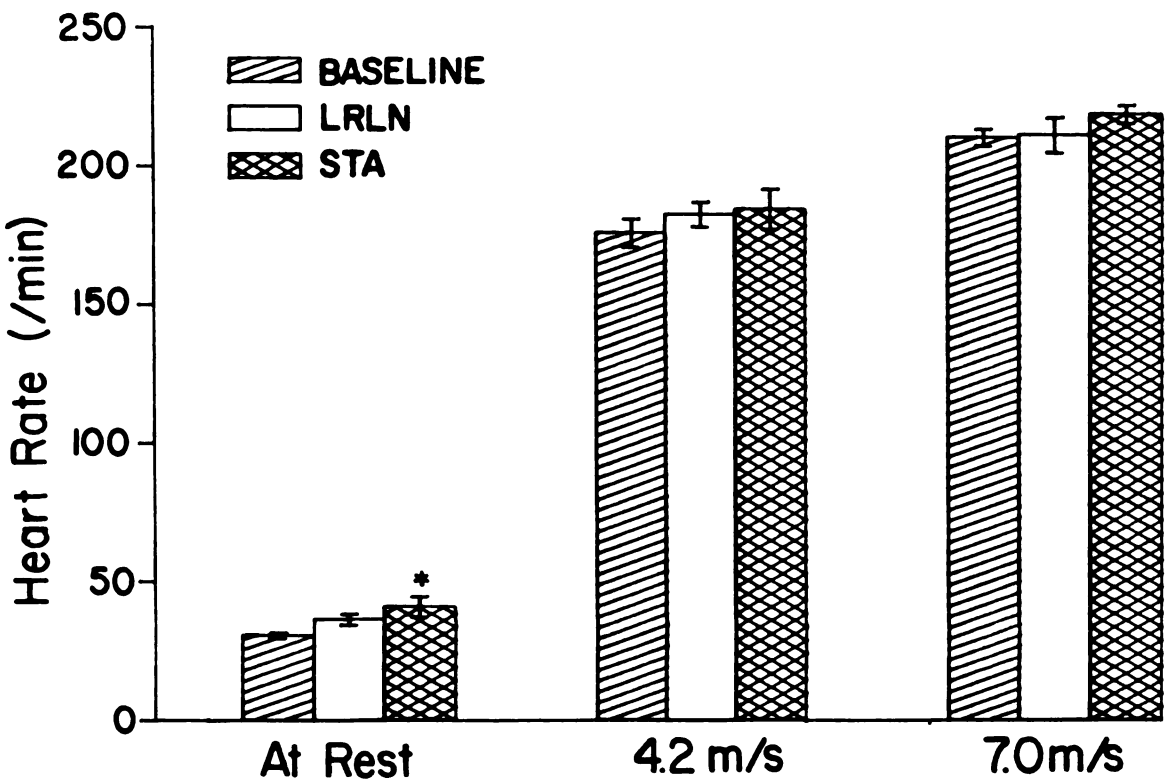

Figure 9. Heart rate at 3 levels of exercise measured prior to left recurrent laryngeal neurectomy (baseline), after left recurrent laryngeal neurectomy (LRLN), and after left subtotal arytenoidectomy (STA).

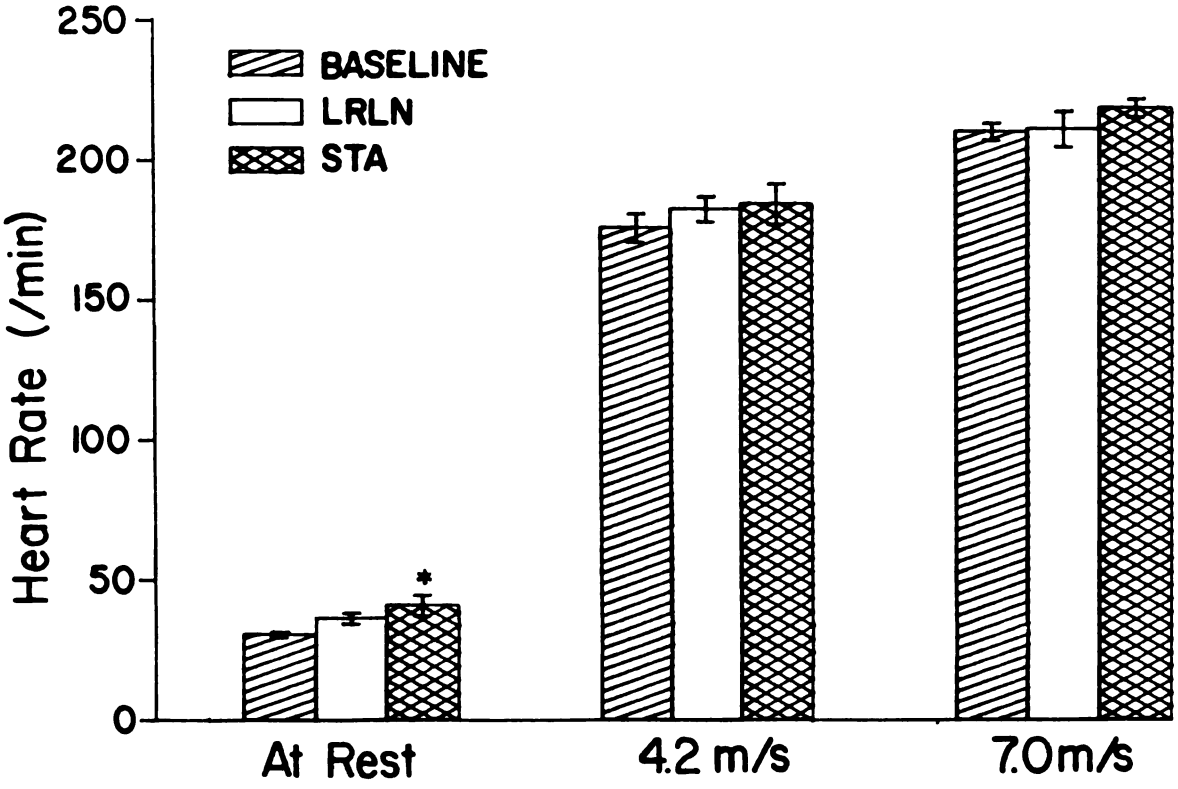

Figure 9. Heart rate at 3 levels of exercise measured prior to left recurrent laryngeal neurectomy (baseline), after left recurrent laryngeal neurectomy (LRLN), and after left subtotal arytenoidectomy (STA).

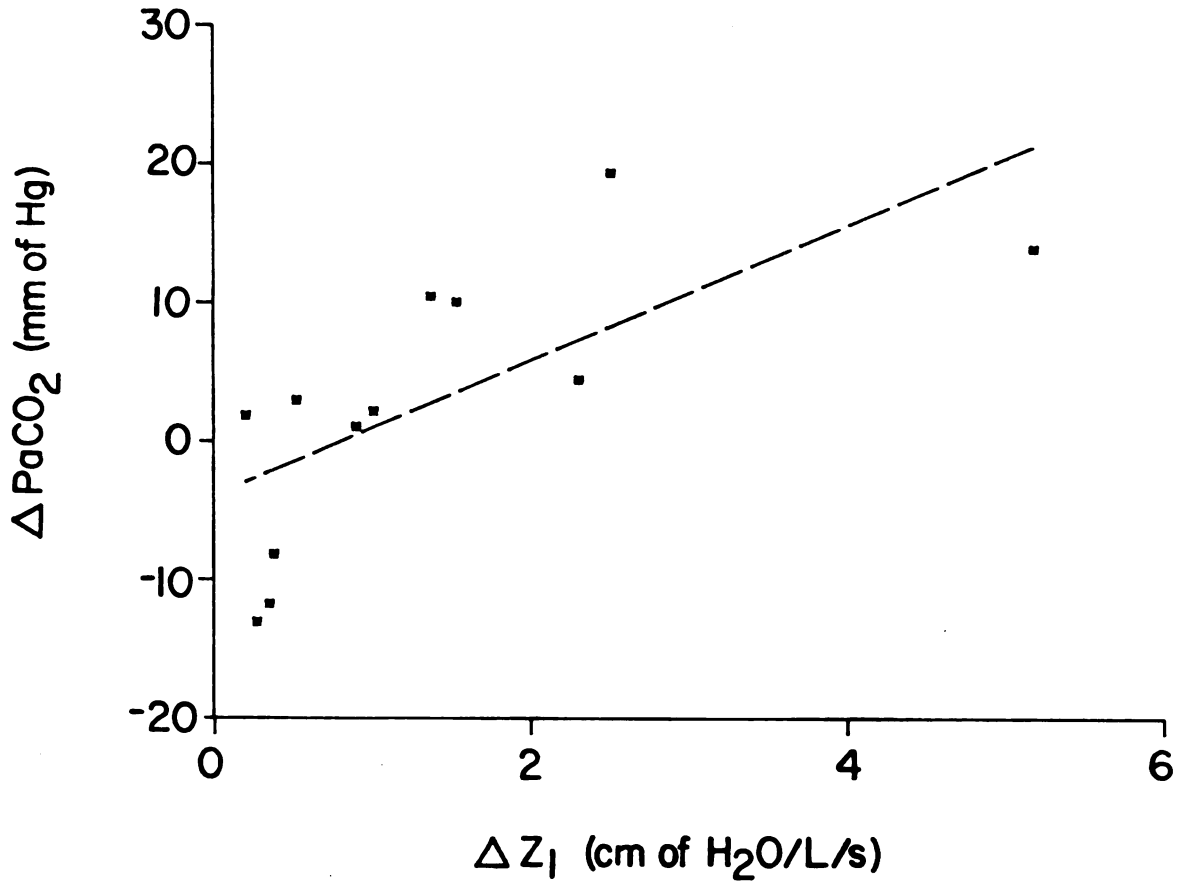

Figure 10. Correlation of change in arterial partial pressure of carbon dioxide ($PaCO_2$) (Y axis) and change in inspiratory impedance (Z_I) (X axis). These measurements were calculated as the change in inspiratory impedance (ΔZ_I) and change in $PaCO_2$ ($\Delta PaCO_2$) between measurements obtained before left recurrent laryngeal neurectomy (baseline) and measurements obtained after left recurrent laryngeal neurectomy, and as the change between baseline measurements and those obtained after left subtotal arytenoidectomy (ΔZ_I). $\Delta PaCO_2 = - 4.28 + 5.20\ \Delta Z_I$.

X. SUMMARY AND CONCLUSIONS

In horses with laryngeal hemiplegia, dynamic collapse of the airways occurs during inhalation.[107] As seen in the present study, the airway collapse resulted in an increase in Pu_I and a decrease in $\dot{V}_I max$. Therefore, the Z_I (the ratio of Pu_I and $\dot{V}_I max$) was greatly increased. To maintain adequate alveolar ventilation with decreased inspiratory airflow rate, there was an increase in the duration of inspiration and consequently a decrease in respiratory frequency (f). Upper airway collapse does not occur on exhalation,and therefore there was no significant change in upper airway flow mechanics during the expiratory phase of the respiratory cycle.

In this study, I tested the hypothesis that subtotal arytenoidectomy reverses the changes in upper airway flow mechanics seen in exercising horses with laryngeal hemiplegia. Subtotal arytenoidectomy did not significantly decrease Z_I or Pu_I, nor did the surgery increase $\dot{V}_I max$ when compared to left recurrent laryngeal neurectomy values. These results indicate that subtotal arytenoidectomy does not significantly change the upper airway measurements obtained after left recurrent laryngeal neurectomy. It can therefore be stated that subtotal arytenoidectomy is not effective in the treatment of induced laryngeal hemiplegia.

The measurements were obtained at speeds lower than racing speeds of the Standardbred. However,the incline of the treadmill greatly increases the workload.[45,108] The average heart rate obtained at 7.0 meters/second (209/min) approximates the heart rate seen at anaerobic threshold in exercising Standardbred horses.[109] In addition, flow rates reported in this study are similar to flow rates

measured in near-maximally exercising Thoroughbreds.[110] Therefore, results obtained in this study may be applicable to racing conditions.

Results of subtotal arytenoidectomy for laryngeal hemiplegia in the present study differ from a previous report of successful correction of equine laryngeal hemiplegia with subtotal arytenoidectomy.[11] However, the previous report used subjective criteria (owners' assessment of exercise tolerance and noise reduction) and not objective data as used in the present study. Improvement in exercise tolerance has also been reported with partial and total arytenoidectomies, but these reports also use subjective criteria for postoperative assessment.[9,10] A high incidence of postoperative complications with the partial arytenoidectomy has been reported which may dissuade one from using this technique.[89] Further investigation into the partial and total arytenoidectomy needs to be performed before the use of these techniques for treatment of LH can be recommended.

Exercise significantly increased $\dot{V}_I max$ and $\dot{V}_E max$, Pu_I and Pu_E, heart rate, $PaCO_2$, and respiratory frequency; PaO_2 significantly decreased. Similar changes with exercise have been previously reported.[12] The V_T obtained in this experiment are greater than those reported in galloping horses,[41,50,110,111] but similar to trotting or pacing Standardbreds.[111] In galloping horses, *f* and stride frequency are linked in a 1:1 ratio.[42,111] Because stride frequency in galloping horses commonly reaches 140/minute,[111] inspiratory time is short and therefore limits V_T. In trotters and pacers, *f* and stride frequency are not coupled in a 1:1 ratio. Instead, a 1:2 or 1:3 ratio is commonly used.[111] It has been reported that Standardbred horses can have

a much higher V_T by decreasing their f at higher speeds.[111] The Standardbred may therefore be capable of a higher V_T by controlling f for optimal ventilation.

Although $PaCO_2$ did not increase significantly following left recurrent laryngeal neurectomy or left subtotal arytenoidectomy, there was a positive correlation ($P < 0.05$) between the change in inspiratory impedance and the change in $PaCO_2$ between baseline and measurements taken after left recurrent laryngeal neurectomy, and between baseline and left subtotal arytenoidectomy in individual horses at 7.0 ms^{-1} (Figure 10). In all animals in which Z_I at 7.0 ms^{-1} increased by more than 0.5 cm $H_2O/l/s$ between baseline and left recurrent laryngeal neurectomy or baseline and left subtotal arytenoidectomy, $PaCO_2$ also increased indicating alveolar hypoventilation. When the change in Z_I was less than 0.5, the changes in $PaCO_2$ were variable. Despite the variability in $PaCO_2$, PaO_2 decreased at 7.0 ms^{-1} in all horses after left recurrent laryngeal neurectomy and left subtotal arytenoidectomy. Because the decrease in PaO_2 was larger and more consistent than the increase in $PaCO_2$, the hypoxemia present after left recurrent laryngeal neurectomy and left subtotal arytenoidectomy at 7.0 ms^{-1} can not solely be explained by alveolar hypoventilation. Dixon observed normocapneic hypoxemia in horses with laryngeal hemiplegia, which he attributed to $\dot{V}:\dot{Q}$ inequalities.[47]

In summary, data presented in this study show that subtotal arytenoidectomy does not significantly change the detrimental effects of laryngeal hemiplegia on upper airway flow mechanics in exercising horses, and therefore is not effective in the treatment of this condition.

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