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By

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ABSTRACT

USE OF FLOW-VOLUME LOOPS TO EVALUATE EQUINE LEFT LARYNGEAL HEMIPLEGIA AND ITS TREATMENT BY PARTIAL ARYTENOIDECTOMY

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Upper airway function was evaluated in 6 horses at rest and during exercise. Expiratory and inspiratory impedance (Z_E and Z_I) were calculated and tidal breathing flow-volume loops (TBFVL) were acquired. TBFVL indices included inspiratory and expiratory flow at 50% of tidal volume (IF_{50} and EF_{50}, respectively). After left recurrent laryngeal neurectomy (LRLN), Z_I and EF_{50}/IF_{50} significantly increased and IF_{50} significantly decreased from baseline (before LRLN) values during exercise. After partial arytenoidectomy, Z_I returned to baseline values though IF_{50} and EF_{50}/IF_{50} remained significantly different from baseline values. After LRLN, TBFVL showed marked inspiratory airflow limitation. Following partial arytenoidectomy, TBFVL shape approximated that seen at the baseline evaluation, although partial inspiratory flow limitation persisted. When obtained during exercise, TBFVL allowed non-invasive, objective, specific, and repeatable detection of upper airway obstruction. Partial arytenoidectomy improved upper airway function during exercise in horses with left laryngeal hemiplegia.

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I. INTRODUCTION

Reduced athletic performance as a result of left laryngeal hemiplegia (LLH) is a common cause of wastage in the racing industry, and may also result in early retirement of non-racing equine athletes (Rossdale et al,1985; Cook,1974). The observed exercise intolerance in horses with LLH is a direct result of paralysis of the left cricoarytenoideus dorsalis (CAD) muscle (Dupey, 1815 in MacQueen,1896; Duncan et al,1974). Paralysis of the CAD muscle, in the majority of cases, has been attributed to a distal axonopathy of the left recurrent laryngeal nerve (RLN) (Cole,1946; Duncan et al,1974). The etiology of this neuropathy remains undetermined.

Use of the flexible fiberoptic endoscope for examination of the upper respiratory tract of horses revolutionized the accuracy with which LLH could be diagnosed (Cook,1974). More recently, videoendoscopic examination of laryngeal function during treadmill exercise has provided more sensitive detection of this upper airway obstruction (Derksen,1988; Morris and Seeherman,1988). Further information, regarding the pathophysiology of LLH at rest and during exercise, has been provided through quantitative evaluation of upper airway flow mechanics and rima glottidis cross-sectional area (Derksen et al,1986; Martin et al,1986). Unfortunately, these objective measurement

techniques have afforded limited clinical use because of their invasive and/or time consuming nature.

In human medicine, objective and sensitive evaluation of upper and lower airway function is routinely achieved in a clinical setting using analysis of maximal effort flow-volume loops (FVL). A maximal effort flow-volume loop represents an x-y plot of airflow rate versus volume, when a patient inspires and then expires with maximal effort (Hyatt et al,1958). This commonly used test of airway function in humans has had limited application in veterinary medicine because of the uncooperative nature of animals. Therefore, the first objective of my study, was to determine if flow-volume loop analysis could be used to quantitate airway obstruction in horses with surgically-induced LLH at rest and during exercise.

Objective evaluation of upper airway function in horses has been reported for treatments of LLH including ventriculectomy, prosthetic laryngoplasty, subtotal arytenoidectomy and laryngeal reinnervation (Shappell et al,1988; Belknap et al,1990; Fulton et al,1991). At present, based on subjective and objective evaluations, prosthetic laryngoplasty, is the preferred method of surgical treatment. Despite this, prosthetic laryngoplasty may be associated with numerous post operative complications, therefore the search for the ideal treatment of LLH continues.

Following the recognition of arytenoid chondropathy and because of the need to treat unsuccessful prosthetic laryngoplasty procedures, arytenoidectomy was advocated in the early 1980's (Haynes et al 1980; White

and Blackwell et al,1980). In addition, surgeons have suggested the use of arytenoidectomy as a primary treatment for LLH (Haynes et al,1984). Presently, recommendations regarding the arytenoidectomy technique of choice remain controversial. Subtotal arytenoidectomy, which leaves the corniculate cartilage in situ, is preferred by some authors because of the high incidence of coughing and dysphagia reported with partial arytenoidectomy, which involves removal of the corniculate cartilage (Haynes,1981;Speirs,1986).

Recent objective information indicates that subtotal arytenoidectomy fails to improve upper airway function and that the upper airway obstruction results from axial displacement of the corniculate cartilage during inspiration (Belknap et al.1990; Stick and Derksen,1989). In addition, recent studies report a lower rate of post-operative complications after partial arytenoidectomy than previously described (Tulleners et al,1988:I). Therefore, the second objective of this study was to evaluate the efficacy of partial arytenoidectomy, in restoring upper airway function in horses with LLH.

II. ASSESSMENT OF UPPER AIRWAY FUNCTION

A. Principles of Flow Mechanics

In its simplest form the upper airway acts as a conduit for airflow from the atmosphere to the lung. The flow of fluid in a rigid cylindrical tube is described and predicted by the laws of fluid mechanics. In contrast, airflow through the mammalian respiratory system is much less well defined by equations used in aerodynamics. Factors limiting application of the principles of hydrodynamics and aerodynamics to airways arise from the complex geometry and dynamic nature of the respiratory tract (West,1990). Despite such limitations, use of laws of fluid mechanics in studies of flow-volume relationships in airways has increased the understanding of mammalian airflow mechanics and has also allowed quantitation of the mechanical properties of the respiratory system.

Laminar flow

Fluid flow, whether it is air or liquid, requires a force. The force for flow in a tube is provided by a pressure difference between the two ends of the tube, referred to as the driving pressure. The flow of air through a rigid smooth cylinder at low flow rates is characterized by stream lines or flow laminae, which are parallel to the sides of the tube. This kind of fluid flow is defined as laminar flow.

As airflow enters a tube, the leading edge of flow is initially flat, because all molecules enter at the same velocity. Over a finite period of time the flow profile becomes parabolic. During the development of this parabolic profile,

high shear forces exist between fluid molecules and the cylinder wall. Shear forces gradually decrease from the periphery, where there is zero velocity of fluid molecules adjacent to the cylinder wall, to the centrally located flow laminae. This allows acceleration of velocities at the center of the cylinder, increasing shear at the center of the cylinder and thus equalizing forces across the profile (Plint and Bosworth,1978). Thus in a finite distance (entrance length) and time, an even distribution of shear between laminae results in a parabolic flow profile where flow near the center has a velocity almost twice the average velocity. Mathematically the relationship between pressure and flow in a laminar flow regime may be described by Poiseuille's Law.

$$\dot{V} = \frac{\pi r^4 P}{8 \mu l}$$

Where $\dot{V}$ = airflow, P = driving pressure, r = tube radius, μ = gas viscosity, and l = tube length. Thus, when tube dimensions are constant, pressure is directly proportional to flow, or $P = K_1\dot{V}$, where K_1 represents the mechanical energy loss within the system from laminar flow.

Laminar flow resistance

In air- or liquid-filled systems resistance to flow is defined as the difference between inflow and outflow pressures divided by the instantaneous rate of flow of fluid (Pride,1970). The term, resistance, is analogous to Ohm's law in electricity, where the resistance of a conducting wire is the potential

difference across its length divided by the instantaneous current. Thus resistance may be represented by:

$$R = \frac{P_1 - P_2}{\dot{V}}$$

where R = resistance, $P_1 - P_2$ = pressure change along the tube, and $\dot{V}$ = flow rate.

By combining the resistance formula and Poiseuilles equation, resistance to flow may be expressed solely by the geometry of the tube and the viscosity of the gas.

$$R = \frac{8 \mu l}{\pi r^4}$$

Where μ = gas viscosity, l = length of the tube, and r = radius of the tube. Clearly from this equation it can be seen that relatively small changes in tube diameter will result in large changes in flow resistance. If the radius is halved the resistance increases by 16-fold. However, doubling the length only doubles the resistance.

Turbulent flow

At higher flow rates complete disorganization of stream lines occurs. Particle velocity throughout the flow varies in magnitude and direction resulting in turbulent flow. The properties of turbulent flow differ from those of laminar flow. The flow profile is flat, flow at the center of the cylinder is only 1.2

times the average velocity and driving pressure is not proportional to flow rate, but approximately to its square. When flow is turbulent, P is equal to the product of K_2 (anatomically dependent constant) and $\dot{V}^2$ (Plint and Bosworth,1978). In addition, the pressure-flow relationship in turbulent flow is dependent on gas density.

Turbulent flow resistance

Turbulent flow results in an increase in shear stresses between flow laminae. This increase in shear stresses is associated with a greater pressure drop for a given flow, and therefore the driving pressure for a given flow is greater when the flow regime is turbulent rather than laminar. When flow through a passage is both turbulent and laminar in places, it may be described by Rohrer's equation, where flow has both laminar and turbulent properties (Hamilton,1979):

$$P = K_1\mu\dot{V} + K_2\rho\dot{V}^2$$

where P = driving pressure, K_1 = mechanical energy loss due to laminar flow, μ = the viscosity of the gas, K_2 = mechanical energy loss due to turbulent flow, ρ = the density of the gas, and $\dot{V}$ = airflow. As flow is not constant when the flow regime is turbulent, resistance is defined as the ratio of the change in pressure over the change in flow:

$$\text{Resistance} = \frac{P_1 - P_2}{\dot{V}_1 - \dot{V}_2}$$

Resistance under turbulent conditions is thus dependent upon the flow rate at which it is measured.

Reynold's Number

Reynolds (1883) was the first to calculate the constant value at which the flow regime in a tube changes from laminar to turbulent. This dimension less value is dependent on the characteristics of the tube, the density, and viscosity of the fluid and flow velocity, and is represented by:

$$Re = \frac{2 \rho \dot{V}}{\pi \mu r}$$

where ρ = density, $\dot{V}$ = airflow velocity, r = radius, and μ = viscosity.

The validity of this equation has been confirmed through experiments using a wide range of tube diameters, flow rates, and fluid properties. Laminar flow occurs when Re is less than 2300 and turbulent flow occurs when Re is greater than 3000 (Patel and Head,1968). Transitional flow, occurring at moderate flow rates, has characteristics of both laminar and turbulent flow and is associated with a Re between 2300 and 3000.

Entrance conditions of a branching system of tubes have been shown to influence the critical Re at which flow regime is altered (Pedley et al,1970). Typically, if incoming fluid has disturbances, then the Re at which turbulence occurs will be reduced, the driving pressure needed for flow will be greater. The larger airways of the respiratory system represent the greatest resistive pressure drop of the respiratory system. This is because airflow velocities are

greater in larger central airways compared to smaller peripheral airways and the total cross-sectional area is much smaller in the central airways than the peripheral airways. Therefore, the driving pressure needed for flow from atmosphere to alveoli is significantly affected by entrance effects in the upper airway and larger diameter parts of the lower respiratory tract (Pedley et al,1970).

B. Flow Mechanics in the Upper Respiratory Tract

The upper airway begins at the nostrils and includes the nasal cavity, the pharyngeal cavity, and finally the larynx. The flow of air from atmosphere through the upper airway, to the alveoli, is the result a force provided by the pressure difference between the pleural cavity and the atmosphere (**driving pressure**). Inspiratory driving pressure is produced by diaphragmatic and intercostal muscle contraction, resulting in a decrease in intrapleural and subsequently alveolar pressure.

The net driving pressure required for gas flow through the upper airway is dependent on the flow rate, whether flow is laminar or turbulent, the density (when airflow is turbulent) and the viscosity of the gas, and several important impedance factors. These impedance factors include airway resistance, resulting from narrow and irregular geometry of the upper airway and reactance, consisting of airway narrowing associated with airway wall compliance and inertial forces created by acceleration and deceleration of airflow when airflow reverses.

Turbulent flow in the upper airway

It has been shown in the upper respiratory tract of humans, that laminar flow only occurs at very low flow rates (<1.0 L/s) (Olson et al,1970). In the horse, the Reynolds number calculated for airflow at 1.3 L/s in the trachea suggests that the flow regime is turbulent (Attenburrow et al,1983). Since airflow in the upper respiratory tract of the horse at rest is approximate 5 L/s and may increase 20-fold during strenuous exercise (Hörnicke et al,1987), the laws of fluid dynamics defining turbulent flow are appropriate.

With the reversal of flow direction during the respiratory cycle, inertial forces are created. This inertance increases the driving pressure required to produce a given flow. At rest, inertance appears to be of minor significance, but when flow rates and respiratory frequencies increase, as during exercise, inertial forces are likely to increase greatly. Techniques used to evaluate upper airway function in man, minimize the need to account for inertial forces associated with measurement of airflow and its' required driving pressure. This is because airflow measurement is performed either during quiet breathing or during forceful, unidirectional, controlled respiration. In contrast, airflow measurement in exercising horses is associated with high airflow rates and respiratory rates and inertance forces are likely to have a significant effect on driving pressure.

Upper airway compliance

An additional complicating factor, making direct application of Rohrers equation inadequate, is that the respiratory system is not a rigid tube, but instead represents a series of airways whose dimensions change throughout the respiratory cycle. Therefore, the constant values used in his equations, representing mechanical losses due to geometry, are unlikely to remain truly constant. The amount of airway diameter change in response to transmural pressure during inspiration and expiration is determined by the compliance of the airway wall. During inspiration, intraluminal upper airway pressure is sub-atmospheric, whereas pressures are positive with respect to atmosphere during expiration. Collapsible structures in the upper airway rely on adequate dilatator muscle function to resist negative intraluminal pressures during inspiration. Dilator muscle contraction maintains airway caliber and thus airflow during inspiration (Robinson and Sorenson,1978). Collapsible structures of the upper airway include the external nares, pharynx, and the arytenoid cartilages of the larynx, which are supported principally by muscle rather than bone or cartilage. The ability of the upper airway to resist dynamic collapse on inhalation is apparently incomplete because, inspiratory resistance has been shown to be 50% and 200% greater than expiratory resistance during quiet breathing at rest and during strenuous exercise respectively (Derksen et al,1986). Other methods that may reduce flow impedance in the upper airway are straightening of the airways and sympathetic vasoconstriction of vascular sinuses in the nasal mucosa (Derksen,1988).

In humans, the effect of compliance on measurement of airway function is reduced by measuring airflows and pressure differences during expiration. Additionally, the minimal contribution of the soft palate to the nasopharynx in man (Procter,1977), results in a low compliance upper airway. In contrast to man, the upper airway of the horse may represent a more compliant conduit, as the horse has a long soft palate that forms an intimate seal with the ventral aspect of the epiglottis (Cook,1981:I). The potential of the equine nasopharynx to narrow during inspiration and the substantial inertia associated with the reversal of flow direction at high flow rates warrant the description of total upper airway resistance to flow as impedance rather than resistance.

Upper airway resistance

The resistance to airflow is a combination of turbulence and drag created by respiratory tract geometry, friction between air and airway walls, and the shear forces present within a flowing gas (Olson et al,1970). Clearly, the upper respiratory tract is anything but a "smooth, rigid, cylinder," but rather a conduit of varying diameter with extensive surface irregularities. Considering the effects of varying airway diameter, we can predict that if flow rate is to remain constant and airway diameter decreases, then flow velocity must increase. This is referred to as "convective acceleration" (Fry and Hyatt,1960). Acceleration requires a force. This force is provided by an increase in driving pressure, that is, a greater pressure drop along the airway. Associated with convective acceleration is a further drop in pressure along the stream in an effort to conserve energy within the system (Bernoulli's principle) (Figure 1).

This additional pressure drop further increases the tendency for collapsible segments of the airway to narrow, thus perpetuating a vicious cycle of

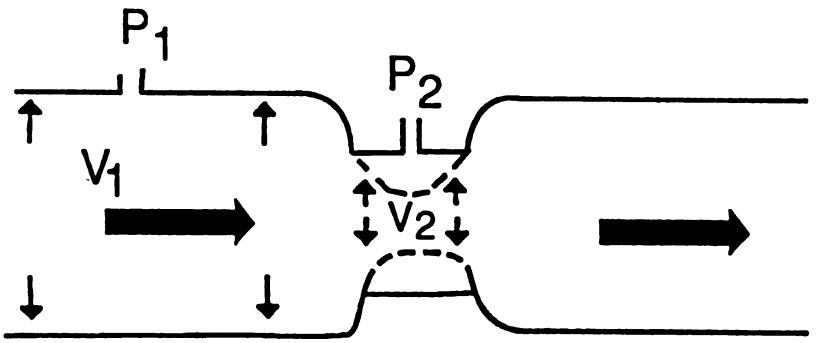

Figure 1. Diagrammatic representation of Bernoulli's effect creating collapse of a narrowed airway. For total energy ($E_{kinetic}$ + $E_{potential}$) conservation within the system, the increase in airflow velocity (V)($E_{kinetic}$) at the narrowed portion of the airway from V_1 to V_2, requires a reciprocal decrease in intraluminal pressure (P)($E_{potential}$) from P_1 to P_2 at the site of the airway narrowing.

This cycle is epitomized in the equine athlete suffering from left laryngeal hemiplegia. Paralysis of the abductor muscle of the arytenoid cartilage prevents the normal dilatator function needed to maintain airflow during exercise. The cross-sectional area of the rima glottidis (opening to the trachea) is smaller than normal as the corniculate cartilage cannot be fully abducted. Air is subject to increased convective acceleration through the narrowed rima glottidis, which is associated with a further pressure drop (Bernoulli effect). The greater

negative intraluminal pressure results in further narrowing, as the corniculate cartilage is unable to abduct, and becomes displaced axially. When subject to high airflow rates, the progressive airway narrowing and negative intraluminal pressure may result in complete obstruction of the rima glottidis by the corniculate cartilage (dynamic collapse) during inspiration (Derksen,1988).

Upper airway impedance

The relationship between resistance and airway radius (Poiseuilles law) provides important insight into the relatively mild changes in airway diameter that can cause significant increases in resistance to flow. In an attempt to better describe pressure-flow relationships in the airway, parallels drawn from the field of electrical engineering accommodate the role of inertance and compliance. The sum of these two components (reactance) is combined with resistance in one term called the impedance (Young and Hall,1989). Impedance is defined as the total opposition to flow in the part of the respiratory tract examined.

$$Z = \frac{\Delta P}{\Delta \dot{V}}$$

where Z = impedance, ΔP = driving pressure, and $\Delta \dot{V}$ = change in flow rate.

C. Upper Airway Resistance Measurement Techniques in Humans

Upper airway resistance in Humans

Early studies showed a nonlinear relationship between pressure and flow in the upper airway, indicative of turbulent flow (Hyatt and Wilcox,1961; Ferris et al,1964). For this reason, resistance was consistently calculated at a low flow rate of 0.5 L/s, at which flow was considered to be laminar. Increase in lung volume decreases upper airway resistance (Hyatt and Wilcox,1961; Ferris et al,1964) because, during maximal inspiration head and neck position straightens the upper airway and widens the rima glottidis.

Partitioning of upper airway resistance

Hyatt and Wilcox (1961) were the first to partition respiratory resistance into lower and upper airway components by measuring intra-tracheal pressure with a blunt 19-gauge needle introduced perpendicularly into the trachea, 2-3 cm below the cricoid cartilage. The intra-tracheal-oral pressure gradient was recorded during various respiratory maneuvers. Oral pressure was recorded just inside to the lips through a 19-gauge needle and subjects mouth breathed with their nose clamped. Airflow was measured using a concentric cylinder flowmeter, and respiratory volumes were recorded using a spirometer. Upper airway resistance was estimated to contribute approximately 45% of total airway resistance in normal subjects. This value is similar to that predicted by Rohrer in 1915 based on computations from anatomical models.

The upper airway not only provides a large portion of resistance to airflow, this resistance is variable within and between subjects (Hyatt and

Wilcox,1961). The observed variability was considered to result from changes in the laryngeal airway size, which comprised the most significant site of airway resistance during mouth breathing. The importance of the larynx as a source of airway obstruction during mouth breathing, was supported by the observation that during hyperventilation the vocal cords remained abducted, and airway resistance decreased by approximately 40%.

In a later study, Ferris et al (1964) suggested that the mouth and pharynx were also significant and variable sources of airway resistance. Spann and Hyatt (1971), after measuring mouth, pharynx, and larynx resistances, considered pharyngeal resistance negligible, and mouth resistance accounted for 45% and 70% of upper airway resistance (Ruaw) during quiet mouth breathing at low and high lung volumes, respectively.

Posterior rhinomanometry

As man is primarily a nasal breather, Ferris et al (1964) attempted to quantify the contribution of nasal passages to upper airway and total respiratory resistance. Upper airway resistance was partitioned by employing a new and less invasive method of obtaining airway pressure. Nasal resistance was measured by obtaining the pressure difference between the inside of a mask placed over the face of the subject and a tube placed via the mouth into the oropharynx . The pressure difference between mask and oropharynx was divided by the measured airflow from a mask flowmeter while subjects breathed through their nostrils. This technique is referred to as posterior rhinomanometry. A similar technique was described by Speizer and Frank

(1964), except that the orally placed catheter measured oropharyngeal pressures through pressure changes in a latex balloon attached to its tip. This technique uses mouth pressure as an index of nasopharyngeal pressure, because upper airway anatomy in humans allows direct communication between the oro-and naso-pharynx (Proctor,1977). Disadvantages of posterior rhinomanometry include, 1) the need to diligently hold the mouth tube to prevent air from escaping around the tube, and 2) avoiding sealing off from the pharynx that part of the oral cavity containing the catheter (Ferris et al,1964; Nolte and Lüder-Lüher,1972). Reports using posterior rhinomanometry concluded that nasal resistance accounts for nearly half the total and two-thirds of upper airway resistance during nose breathing (Ferris et al,1964; Speizer et al,1964). It has been stated that nasal breathing nearly doubles the total respiratory resistance compared to oral breathing (Proctor,1977).

Anterior rhinomanometry

During anterior rhinomanometry one nasal passage contains a catheter for measurement of pharyngeal pressure while the patient breaths through the other nasal passage (Nolte and Lüder-Lüher,1972). This method has clinical advantages over posterior rhinomanometry in that it eliminates the inconvenience of a pharyngeal tube and the inability of some patients to hold the tube correctly.

Anterior rhinomanometry assumes that left and right nasal resistance are equal. The limitations of this measurement technique were documented by Nolte and Lüder-Lühr (1972) in a study comparing measurement of nasal

resistance by posterior rhinomanometry, anterior rhinomanometry, and whole-body plethysmography. They concluded that anterior rhinomanometry over-estimates the measured resistance when laminar flow is assumed and under-estimates the value when turbulent flow is assumed.

Body plethysmography

Early on in the search for a clinical, quantitative, and practical method of measuring nasal resistance, body plethysmography was suggested as a potential diagnostic tool (Butler,1960). Dubois et al (1955) performed pulmonary function tests using a non-invasive technique that employs a constant-volume, variable-pressure, whole-body plethysmograph.

Measurement of nasal resistance (Rn), using body plethysmography is based on the fact that total resistance between alveoli and nose openings consists of two partial resistances: the resistance while mouth breathing (Raw) and Rn. Thus the difference in resistance measurements during mouth breathing and nose breathing will represent nasal resistance. The advantages of body plethysmography as a clinical diagnostic tool are that it is efficient and reliable and requires minimal demand for skill and cooperation by the patient. The obvious limitation of this technique is the cost of equipment and technical skill necessary.

D. Measurement of Upper Airway Obstruction in Horses

Measurements of inspiratory and expiratory airflow in horses walking on a treadmill were performed as early as 1898 (Zuntz and Hagemann,1898). In

1966, airflow measurements were obtained from standing horses, using a pneumotachograph attached to a close-fitting face mask covering the horse's nose and mouth (Gillespie et al,1966). The pneumotachograph functions as a flow laminator and provides a constant resistance. Differential transducers connected to either side of the pneumotachograph, provide a measurement of the change in pressure across the pneumotachograph, which is proportional to flow rate.

Calculation of upper airway impedance in the resting horse was initially described by Robinson et al, (1975). Airflow was measured through a pneumotachograph attached to a face mask, and trans-upper airway pressure was determined as the difference in pressure between a catheter at the level of the nares and an 18-gauge needle inserted into the trachea just below the larynx. The contribution of upper airway resistance to total airflow resistance was further investigated by measuring pressure in the trachea and in the pleural space. Using a dead horse head, upper airway resistance was partitioned by a catheter pull through technique at constant airflows of 4 and 7 L/s. In the upper respiratory tract 80% of resistance to airflow was at the nostrils, with the larynx contributing the other 20%. The upper respiratory tract was determined to contribute only 30% of total airway resistance. In contrast, in a later study by Art et al (1988) upper airway resistance, principally that of the external nares, was considered to account for 82% of total respiratory resistance. The differences in these two studies may be due in part to differences in measuring techniques of pleural pressure. The

intercostally-placed mushroom catheter used by Robinson et al,(1975) to measure pleural pressure may result in pleural deformation and altered pressure values, whereas the indirect pleural pressure measurement via a esophageal balloon used in the study by Art et al,(1988) does not cause such errors. In addition, Art et al, positioned their intra-tracheal catheter closer to the thoracic inlet than that of Robinson et al,; consequently, the measured pressure gradient between trachea and pleural cavity may have been smaller.

Efforts to quantify upper airway function in exercising horses, began with the measurement of airflow rates while riding a horse wearing a face mask attached to a respiratory tube (Hörnicke et al,1983). Flow was sensed by a tube-mounted flag whose deflection was measured electronically. The electrical signals were transmitted telemetrically and stored on magnetic tape. The ability to quantify upper airway flow mechanics during exercise, was further advanced with the development of a technique for measuring intra-tracheal pressure in the horses during exercise (Mangseth,1984). The technique involved the percutaneous placement of an intra-tracheal catheter, which was connected to a differential pressure transducer. Upper airway pressure changes were defined as the pressure difference between atmospheric and intra-tracheal pressure. In later studies, this percutaneous intra-tracheal catheter technique was compared to a nasotracheal catheter in maximally exercising horses with and without surgically-induced LLH (Williams et al,1990:I). Pressure measurements obtained using these two catheter systems were found not to differ significantly. Subsequently, intra-tracheal pressure

measurements were obtained before and after surgical treatment of experimentally induced and naturally occurring upper airway obstructions (Williams et al,1990:I,II).

Because variations in flow rates rather than changes in airway geometry may account for differences in intra-tracheal pressures within and between horses, studies in which only intra-tracheal pressure is measured should be interpreted with caution. Therefore, in 1986, Derksen et al. quantified upper airway impedance in the horse at rest and during treadmill exercise. Airflows were measured via a mask-pneumotachograph unit. Trans-upper airway pressure, was the difference between mask pressure and mid-cervical intra-tracheal pressure. Impedance was determined as the ratio of peak trans-upper airway pressure and peak flow for a given breath. Subsequently, impedance values were calculated in horses to evaluate numerous surgical treatments for induced left laryngeal hemiplegia (Derksen et al,1986; Shappell et al,1988; Belknap et al,1990; Fulton et al,1991).

Recently, measurement of airflow rates using ultrasound has been adapted to the exercising horse (Woakes et al,1987). As the pneumotachograph used by Derksen et al, was of considerable weight, airflow measurement by ultrasound greatly reduces the weight of the mask worn by the horse. Variation in airflow rates change the transit time of ultrasound beams projected diagonally across flow tubes mounted on a mask. The resulting phase shift of the received signal is detected and produces a voltage output proportional to flow.

Intra-tracheal pressure measurement using a lateral tracheal catheter has clinical limitations because of the invasive nature of the procedure and complications such as cellulitis, granulomas and chondritis (Nielan et al,1992). Although nasotracheal catheter systems may be less invasive, ventilatory impairment (although small), is likely to be greater than that seen with a lateral transtracheal catheter (Nielan et al,1992). In addition to the invasive nature of tracheal pressure measurement, the time-consuming calculation of impedance values from pressure and flow tracings is clinically undesirable. For these reasons, quantitation of upper airway obstructions is rarely used in a clinical setting.

In human medicine, flow-volume loop analysis allows clinically useful, quantitative evaluation of upper airway obstructive diseases, and it is possible that the technique may be clinically useful for quantifying upper airway obstruction in the horse. Therefore, I chose to document this technique in horses with surgically-induced LLH at rest and during exercise.

E. Development of Flow-Volume Loop Analysis

Currently, the most commonly used human pulmonary function test is the forced vital capacity (FVC) maneuver. To complete this procedure the patient inhales to maximal lung volume then immediately exhales as rapidly, forcefully and completely as possible. This maneuver requires patient cooperation, and coaxing is often necessary to generate maximal effort. This test is performed at rest, breathing into a heated pneumotachograph, which is

considered the most accurate flow monitoring system (Yeh et al,1987). During a FVC maneuver, the x-y plot of airflow rate and its' integral with time (volume), produces a maximum expiratory- and-inspiratory flow-volume curve (MEFVC and MIFVC, respectively). These 2 curves comprise a **maximal effort flow-volume loop (FVL)**. Flow-volume loop analysis involves qualitative and quantitative evaluation of this continuous x-y plot of airflow versus volume (Hyatt and Black,1973). As a clinical diagnostic test, FVL analysis approximates the criteria stated by Cochrane and Holland (1971) for the goals of any diagnostic test: simplicity, patient acceptability, accuracy, repeatability, sensitivity, specificity, and cost. For this reason it is well established as a reproducible and sensitive indicator of respiratory disease in man (Becklake and Permutt,1977).

The use of the FVL, as a pulmonary function test occurred following the recognition of the functional relationship existing between transpulmonary pressure, airflow rate and degree of lung inflation (Fry et al,1954; Hyatt et al,1958). The relationship between pressure and flow was expressed as a family of isovolume pressure-flow (PF) curves differing in shape at varied lung volumes. Figure 2 shows 4 PF curves obtained from initial experiments performed on healthy people by Hyatt et al (1958). The expiratory flows of PF curves 1, 2, and 3, measured low in the vital capacity, increase to a maxima, A, B, and C respectively, and then diminish with increasing transpulmonary pressure. Therefore, despite increasing effort (increasing transpulmonary pressure), once a flow maximum for that volume is reached, increasing

transpulmonary pressure results in dynamic compression of airways and flow rate can not be increased (flow limitation).

At lung volumes less than approximately 70% of vital capacity, flow is effort independent, as increasing transpulmonary pressures do not result in an increase in airflow. Therefore, the maximal achievable expiratory flow over the lower half of the vital capacity theoretically bears a constant relationship to lung inflation, that is uniquely determined by the physical properties of the lower respiratory tract and does not depend on maximal effort (Fry et al,1958). Using the plot of flow maxima at various lung volumes, the information obtained through measurement of transpulmonary pressure and flow can be represented as a flow-volume (FV) curve (Figure 2b). Representation of a FVC maneuver as a FV curve, rather than a PV curve, is clinically desirable as the measurement of pleural pressure required to derive transpulmonary pressure, involves the invasive placement of an esophageal balloon. In a series of studies evaluating the factors influencing FV curves at lung volumes less than 70% of vital capacity, Hyatt et al (1958) and Fry et al (1960), repeatedly showed that increased extrathoracic resistance had minimal effect on this effort independent portion of the FV curve. Therefore, this characteristic portion of the MEFVC, termed the alpha segment, is relatively invariant within an individual and is therefore a potential indicator of pulmonary disease states.

Over the upper 30% of vital capacity, the relationship between maximal expiratory flow and degree of lung inflation is influenced by the generated transpulmonary pressure and therefore the shape of the FV curve is effort

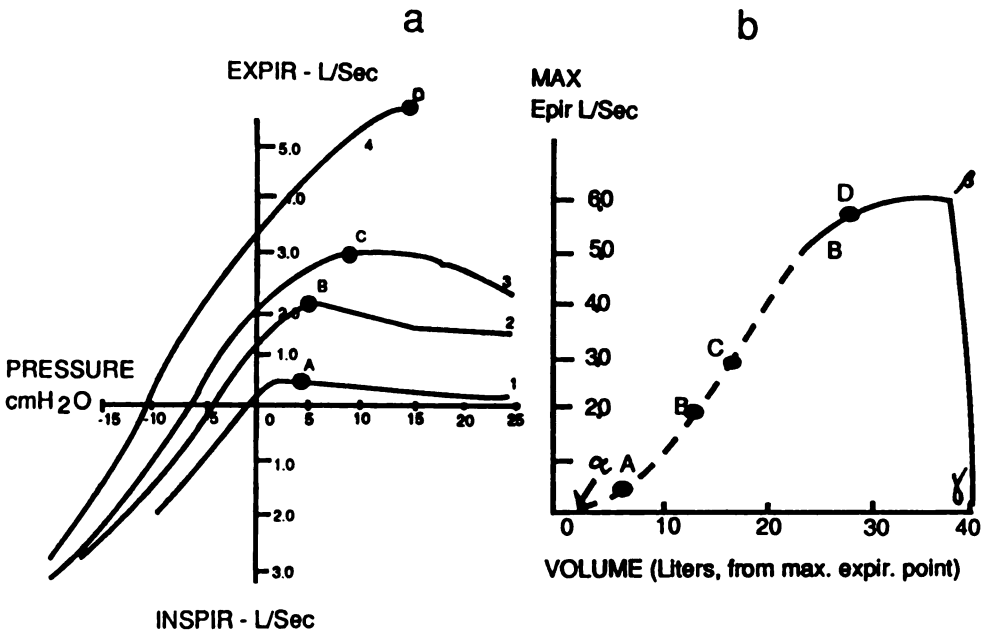

Figure 2. a, Relationship of transpulmonary pressure and flow for a normal subject at differing degrees of lung inflation (curves 1, 2, 3, and 4). b, A plot of maximum achievable flow against degree of lung inflation. Flow and volume co-ordinates of points A, B, C, and D from Figure 1a are plotted as closed circles on this curve. *α* corresponds to maximum expiration point and *γ* to maximum inspiration point (From Hyatt et al,1958).

dependent. As seen in Figure 2a, the PF curve high in the vital capacity (4) does not achieve expiratory flow maxima, presumably because the patient cannot generate sufficient transpulmonary pressure to cause dynamic compression of larger more rigid airways (Hyatt et al,1958). The effect of added extrathoracic airway resistance on the effort dependent portion of the FV curve has been shown to significantly decrease peak expiratory flow and the volume of air expired in the first second ($FEV_{1.0}$). Therefore, in contrast to the alpha segment of the MEFVC, this effort-dependent, beta-gamma segment is

related to the dimensions and physical properties of the entire airway in a complicated manner and therefore its' contour is not consistent.

In addition to reflecting the properties of the respiratory tract, the effort dependent nature of this part of the FV curve is influenced by variation in flow rates with effort within individuals. Therefore, in order to standardize the contour and indices describing the FV curve, peak expiratory flow and flow generated early in the upper half of the MEFVC at high lung volume requires a maximal expiratory effort to attain a reproducible beta-gamma FV curve (Fry and Hyatt,1960). In practice, the effort dependent segment acquired from a FVC maneuver has been shown to be remarkably repeatable and therefore clinically useful (Fry et al,1960; Hyatt and Black,1973).

Effect of lung disease on MEFVC shape

In man certain pulmonary diseases produce characteristic MEFVC shapes. The interpretation of the contour of the MEFVC generated, in conjunction with evaluation of indices quantifying the MEFVC such as the ($FEV_{1.0}$), peak expiratory flow (PEF) and expiratory flow at 50% of lung volume (EF_{50}), have become the backbone of clinically used screening programs for a plethora of pulmonary conditions (asthma, emphysema, cystic fibrosis etc.) as well as providing prognostic measurement of airway function (Hyatt and Black,1973).

Effect of airway obstruction on MIFVC

In contrast to expiratory PF curves, inspiratory PF curves at all lung volumes increase monotonically with decreasing transpulmonary pressure (Hyatt et al,1958). Thus, flow throughout the inspiratory FV curve is effort

dependent. The effort dependent portions of the FVL, the inspiratory curve and the upper one third of the MEFVC, are affected by alveolar pressure (elastic recoil and pleural pressure) and resistance of the respiratory tract. Therefore, maximal flow is directly proportional to the driving pressure and inversely proportional to the resistance (Miller and Hyatt,1969). As inspiratory flow is effort dependent at all lung volumes the muscle force dissipated to overcome added airway resistance, renders less force available to overcome normal airway resistance, and as a result maximal flow decreases (Miller and Hyatt,1969).

In 1968 Jordanoglou and Pride reported the clinical use of flow-volume loop analysis to detect an upper airway obstruction. This was the first report of the use of this non-invasive pulmonary function test in the detection of changes in upper airway resistance. Subsequent to this, Miller and Hyatt (1969) studied the pathophysiology of upper airway obstructions and described how these abnormalities could be reflected by spirometry and FVL. When pressure and flow rates are high, typically at high lung volumes, a given upper airway resistance should reduce flow more than at flow rates observed at lower lung volumes. At lower volumes a greater resistance should be required to permit detection of reduced flow. These properties were demonstrated by evaluating normal patients breathing through different sized orifices and in clinical patients with upper airway lesions. Indices describing the FVL generated in these patients, afforded detection of upper airway obstructions (UAO) at high flow rates. In addition, subsequent clinical studies have

documented that only severe upper airway obstruction can be detected if low flow rates are used (Abramson,1982; Amis and Kupershoek,1986).

From these initial studies Miller and Hyatt proposed a classification of upper airway obstructions (UAO) into two functional groups based on the pressure-flow relationships around the site of obstruction.

Fixed obstruction - The airway is unable to appreciably change cross-sectional area in response to transmural pressure differences during either inspiration or expiration. Qualitatively this lesion would be represented by equal reduction of both inspiratory and expiratory flow and hence appear as a flattening of inspiratory and expiratory curves of the FVL (Figure 3). Quantitative description of this loop shape includes reduced inspiratory and expiratory flow rates and near normal ratios of expiratory-to-inspiratory flow at mid-tidal volume. This characteristic pattern is seen in lesions such as "fixed high tracheal stenosis" in man.

Variable extra-thoracic obstruction - The airway responds to increased transmural pressure on inspiration. When intraluminal pressure is negative with respect to atmospheric pressure, cross-sectional area is reduced resulting in obstruction to airflow. During expiration, intraluminal pressures are positive with respect to extraluminal pressures which tends to dilate the airway and reduce the degree of the airway obstruction. The characteristic appearance of the FVL is a flattened inspiratory curve, representing a low, fairly constant flow and a near normal shaped expiratory curve (Figure 3). Quantitatively, FVL analysis of this type of lesion is typified by an increase in the ratio of peak

expiratory-to-inspiratory flow and ratio of flows at mid-tidal volume, as well as a reduction in inspiratory flow rates throughout inhalation. This characteristic FVL pattern is typically associated with patients with laryngeal paralysis and laryngeal space occupying lesions (Miller and Hyatt,1973; Kashima,1984).

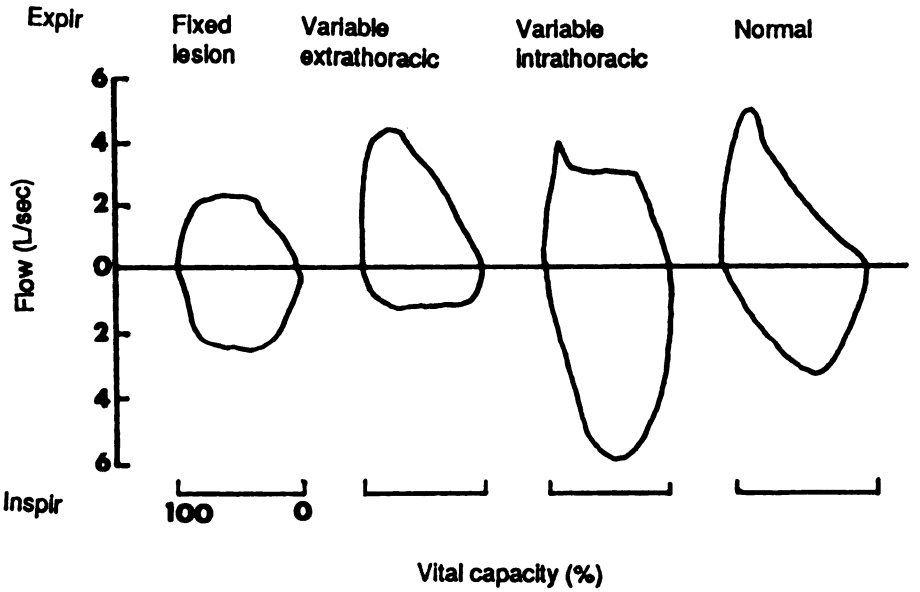

Figure 3. Representative flow-volume loop shape, showing the effect of fixed, variable extrathoracic, and intrathoracic airway obstructions, (Hyatt and Black,1973).

In addition to the 2 defined UAO types, a characteristic FVL pattern expected to occur with **variable intra-thoracic obstruction** was proposed. The expiratory FV curve tends to have a fixed flow over a large portion of the vital capacity, with the mid-tidal flow being extremely low. The constant expiratory flow suggests a lesion such as intra-thoracic tracheal tumor which develops an orifice like configuration shortly after onset of expiration.

Quantitative FVL analysis

Since this initial report, FVL analysis has been used extensively in the clinical diagnosis and evaluation of upper airway obstructions (Miller and Hyatt,1973; Kashima,1984; Polverino et al,1990). Peak, mid-tidal-volume flows and their ratios were initially proposal by Miller and Hyatt (1969) as useful indicators of airway resistance. Subsequently, several other FVL indices and their "normal" values have been suggested as being beneficial in the diagnosis of UAO. Evaluation of FVL from healthy patients and from those with confirmed fixed UAO, has shown that reduction in flow occurs mainly at high lung volumes, while the $FEV_{1.0}$ could be almost normal. The $FEV_{1.0}$ is relatively unaffected by upper airway obstruction as the volume exhaled in 1 second incorporates a whole range of lung volumes many of which are on the effort-independent part of the FVL. It was therefore suggested that an increased in $FEV_{1.0}$/PEF would be a useful indicator of UAO (Empey,1972). Topham (1974) also recommended use of this index, particularly in preference to PEF/PIF. He considered $FEV_{1.0}$/PEF advantageous, because of the difficulty experienced by many patients when performing the forced inspiratory maneuver, resulting in inadequate inspiratory efforts.

Evaluation of the extrathoracic respiratory tract in conjunction with the lower airway, provides a simple and rapid assessment of respiratory function (Carilli et al,1974; Bass,1973). FVL indices permit differentiation of patients with UAO from patients with chronic obstructive pulmonary disease. Rotman et al (1975) suggested that when $FEV_{1.0}/PEF > 10$ and/or $EF_{50}/IF_{50} > 1.0$, then

the possibility of UAO should be further investigated. Numerous other investigators have published "normal" values, obtained from a relatively small number of subjects, for various FVL indices useful in diagnosing UAO (Shim,1972; Bass,1976; Hoffstein,1986). The mid-tidal expiratory-to-inspiratory flow ratio is considered a sensitive indicator of UAO by many investigators (Miller et al,1973; Rotman et al,1975; Shim et al,1972; Kashima,1984). Unfortunately, reported normal values vary from as high as 1.5 (Shim,1972; Haponic et al,1987) to as low as 0.8 (Vincken et al,1987). Recently, values were reported for FVL indices obtained from a study of a large number of healthy subjects. By documenting mean values and the distribution of various FVL indices from a large population, these values may represent a more accurate account of the degree of variation that exists (Polverino et al,1990). In that study, the normal EF_{50}/IF_{50} was reported as 1.3+/- 0.288, and interestingly, when "normal" values for various indices were compared to values obtained from 17 patients with UAO, IF_{50} was found to be the most consistent indicator of UAO.

Tidal breathing flow-volume loops

The FVC maneuver (recorded as a FVL) as described in man obviously necessitates patient cooperation for a maximal (voluntary) effort. Children younger than 6 years of age are usually unable to perform a full FVC maneuver (Wall et al,1984). Evaluation of pulmonary function in such patients has been performed using partial expiratory flow-volume curves (PEFVC), generated as a result of an expiratory effort which is greater than obtained during quiet

breathing at rest ,though not originating at total lung capacity (Taussig,1977). When used in conjunction with measurement of functional residual capacity, to standardize lung volume, the technique has been reported as a useful clinical tool in the assessment of lung function in infants and neonates (Buist,1980; Wall et al,1984). Although PEFVC are considered useful in the detection of more severe lower airway obstructive diseases such as cystic fibrosis, mild airway dysfunction may not be accurately detected because of variable flow rates within healthy children (Wall et al,1984). In addition to evaluation of lower airway function, the shape and indices of flow-volume loops generated from less than maximal respiratory effort have been reported as a useful indicator of upper airway obstructions in young children (Smith and Cooper,1981).

Use of PEFVC and flow-volume loops in infants involves some degree of voluntary respiratory effort, and for that reason it is not a test that can be executed in human neonates and animals because of lack of subject compliance. For this reason, the technique would seem limited as a diagnostic tool in veterinary medicine. Despite this fact, flow-volume loops may be recorded from such non cooperative subjects during quiet breathing at rest with resultant graphs representing **tidal breathing flow-volume loops (TBFVL)**. Tidal breathing flow-volume loops have been used to evaluate sleeping neonates suffering from laryngotracheal disease (Abramson et al,1982). The TBFVL obtained were useful in detecting upper airway obstruction based on characteristic shapes, though no correlation between TBFVL indices and clinical

degree of airway obstruction was demonstrable. This study suggested that the low airflow rates associated with tidal breathing limit the diagnostic sensitivity of the TBFVL. At low flow rates, relatively severe airway obstruction is necessary to detect flow changes, and the associated low transmural pressures may be insufficient to cause dynamic collapse of variable extrathoracic lesions. The significance of the severity and nature of the airway obstruction in permitting quantitative detection by TBFVL is seen in patients suffering from sleep apnea, where this severe airway obstruction is associated with characteristic TBFVL shape and indice changes (Haponik et al,1981; Tammelin et al,1983). Although TBFVL analysis has some benefit in aiding detection of airway obstruction in non cooperative patients, the ability of these subjects to voluntarily increase driving pressure, and thereby increase airflow, may obscure flow limitation. For these reasons, the lack of standardization of TBFVL makes strict numerical interpretation difficult (Abramson et al,1982).

In 1986, Amis and Kurpershoek first introduced the TBFVL analysis technique to clinical veterinary practice. In this initial report TBFVL from normal dogs (33) were categorized into 4 predominant TBFVL shapes. In the predominant TBFVL shape (20 dogs), PEF occurred early in expiration , and PIF occurred late in inspiration. In their evaluation of dogs with fixed upper airway obstructions and chronic bronchitis, the TBFVL shapes generated by these conscious dogs were useful in their assessment of airway obstruction. Significant differences in TBFVL indices from dogs with airway obstruction, compared to indices obtained in normal dogs were scarce and significant

changes tended to be associated with the most severe clinical airway obstructions. Repeatable quantitative assessment of airway function using TBFVL analysis was limited by body size, amount of respiratory effort, variation in breathing pattern and respiratory rate. This variability of TBFVL observed in normal subjects was documented by the high coefficients of variation for TBFVL indices (up to 46%).

In a subsequent study, evaluating upper airway function in dogs with bilateral laryngeal paralysis, 2 TBFVL shape types were reported in the 27 of 30 TBFVL evaluations considered abnormal (Amis et al,1986). All dogs in this study had stridor or respiratory distress, suggesting moderate to severe airway obstruction. Although inspiratory airflows were reportedly reduced in many of the dogs, TBFVL indices consistent with a variable extrathoracic lesion (decreased inspiratory flows and increased in expiratory-to-inspiratory flow ratios) were not significantly different from their normal values. This lack of significance would suggest either large variability and/or insensitivity in detecting less severe airway obstruction.

Despite the limitations in strict quantitative assessment of airway function using TBFVL, the technique has been reported as being useful in evaluating surgical treatment of various upper airway obstructions in dogs (Smith et al,1986; 1990). In a recent study, TBFVL were used to evaluate airway function in healthy cats, and cats with bronchial disease. Using the technique, investigators were able to detect lower airway obstruction (McKiernan et al,1993). In this study, as with that reported by Amis et al

(1986) significant changes in TBFVL indices were associated with moderate to severe lower airway obstructions. In the past, clinical application of TBFVL analysis involved laborious, time consuming measurement of TBFVL indices from either photographs, storage oscilloscopes or x-y plotter graphs. Recently, TBFVL analysis has become more clinically feasible with the availability of computer assisted flow-volume analysis programs[1]. This program has been used to evaluate TBFVL from normal dogs with similar results to those previously reported (Amis and Kurpershoek,1986), but was much easier and rapid to use (McKiernan et al,1987).

Stimulation of respiratory effort in noncooperative subjects

Although TBFVL are considered of value in non cooperative patients, methods of improving diagnostic sensitivity by stimulating increased airflow rates and lung volumes have been investigated. Motoyama (1977) produced MEFVC in children by applying negative pressure to the airway via an endotracheal tube, though obviously this technique has clinical limitations, as subjects need to be either deeply sedated or anesthetized. Other investigators have measured MEFVC in infants by application of positive pressure to the external chest wall by use of a chest chamber (Adler and Wohl,1978). In further attempts to obtain maximal flow curves in newborns and infants, vital capacity of the crying infant has been measured (Wise et al,1980). In crying infants, it is difficult to distinguish voluntary vocal cord apposition from airway obstruction.

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[1]Respiratory Loop Analysis Software, BUXCO Electronics, Inc., Sharon, CT

In veterinary medicine the use of respiratory stimulants such as increased concentrations of inspired carbon dioxide in cats (McKiernan et al,1989) and horses (Tesarowaski et al,1989) have been investigated. Whiting (1988), used 10% CO_2 inspired air to stimulate tidal volumes which approached predicted vital capacities in horses (Davidson et al,1986), however, maximum flows predicted for adult horses of 65-90 L/sec were not approached. In Whitings' study, although patient acceptance of the technique was good, coefficients of variation of FVL indices were approximately twice those reported in human PEFV studies (Barnes et al,1981), suggesting poor repeatability. Although, TBFVL indices were significantly increased in all of these studies, their usefulness and suitability as a routine diagnostic procedure in clinical veterinary practice remains to be determined.

The effect of exercise-associated ventilatory mechanics and increased airflow on the TBFVL has been evaluated in normal humans during exhausting exercise (Olafsson and Hyatt,1969; Babb et al,1991). The TBFVL, from healthy non-athletic people, obtained during strenuous exercise impinges on their FVL only near end expiration. In contrast, patients with obstructive lung disease breathe along or outside their MEFVC during exercise (Grimby and Stiksa,1970). In well trained athletic young men, TBFVL obtained during sub-maximal exercise generally do not approach their FVL (Grimby et al,1971). In contrast, during maximal exercise in the same subjects airflows are near-maximal, and flow approaches much of their MEFVC, and tidal volumes are approximately 50% of vital capacity.

In exercising horses, airflow rate is greatly increased whereas variability in breathing strategy is reduced (Hörnicke et al,1983; 1987). In 1988, Art et al, evaluated the sub-maximal exercise-induced changes in breathing pattern in ponies by analyzing TBFVL. This study reported that TBFVL were variable between ponies though relatively constant within individuals. The TBFVL indices which significantly changed in response to exercise were poorly correlated with pulmonary resistance. Based on these findings the authors questioned the diagnostic usefulness of exercise associated TBFVL in pulmonary function testing. However, the relatively low airflow rates reported (23.56 +/- 1.26 L/s) in Art's study during submaximal exercise, are likely to limit the sensitivity of the test in assessing airway function under those exercise conditions.

The sensitivity of TBFVL in detecting airway obstruction may improve as airflow rates approach maximum (Abramson et al,1982), and the usefulness of TBFVL in detecting airway obstruction in non-cooperative patients, like horses, may be enhanced during more strenuous treadmill exercise. Furthermore, it is possible, that if a ventilatory response to exercise in performance horses is similar to that reported in well trained young men, then TBFVL obtained during maximal exercise may approach their FVL. The increased sensitivity of TBFVL obtained during exercise may therefore allow detection of less than severe upper airway obstruction.

III. EQUINE LEFT LARYNGEAL HEMIPLEGIA - A REVIEW

A. Anatomy and Physiology of the Larynx

The equine larynx consists of a framework of cartilages and associated tissues which provide a conduit for the flow of air from the pharynx to the trachea. The larynx contains 3 paired cartilages (cuneiform, corniculate and arytenoid) and 3 unpaired cartilages (cricoid, thyroid and epiglottis).

The pyramidally shaped arytenoid cartilages are located rostral to the cricoid cartilage and medial to the laminar portion of the thyroid cartilage. Each arytenoid cartilage consists of a caudo-dorsal base and a rostrally located apex. Caudally, each arytenoid cartilage has a synovial articulation with the cricoid cartilage, and rostrally the apex fuses with the corniculate cartilage. Lateral and rostral to the base is a large muscular process, while the vocal process is situated ventrally (Getty,1975). The arytenoid cartilages, and the epiglottis, have the greatest range of motion of the laryngeal cartilages. The cuneiform cartilages represent two caudal extensions from the epiglottis which are situated just rostral to the thyroid cartilage.

Broad fibro-elastic ligaments exist between the cricoid cartilage and the first tracheal ring, and between the cricoid and the thyroid cartilage. The transverse arytenoid ligament is a narrow band that connects the dorsomedial angles of the opposing arytenoid cartilages. The vestibular ligament extends from the cuneiform cartilages and lateral aspect of the epiglottis, to the ventral aspect of the arytenoid cartilages. The vocalis ligament spans the distance between the vocal process of the arytenoid cartilage to the caudal border of the

body of the thyroid cartilage. The mucous membrane lining the vocalis ligament and muscle (vocal folds), and medial surface of the arytenoid cartilage, outlines the narrowest cross sectional area of the laryngeal airway; the rima glottidis. The lateral ventricles constitute an infolding of mucous membrane between the vocal fold and the vestibular fold (covering the vestibularis muscle and ligament). The aryepiglottic folds consist of mucous membrane gathered into discrete folds extending from the caudo-lateral aspect of the epiglottis to the corniculate and arytenoid cartilages. The folds are continuous on either side of the epiglottis ventral to the epiglottis and are contiguous with the glossoepiglottic fold rostrally.

The extrinsic muscles of the larynx; the thyrohyoideus, hyoepiglottis, sternothyroideus and omohyoideus muscles, move the whole larynx as a unit. The hypoglossal nerve (cranial nerve XII) is the efferent nerve to the thyrohyoideus and hyoepiglottis muscles, whereas the ventral branches of the first and second cervical nerve innervate the sternothyrohyoideus and omohyoideus.

The intrinsic laryngeal muscles, which originate from the muscular process (except the vocalis, cricothyroideus and tensor ventriculi lateralis mm.), move individual cartilages in relation to each other. The cricothyroideus muscle tenses the vocal ligaments by moving the thyroid cartilage caudally, causing adduction of the vocal folds and increased dorsoventral diameter of the rima glottidis. Adduction of the vocal process of the arytenoid cartilage and vocal fold results from contraction of thyroarytenoideus (vocalis and vestibularis

components), arytenoideus transversus and cricoartenoideus lateralis muscles. The cricoarytenoideus dorsalis (CAD) muscles cause abduction and dorsal displacement of the arytenoid cartilage and vocal fold. The tensor ventriculi lateralis also causes abduction of the vocal fold.

The innervation of the intrinsic muscles, except for the cricothyroideus muscle, is via the recurrent laryngeal nerves (RLN). Unlike the dog and man, there is no passage of motor nerve fibers from one side of the larynx to the other (Quinlan et al,1982). The cell bodies of the RLN are located in the nucleus ambiguus of the medulla oblongata. Nerve fibers of the RLN travel within the vagus nerve then branch from the right vagus nerve at the level of the first or second rib, and from the left vagus nerve at the aortic arch. After passing over the ligamentum arteriosum, the left RLN then ascends to the larynx along the ventral surface of the common carotid artery within the carotid sheath, as does the right RLN. Only the cricothyroideus muscle is innervated by the cranial laryngeal nerve, which also is sensory to the mucous membrane of the larynx.

In addition to providing a patent airway for respiration, the complex structure of the larynx is involved in swallowing, phonation, coughing, explosive efforts (straining) and airway protection from aspiration (Bartlett,1989). Laryngeal movements are coordinated in the central nervous system during respiration. Laryngeal response to respiratory demands is regulated through afferent nervous input and numerous reflexes involving the entire respiratory tract. Central stimulus of the RLN, supplying intrinsic

laryngeal muscles, results in abduction of the arytenoid cartilage and vocal fold during inspiration and relative adduction during expiration. Abduction of the vocal fold occurs prior to contraction of the diaphragm, thereby ensuring minimal resistance to airflow at the larynx during inspiration. In addition to the CAD muscle, contraction of the cricothyroideus muscle may also aid abduction (Suzuki and Kirchner,1969). Decreased motor tone is observed in the RLN during expiration and therefore, the decreased CAD muscle activity is thought responsible for the relative adduction of the vocal folds. This adduction of the vocal folds may play a role in the control of respiratory frequency, by slowing expiratory airflow (England et al,1982).

The controlled movement of the vocal folds by the respiratory center may be influenced by reflexes arising from receptors sensitive to changes in pH of cerebrospinal fluid, stretch receptors in the lung and chemoreceptors in the carotid sinus. Physiological states, such as hypercapnia which may cause prolonged vocal fold abduction, alter laryngeal function (Bartlett,1989). Increased RLN activity associated with abduction of vocal folds and arytenoid cartilage in response to increased resistance to airflow has also been reported (Glogowska et al,1974).

Receptors in the airway epithelium, including the laryngeal epithelium may alter the cross sectional area of the rima glottidis. Stimulation of irritant receptors in the laryngeal mucosa causes adduction of the vocal folds and therefore increased laryngeal resistance to airflow (Stransky et al,1973). Laryngeal stretch receptors have also been described (Bartlett,1989). The

reflex activity of the larynx is also associated with changes in respiratory pattern and depth of breathing. Thus, afferent laryngeal nerves are involved with the control of ventilation (Bartlett,1989).

B. Incidence of LLH

As a cause of wastage in athletic horses, respiratory disorders are second only to lameness (Rossdale et al,1985). Although the exact prevalence of upper airway obstructions, as performance limiting diseases, is difficult to determine due to their varied clinical manifestations, LLH has been reported as the next most common disease of the respiratory system after respiratory infections (Cook,1970). The disease, LLH, has been considered to range from a subclinical hemiparesis to hemiplegia associated with overt clinical signs. Therefore, the reported incidence of LLH will depend on the manifestation of the disease and the diagnostic criteria used. A subclinical form of LLH has been reported to occur in as many as 77% of clinically normal horses greater than 14.2 hands, and recently a 95% incidence was reported from evaluation of a large number of Thoroughbreds, based on palpation of the atrophied CAD muscles (Duncan et al,1974: Cook,1988).

Based on endoscopic evaluation in the resting horse, the prevalence of the clinical form of laryngeal hemiplegia has been reported to range from 1.3% to 8% (Pascoe et al,1981; Raphel,1982; Baker,1983:II; Hillidge,1985; Sweeney et al,1991). Breeds recognized as being commonly affected with LLH are the Thoroughbred, Standardbred, Quarterhorse and draught type horses,

though the observed breed distribution may be skewed by the athletic use of such breeds. The incidence of LLH in draught horses has been reported from 9.0% and 22% (Goulden et al,1985; Archer et al,1989).

Many of the reported surveys were conducted on Thoroughbreds in race training, except for Hillidge's study who reported an 8% incidence. Therefore, the incidence of LLH reported by others (1.3-4.7%), may be artificially low, as horses are likely to be culled at the earliest signs of a performance limiting disease. In a study of horses presented for poor performance, endoscopic examination of the larynx during high speed treadmill exercise, identified LLH in 36% of horses that had an upper airway abnormality detected (Morris and Seeherman,1991).

In a number of surveys, entire and castrated males are found to be more commonly effected by LLH than females (Cook,1970; Goulden and Anderson, 1981:I). Goulden and Anderson (1981:I), reported 6 times as many Thoroughbred males to be suffering from LLH than females. In addition, all horses diagnosed with LLH were shown to be significantly ($P<0.05$) heavier and taller at the withers than unaffected animals. Although foals and geriatric horses have been observed with LLH (Hillidge,1985), the condition is more commonly diagnosed in Thoroughbred horses between 1 and 5 years of age, and in draught horses at 8 years (Archer et al,1989). In contrast to the findings cited above, using percutaneous palpation of laryngeal musculature as the criteria for a diagnosis of LLH, a poor correlation was found between LLH and large horses and males (Cook,1988). These findings, although

controversial, primarily serve to emphasize the lack of agreement between investigators, regarding the disease syndrome being described and the method of diagnosis.

C. Pathogenesis

Nerves

The major neural lesion in LLH is suggestive of a progressive axonal degeneration in the face of attempted repair. The disease selectively effects large myelinated nerve fibers in the distal regions of the left, and to a lesser extent the right recurrent laryngeal nerves (Duncan et al,1974; Cahill and Goulden,1986:I,II). There is loss of large diameter myelinated fibers distally, in conjunction with regeneration of axonal clusters, thinly myelinated axons and "onion bulbs", particularly in the middle and proximal portions of the nerve. These characteristic neural changes, referred to as a distal axonopathy, were originally described by Cole (1946), though it wasn't until later, after Duncan et al,(1974) confirmed these findings that this terminology became recognized.

Muscles

The intrinsic laryngeal muscle lesions, in clinical and sub-clinical LLH, are typical of chronic neurogenic atrophy (Cole,1946; Duncan et al,1974). Fiber type grouping, evidence of denervation and reinnervation by separate nerve fibers, has been reported in all muscles supplied by the RLN (Cahill and Goulden, 1986:III). Fiber type grouping occurs when denervated muscle fibers in the vicinity of a surviving nerve fiber are reinnervated by collateral sprouts

from this fiber, and thus assume the same metabolic type, as determined by the innervating nerve fiber. Other changes consistent with neurogenic atrophy include the presence of atrophic and hypertrophic muscle fibers (Duncan et al,1974), variation in muscle fibre size, and degenerate muscle fascicles being replaced by connective tissue (Cole,1946).

Of the intrinsic laryngeal muscles, the earliest and most pronounced atrophy occurs in the cricoarytenoideus lateralis (CAL), the main adductor (Duncan and Griffiths 1973; Duncan et al,1974; Cahill and Goulden,1986:III). The preferential denervation of the adductor muscles, CAL and transverse arytenoid muscles, has recently been quantified (Duncan et al,1991:I). Presently, the reason for the observed preferential adductor muscle denervation is unknown. Previously, it has been suggested that the adductor muscles may be innervated by a greater percentage of large diameter nerve fibers, which are more severely affected in LLH (Duncan and Griffiths,1973). Recent morphometric studies of the adductor and abductor branch of the RLN, showed no significant difference between the population of large diameter fibers in these nerves (Duncan et al,1991:II). It has also been proposed that preferential adductor muscle denervation is due to the fibers innervating the CAL muscles being more distal than that of the CAD muscle.

Neurogenic atrophy, although less severe, is also commonly observed in the right intrinsic laryngeal muscles (Cole,1946), as well as the extensor digitorum longus muscle (Cahill and Goulden 1986:III) in horses with LLH, supporting the view that the disease is a generalized peripheral neuropathy.

Although mild degenerative changes in the more distal parts of longer limb nerves have been reported, their clinical importance is questionable, as they may represent age related changes rather than that of a generalized disease state (Wheeler and Plummer,1989). Therefore, whether the pathology associated with LLH is a generalized process or not is unclear.

Despite the characteristic neuromuscular findings in clinical cases of LLH, it is now well established that many horses may have histologically apparent neuromuscular changes in the absence of clinical LLH. In one study, where laryngeal asynchrony and trembling, but not paralysis was observed endoscopically in 6 horses, neuromuscular changes were found, similar to those reported in clinical cases of LLH (Duncan et al,1977). This study suggested these endoscopic findings represent the early signs of a progressive lesion which may develop into left sided laryngeal hemiplegia. This subclinical or early stage of LLH has been termed "recurrent laryngeal neuropathy", as opposed to laryngeal hemiplegia, which is considered by Cook to more accurately describe a total inability to abduct the arytenoid cartilage (Cook,1988). In contrast to the conclusions drawn from Duncan et al's(1977) study, results from a large number of endoscopic examinations in horses over a 5 year period suggested that the observed variations in symmetry and synchrony were a normal finding (Baker,1983:I). Baker (1983:I) reported that none of the 168 horses exhibiting asynchronous laryngeal activity, progressed to clinical disease, and questioned whether these endoscopic findings were a prelude to the clinical state of LLH.

Cartilages

Little attention has been paid to the effect of LLH on the cartilages of the larynx. In a study were the RLN was sectioned in 30 horses, bony ankylosis of the crico-arytenoid joint was reported to develop in 10 horses within 1 year (Denecke in Elies et al,1983). These changes may be of significance when considering the prognosis following prosthetic laryngoplasty in long standing cases of LLH.

ETIOLOGY

The etiology of the neuromuscular pathological findings in LLH is most commonly idiopathic, hence the common use of the term "idiopathic laryngeal hemiplegia" in place of LLH. The involvement of both right and left RLN make focal injury or compression unlikely as major factors. If LLH is part of a generalized neuropathy, possibly involvement of the left RLN may be exacerbated by, as yet undefined, "local factors" (Griffiths,1991).

Injury

In a small number of cases, isolated incidents of known injury have been reported to result in laryngeal hemiplegia, including cervical lacerations and blunt trauma (Gilbert,1972 and Goulden and Anderson, 1981:II). Known causes of recurrent laryngeal nerve injury also include, injection of perivascular irritants and a retropharyngeal abscess caused by Staph. aureus (Barber,1981).

Mechanical causes of left RLN injury have been proposed based on the unique anatomy of the RLNs. A flattening of the left RLN, reported in some horses, as it passes around the aorta was thought associated with the site of

nerve damage (Argyle in Mason,1973). The lack of pathology at this site and the similar flattening of the right RLN observed by Cahill and Goulden (1986:I), do not support this theory.

In 1970, Rooney suggested the anatomical path of the left RLN, compared to the right RLN results in greater tensile forces experienced by the left RLN when the neck is stretched. In a recent report, head position during general anesthesia was postulated to result in bilateral laryngeal paralysis after general anesthesia (Abrahamson et al,1990). Despite the theory that this periodic stretching would result in ischemia and nerve damage, peripheral nerves can be stretched up to 8% of their length before there is vascular compromise (Lundborg,1988). Further evidence questioning Rooney's theory is that microscopic lesions in the left RLN of horses with LLH are not typical of ischemic nerve injury (Duncan and Hammang,1987).

Central nervous system lesions

Focal CNS lesions have been reported in horses with LLH. Significantly higher numbers of axonal spheroids (areas of degenerating and regenerating axons), have been described in the lateral cuneate nuclei of horses with LLH compared to horses unaffected by the disease. Despite the difference observed between these 2 groups, the increased frequency of axonal spheroids may be an age related process, and therefore their significance remains uncertain (Cahill and Goulden,1986:IV; Cahill and Goulden,1989).

Causes of peripheral neuropathy

Polyneuropathies with a distal distribution can have a variety of causes including inherited, toxic, nutritional deficiencies, and metabolic disorders. Despite the fact that in the majority of cases the etiology of LLH is unknown, isolated reports of laryngeal hemiplegia resulting from poisonings such as organophosphates (Rose et al,1981; Duncan and Brook, 1985), lead (Burrows,1982) and plant toxicities from Lathyrus, alfalfa, and false dandelion (Cahill and Goulden,1987; Huntington et al,1989) exist. Thiamine (vitamin B_1) deficiency was proposed as a possible cause of LLH, based on a similar association known to occur in people (Loew,1973). Despite the fact that low thiamine levels have been recorded in horses with LLH, the disease has not been induced by a thiamine deficient diet (Cymbaluk et al,1977). Other suggested causes have included various viral and bacterial respiratory tract infections (Goulden and Anderson,1981:II).

Genetics

The possibility of an inherited basis for LLH has substantial evidence. Clinical LLH (Cook,1988) and fiber type grouping (Gunn,1973) in laryngeal muscles of foals has been reported. Clearly, the demonstration of the disease in very young foals or even near-term fetuses (Gunn,1973), would be indicative of a congenital or hereditary association. Cook postulated that a single recessive gene was responsible for LLH (Cook,1981:II). To date, no recorded matings between horses with clinical LLH have produced 100% affected foals (Hillidge, 1985). The inheritance of phenotype was thought to be the only

genetic component to LLH since affected horses tended to be taller and heavier (Marks et al,1970:I).

In a recent report, 47 offspring of an affected stallion were compared with a similar number of controls. A significantly greater number (11) of the stallions offspring had LLH compared to the controls (Poncet et al,1989). In this study a dominant gene was hypothesized as explaining the high occurrence rate, rather than the high incidence having a congenital basis. The findings from such organized breeding studies should be viewed with caution, as the widespread nature of LLH, make selection of an adequate control population difficult.

D. Diagnosis

Clinical Signs

Decreased ability to abduct the arytenoid and corniculate cartilages during exercise causes inspiratory dyspnea, reduced tolerance for sustained high intensity exercise, and a characteristic stridor or "roaring" sound during exercise. Loss of adductor tone may result in a voice of lower than normal pitch. Typically these clinical signs gradually increase in severity over a period of weeks to months. A diagnosis of LLH requires consideration of the animals signalment (breed and height), history (previous performance, race times), careful physical examination and an endoscopic examination of the larynx (Baker,1983:II).

Physical Examination

A general physical examination is particularly important to identify other potential performance limiting conditions such as lameness and lower airway disease. The presence of fibrous scars in the skin from previous laryngeal surgery should be ascertained, either ventral to the larynx or immediately ventral to the linguofacial vein. Percutaneous laryngeal palpation may demonstrate evidence of CAD muscle atrophy, by a more prominent muscular process of the left arytenoid cartilage compared to the right. Although such atrophy is pathognomonic for LLH, experience is necessary for the examiner to be comfortable with such findings. An "arytenoid depression test" may also be performed. This test involves manual depression of the muscular process in a medial, rostral, and ventral direction which may reveal reduced abductor tone and inspiratory stridor in horses with LLH (Marks et al,1970:I).

Tests of adductor muscle function

Knowledge that adductor muscle dysfunction precedes abductor muscle dysfunction (Duncan et al,1974), potentially provides an avenue for tests that may allow early detection of LLH. In the "grunt test", the horse attempts to close its larynx in response to having its abdomen or thorax threatened. In affected horses this is associated with a "grunt" as air is able to escape through a partially occluded rima glottidis (Cook,1965). The "slap test", involves 3 or 4 sharp slaps on either side of the withers to evoke an adductory movement from the contralateral arytenoid (Greet et al,1980). A normal response requires that the reflex arc terminating in the recurrent laryngeal nerve

be intact. Although it may be useful to verify laryngeal hemiplegia, it does not allow differentiation of degrees of paresis, it becomes less responsive with repeated stimulation, and is absent in tense or frightened horses and in horses with cervical spinal cord lesions. Generally adductor function tests are considered less reliable than abductor function evaluation via endoscopic examination of the larynx.

Recently, objective evaluation of the integrity of the reflex arc associated with the slap test has been attempted by the use of measured latency times of the left and right reflex arcs (Cook and Thalhammer,1991). The validity of this measurement in detecting and grading recurrent laryngeal neuropathy remains unproven. Previously, electromyographic studies have been shown to detect CAD muscle paralysis (Moore et al,1988). However, this diagnostic technique has limited ability to discern grades of LLH and appears impractical because of its invasive nature, cost and operator skill required.

Endoscopy

Although history and laryngeal palpation are useful in attaining a diagnosis of LLH, definitive diagnosis and identification of other potential upper airway causes of stridor is accomplished by use of endoscopy (Cook,1965). Endoscopic evaluation of the larynx is presently regarded as the most accurate and specific diagnostic test for LLH. Careful endoscopic evaluation of laryngeal form and function facilitates differentiation of LLH from other upper airway conditions associated with exercise intolerance and respiratory noise during exercise. These include arytenoid chondropathy (Haynes et al,1980),

ossification of the arytenoid cartilages (Shapiro et al,1979), epiglottic entrapment (Boles et al,1978), dorsal displacement of the soft palate (Cook 1974) and subepiglottic cysts (Raker,1976). Further diagnostic assistance with differentiation between these upper airway obstructions may be obtained from pharyngeal radiography (Linford et al,1983; Orsini et al,1989).

The endoscopic appearance of the larynx may vary with the degree of abductor muscle atrophy and loss of function (Duncan et al,1977). With hemiplegia, there is obvious asymmetry of the rima glottidis, failure of the arytenoid and corniculate cartilage to abduct normally, a kinking of the aryepiglottic fold and dilation of the laryngeal ventricle on the left side (Cook,1965). Evaluation of abductor muscle function may be enhanced by stimulation of swallowing, nasal occlusion, exercise and systemic administration of doxapram hydrochloride (Marks et al,1970:I, Baker 1983:II, Lane,1987). The repeatability of some of these techniques has recently been evaluated, using measurement of rima glottidis cross sectional area and multiple independent observers. Nasal occlusion was considered the most simple and reliable method of inducing arytenoid abduction (Archer et al,1991). Although in the clinical setting, induction of swallowing is currently considered the "acid test" in post-sale examinations of laryngeal function.

The significance of tremor, asynchronous movement, and reduced abductor activity of the arytenoid cartilages as a cause of upper airway obstruction remains a controversial issue. The prevalence of asynchronous movement of the arytenoids has lead to it's incorporation into a grading scheme

for laryngoscopic examinations. Recently a grading scheme has been proposed for clinical use (Rakestraw et al,1991), based on endoscopic classifications previously reported (Goulden et al,1985).

Grade I. Synchronous full abduction and adduction of the left and right arytenoid cartilages

Grade II. Asynchronous movement of the left arytenoid cartilage during any phase of respiration. Full abduction of the left arytenoid cartilage (as compared to the right) inducible by nasal occlusion or swallowing.

Grade III. Asynchronous movement of the left arytenoid cartilage during any phase of respiration. Full abduction of the left arytenoid cartilage cannot be induced and maintained by nasal occlusion or swallowing.

Grade IV. Marked asymmetry of the larynx at rest and no substantial movement of the left arytenoid cartilage during any phase of respiration.

Several commonly used practices may influence the appearance of the larynx. These include sedation, use of a twitch and endoscopy through the right or left nostril. In 1975, Robinson and Sorenson reported altered upper airway function following xylazine administration in the resting horse, and recommended that upper airway endoscopy should be performed in the unsedated horse. Despite their findings, Cook (1988) has recommended the use of tranquilizers to facilitate examination of the larynx. Recently, some of

the potential factors influencing laryngoscopic appearance were evaluated by multiple experienced observers, using the above cited laryngeal function grades, in conjunction with measurement of the cross sectional area of the rima glottidis. Sedation with xylazine, use of the alternate nostril and day of examination had a statistically significant influence on the laryngeal score and rima glottidis measurement (Archer et al,1991; Ducharme et al,1991; Hackett et al,1991). These studies suggest that the most reliable evaluation of laryngeal function at rest is obtained in the twitched, unsedated horse, viewing the larynx via the left nasal passage and stimulating arytenoid cartilage abduction by nasal occlusion.

Endoscopy During Exercise

In some horses the larynx may appear normal at rest but during and immediately after exercise, signs of LLH may be present. Strenuous exercise, sufficient to reveal exercise intolerance and respiratory noise as described by the owner, immediately followed by endoscopic examination may demonstrate incomplete arytenoid abduction (Lane,1987). This technique may be useful in detecting LLH in horses which may not have typical signs of LLH at rest (recurrent laryngeal neuropathy). Despite this, examination in the resting horses immediately after exercise is of limited value in detecting the dynamic nature of LLH, as respiratory airflow rates rapidly return toward normal resting values. The sensitivity of laryngoscopy has recently been enhanced through videoendoscopic examination of larynx during high speed treadmill exercise (Derksen,1988; Morris and Seeherman,1988).

During exercise, high airflow rates and negative upper airway pressures compared to atmosphere, may result in axial displacement or "dynamic collapse" of the left corniculate cartilage across the airway in horses with LLH (Robinson and Sorenson,1978; Derksen,1988). Recently, the graded endoscopic appearance of horses larynges at rest where compared to videoendoscopic evaluation during strenuous treadmill exercise (Rakestraw et al,1991). All grade I and II horses were able to fully abduct the left arytenoid cartilage during exercise, and all grade IV horses showed evidence of airway closure, "dynamic collapse", during inspiration. However, in horses with grade III resting laryngeal function, videoendoscopic findings during exercise could not be predicted. This suggests that endoscopic evaluation of resting horses with grade III LLH is an unreliable method for assessing laryngeal function during exercise.

The controversy surrounding the interpretation and clinical significance of endoscopic findings at rest, and to a lesser extent during exercise, is confounded by the fact that evaluation is based entirely on subjective impressions. In the last few years there has been an increasing effort to adapt quantitative measurements of upper airway function, used at an experimental level, to enable their use in a clinical setting. Such objective evaluations of the upper airway include measurements of upper airway impedance (Derksen et al,1986) and measurement of rima glottidis cross sectional area (Martin et al,1983).

Recently, tracheal pressure measurements from exercising horses with LLH have been used as an indicator of upper airway function in the diagnosis and surgical treatment in a clinical setting (Williams et al,1990:I). Similarly, quantitative evaluation of the rima glottidis has been determined in a limited number of clinical cases, and may have potential as a indicator of airway obstruction during exercise (Rakeshaw et al,1991). Upper airway impedance measurements document airway function more thoroughly than these techniques, as discussed in Chapter I. Although it has been used clinically on a single horse (Stick and Derksen,1989), the technique has clinical limitations, which were discussed in the Chapter II (E).

In chapter V, I will show for the first time that TBFVL analysis in exercising horses may prove to be a clinically useful, sensitive, and quantitative test of upper airway function. In the present chapter, I reviewed the incidence, pathogenesis, etiology and diagnosis of LLH. In the next chapter I will review the surgical treatments of this condition.

IV. TREATMENT OF LEFT LARYNGEAL HEMIPLEGIA - A REVIEW

As early as 1664 horsemen reported horses making an abnormal "roaring" sound during exercise, which was associated with a diminished tolerance for work (in MacQueen,1896). The relationship between "roaring" and left laryngeal paralysis was reported by Dupuy in 1807 and subsequently confirmed in 1815 after he induced "roaring" by transecting the recurrent laryngeal nerve (in MacQueen,1896).

Soon after the recognition of the association between the degeneration of the abductor muscle of the larynx and the commonly observed clinical signs of LLH, the search for a treatment was undertaken. Fleming stated that "roaring" and reduced exercise tolerance resulted from the ventricle filling with air and billowing into the airway and upon severe exercise the arytenoid cartilage also contributing to airway narrowing (Fleming,1882). The basic principle of all the techniques attempted for treatment of LLH is to relieve the airway obstruction, by either by-passing the larynx or removal or stabilization of the lateral ventricle, vocal fold, and corniculate and arytenoid cartilages.

For horses that are only required to perform minimal exercise or race for short distances, surgical intervention with its associated cost, potential complications and predicted success rate, may be unnecessary. However, effective surgical intervention is necessary for horses to exercise maximally.

A. Ventriculectomy

Ventriculectomy or sacculectomy involves the removal of the mucosal lining of the lateral ventricle. A form of ventriculectomy was first described by Gunther Junior in 1866 (in Williams,1911). The goal of this procedure is to induce a fibrous scar between the vocal fold, thyroid and arytenoid cartilages and thereby abduct and stabilize the vocal fold and arytenoid cartilage. The modern version of ventriculectomy was initially used by Williams in North America in 1906 (Williams,1911), and subsequently popularized by Hobday in Great Britain. As the lateral ventricle is considered the primary site of respiratory noise during exercise in horses with LLH (Attenburrow et al,1983), it has considerable value in reducing and modifying exercise related stridor. Although the procedure can be performed in the standing horse, it is usually performed with the horse in dorsal recumbency (Haynes,1984). The lateral ventricle is exposed through a laryngotomy created by a midline incision through the skin and subcutaneous tissues. Subsequently, the paired sternothyrohyoideus muscles are separated, and the entire length of the cricothyroid ligament is incised. Eversion of the ventricle may be accomplished using either a toothed burr or traction with forceps. After excision of the everted membrane the edges of the ventricle may be sutured (Pouret,1966) and the vocal cord removed (Baker,1983:II), though no extra benefit is considered to be gained from these additional procedures (Haynes,1984). Recently ablation of the lateral ventricle by use of transendoscopic laser produced satisfactory results, although thermal damage to structures adjacent the treated

ventricle were reported (Shires et al,1990). The advantages of the laser technique are that it obviates the need for general anesthesia and laryngotomy.

The laryngotomy wound is usually left to heal by secondary intention. Primary closure is possible, and it may be associated with more rapid healing, and decreased discharge from the wound. If primary closure is attempted, a meticulous airtight seal of the cricothyroid membrane and thorough wound lavage is paramount in preventing the development of subcutaneous edema and wound abscessation. Complications following ventriculectomy are rare, though may include, inflammatory polyps, laryngeal edema, chondritis and wound infections. Post-operatively, horses are stall rested and observed closely for 48 hours for signs of respiratory distress associated with laryngeal edema. Healing is generally complete within 21-30 days and training generally should resume after 45 days of rest.

Early reports of the use of ventriculectomy for treatment of LLH, document restoration of athletic endeavors and reduction in respiratory noise in 85-95% and 20-71% of horses, respectively (Williams,1911; Hobday,1935). Subjective evaluations of the ability of ventriculectomy to successfully reduce stridor during exercise, and/or improve tolerance to exercise range from 28% to 99% (Baker,1983:II; Pouret,1966). This large range reported reflects variation between authors as to the criteria determining success or failure. Recently, a successful outcome, defined as a reduction in inspiratory noise and improved exercise tolerance, was reported in 82% of draft horses with LLH treated by ventriculectomy (Bohannon et al,1990). From this study it may be

concluded, that ventriculectomy may be sufficient to allow sustained low level exercise.

To date only 1 study has objectively evaluated the efficacy of ventriculectomy. Shappell et al (1988) evaluated the effect of ventriculectomy in horses with surgical-induced LLH using measurements of airflow and airway pressure to evaluate airflow mechanics. This study found that unilateral ventriculectomy did not reduce resistance to airflow in these horses at either sub-maximal or near maximal exercise levels. Others have also deemed ventriculectomy an unjustifiable procedure on its own in horses with LLH (Speirs,1987; Cook,1988). Despite the findings of Shappell et al (1988), many surgeons treat equine athletes suffering from LLH by ventriculectomy in conjunction with prosthetic laryngoplasty.

B. Prosthetic Laryngoplasty

Based on published literature to date, their appears to be a consensus that, when performed by experienced surgeons, prosthetic laryngoplasty (PL) is currently the best available method for treating horses suffering from LLH. The objective of PL, or abductor muscle prosthesis, is to abduct and stabilize the affected vocal fold, and corniculate and arytenoid cartilage. The first detailed report of the use of this procedure, whereby a prosthetic suture is placed to mimic the abductor function of the CAD muscle, appeared in 1970 (Marks et al,1970:II).

For prosthesis placement, the horse is positioned in lateral recumbency, under general anesthesia, with the affected side uppermost. An 8 cm curvilinear incision is made from the level of the cricotracheal space extending rostrally along the ventral border of the linguofacial vein. The plane of dissection is continued between the omohyoideus muscle and the linguofacial vein to the lateral wall of the larynx. The crico- and thyropharyngeus muscles are then separated along their septum. After identification of the cricoid cartilage, a cutting curved or half circle needle is passed from the caudal border of the cricoid rostrally about 1.0-1.5 cm. The needle should be directed submucosally and penetrate the dorsal lamina as close to the median ridge of the cricoid cartilage as possible. Generally the prosthesis consists of No.2 nonabsorbable material, either single or double strand. The suture ends are then passed under the cricopharyngeus muscle emerging at the septum between the crico-and-thyropharyngeus muscles. Using a 16 gauge needle a hole is drilled through the muscular process of the arytenoid cartilage and the suture end arising from the most cranial aspect of the cricoid cartilage is pulled through with a #10 crochet hook from medial to lateral. The site of suture placement should be through the cranial half of the base of the muscular process, rather than at the apex. Accurate placement through the dorsal lamina of the cricoid and muscular process of the arytenoid cartilage is essential. The prosthesis must be positioned to approximate the normal line of action of the CAD muscle, and also to minimize migration of the prothesis through the cartilage when tension is applied. The suture is then tied to create permanent

abduction of the arytenoid cartilage. The pharyngeus muscles, subcutaneous tissue and skin are then apposed. A unilateral or bilateral ventriculectomy may then be performed via laryngotomy.

Since the original description of the technique, various modifications have been described including an approach dorsal to the linguofacial vein (Merriam,1973). The elastic material described with the original technique (Marks et al,1970:II), is now rarely used because of the difficulty of achieving sterility, inferior long term strength, and increased tissue reactivity (Merriam,1973). Use of a trocar surgical needle to pass the prosthesis through the muscular process is now commonly used in place of a crochet hook (Shappell et al,1988). Speirs (1983) considers placement of a second prosthesis beneficial, although placement of the second suture in the cricoid cartilage too far lateral to the first may result in adduction, rather than abduction of the vocal fold and process (Speirs,1987).

The degree of abduction of the arytenoid cartilage by the prosthesis remains a controversial issue. Some surgeons suggest that maximum arytenoid abduction is necessary while others propose that maximum abduction may result in chronic coughing, dysphagia and interference with the lateral food channel (Greet et al,1979). At present it is generally recommended that the left corniculate cartilage is positioned midway between full abduction and the resting position.

There are many potential complications associated with laryngoplasty including coughing, chondritis, fistulation, laryngeal granuloma due to

penetration of mucosa, dysphagia, laryngospasm, tracheitis, pneumonia, seroma formation, wound sepsis and dehiscence, choke, and osseous metaplasia of cartilage (Marks et al,1970:II, Mackay-Smith et al,1973; Merriam,1973, Haynes et al,1980; Goulden and Anderson,1982; Speirs,1987). Fortunately, the incidence of complication is low, with seroma, coughing and nasal discharge of food and water being the most common complications reported (Goulden and Anderson,1982). Coughing is reported to occur in up to 57% of horses immediately post operatively (Merriam,1973) and to remain chronic in 4% to 6% (Speirs,1987). Aspiration of food particles during eating may be confirmed by endoscopic examination of the proximal trachea, and would appear the most common reported cause of coughing. In some horses, chronic coughing will resolve if the prosthesis is cut or removed (Greet et al,1979). The incidence of nasal reflux has been reported from 1% to 43% (Speirs,1983; Goulden and Anderson,1982). Although regurgitation may be associated with excessive arytenoid cartilage abduction, coughing and dysphagia have been observed after a sham operation in which no suture was placed (Greet et al,1979). This suggests that interference with neuromuscular control of deglutition resulting from the surgical approach for laryngoplasty may be involved in the pathogenesis of this complication.

Based on relatively large numbers of horses treated by PL, a "successful" outcome, determined from subjective evaluation of performance and stridor, has been reported in 44% to 90% of cases (Goulden and Anderson,1982; Baker,1983:II; Marks et al,1970:II; Haynes,1984). These reports were

supported by the finding that post-operative racing performance between treated horses and a control group of horses of similar ability was not significantly different (Speirs,1983).

Objective assessment of this surgical procedure using evaluation of airway flow mechanics was initially provided by Derksen et al (1986). Although horses were evaluated at speeds substantially less than experienced during racing, PL significantly reduced the resistance to inspiratory airflow in horses with surgically induced LLH. This finding was later substantiated using treadmill speeds, which resulted in airflow rates in horses approaching that experienced during racing (Shappell et al,1988). Recently, tracheal airway pressure was measured in induced and naturally occurring forms of LLH, before and after PL (Williams,1990:I,II). These measurements were performed under simulated race conditions, and showed that pressure measurements were substantially reduced following prosthetic laryngoplasty, further supporting the initial objective evaluations of this surgical procedure (Derksen et al,1986). Laryngoplasty has also been shown to reduce the level of hypoxemia recorded in exercising horses with LLH (Bayley et al,1984; Tate et al,1993).

The long term effects of laryngoplasty on performance are less well documented. Failure of the prosthesis to maintain arytenoid cartilage abduction, is reported to occur in some horses (Marks et al,1970:II; Baker,1983; Goulden and Anderson,1982). Loss of abduction may be sudden, as a result of suture breakage or loosening, or gradual over a period of years, due to migration of the prosthesis through laryngeal cartilage. Variations of the

original technique described have been aimed at decreasing the incidence of the prosthetic material tearing from the muscular process. Goulden and Anderson (1982) reported on placement of a second suture, anchored to the prosthesis, through the arytenoid and thyroid cartilages, as well as a teflon implant between the caudal border of the cricoid cartilage and the prosthesis. Placement of the prosthesis using a horizontal mattress pattern in the cricoid cartilage and use of an additional prosthesis have also been advocated (Speirs,1983). In vitro studies suggest that the age of the horse and type of prosthetic material, are unlikely to influence the rate at which abduction is lost, and the most common place for the prosthesis to pull through the cartilage is at the muscular process of the arytenoid cartilage (Dean et al,1990).

Recent reports suggest that transection of the left RLN, preventing any residual contraction of the CAD and CAL muscles, following prosthesis placement may reduce the rate at which the prothesis cuts through laryngeal cartilage (Ducharme and Hackett,1991). Convincing justification for these additional procedures is lacking at the present time.

C. Arytenoidectomy

In the late 19th century, Günther (Hanover,1845) and Möller, in their attempts to find a surgical treatment for LLH, performed partial and total arytenoidectomies with the aim of removing the obstructing arytenoid cartilage (in Liautard,1892). Subsequently, Günther Junior reported that total arytenoidectomy often resulted in severe post-operative hemorrhage and

dysphagia with death from aspiration pneumonia (in Williams,1911). He also found that although these life threatening complications could be avoided by removing less cartilage, particularly the corniculate cartilage, his results were still unsatisfactory because the remaining cartilage continued to interfere with air flow. The introduction of the ventriculectomy in 1906 (Williams,1911) provided a less traumatic method of improving horses that had LLH, and subsequently arytenoidectomy fell into disuse.

The terminology classifying the 3 types of arytenoidectomy, although adequate, remains somewhat confusing. Total arytenoidectomy involves the complete removal of both the corniculate and arytenoid cartilages. Partial arytenoidectomy involves resection of both cartilages with retention of the muscular process, while in the subtotal method, only the arytenoid cartilage is removed with both the corniculate cartilage and usually the muscular process being retained (Haynes,1984). More recently an alternative classification scheme has been proposed based on incorporating the arytenoid and corniculate cartilage into the terminology, and is suggested to be more anatomically correct (Speirs,1987).

Use of the modern day form of arytenoidectomy was stimulated in the late 1970's by isolated reports describing the successful treatment of horses with arytenoid chondropathies, and of horses in which a PL had failed, using either subtotal or partial arytenoidectomy (Wheat,1978; White and Blackwell,1980; Haynes et al,1980). These reports suggested that the life threatening post-operative complications experienced in the 19th century were

not observed, presumably the result of improved anesthetic and surgical technique, and the availability of anti-inflammatory drugs.

Following recognition of the performance limiting effects of arytenoid chondropathy (Haynes et al,1980), and it's apparent increasing incidence, arytenoidectomy has become a common place procedure (Tulleners et al,1988:I; Speirs,1987). Although the other main indication for arytenoidectomy is management of unsuccessful prosthetic laryngoplasties, some authors consider arytenoidectomy a primary treatment for LLH, as the potential coughing, aspiration and short lived abduction associated with the prosthesis may be avoided (Haynes et al,1984; McIlwraith and Turner,1987).

The objective of arytenoidectomy is to remove sufficient cartilage to produce an airway adequate for the projected activity of the horse. Anesthesia is maintained via an endotracheal tube placed through a mid cervical tracheotomy which can be performed either before or after induction of general anesthesia (Haynes,1984). With the horse in dorsal recumbency, a laryngotomy is performed and the ventricle on the same side as the affected arytenoid cartilage is usually removed first. Subsequently, mucosal incision and dissection allows complete or partial removal of the arytenoid and corniculate cartilages. Mucosal edges are then apposed in a continuous or interrupted pattern using absorbable suture material.

A tracheostomy tube is often required for up to 5 days post-operatively. The laryngotomy is left to heal by second intention and anti-inflammatory drugs and broad spectrum antibiotics are commonly employed for 2-5 days. Stall rest

is recommended for 30 days and followed by an additional 30-60 days of paddock turnout. A more detailed surgical description of partial arytenoidectomy is found in Chapter VI.

Numerous variations regarding surgical technique have been described since the resurgence of this surgical procedure including, not transecting the cricoid or thyroid cartilages (Speirs,1986), and the submucosal injection of 1:10,000 epinephrine prior to mucosal incision (White and Blackwell,1980). Others have suggested that the inter-arytenoid ligament should be preserved to minimize post operative dysphagia (Speirs,1986). Excision of the corniculate and arytenoid cartilages using CO_2 and Nd:YAG laser has been performed in the standing and anesthetized horse (Montgomery,1985; Tate et al,1986; 1989), and recently partial arytenoidectomy has been reported using an extra-laryngeal approach (Hay and Tulleners,1993).

Some authors advocate healing of mucosal defects, particularly in the treatment of arytenoid chondropathies, by second intention rather than attempting primary closure. Second intention healing following partial arytenoidectomy is associated with shorter surgery times, reduced hematoma formation, and comparable healing quality when compared to primary closure techniques, though healing time appears longer compared to primary closure (Tulleners et al.1988:II). Recently, the use of systemic corticosteroids has been recommended to control post-operative swelling (Dean,1990).

Intra-operative complications include difficult access and visualization, hemorrhage, and defects in the mucous membranes. Post-operatively

complications may include wound swelling and dehiscence (Tulleners et al,1988:I), coughing, dysphagia, nasal discharge of food and water, and cartilage mineralization (Haynes,1984; Speirs,1986). Complications referable to dysphagia and inadequate laryngeal protection of the lower airway during swallowing are reportedly more common after partial arytenoidectomy (Speirs,1986) and have been suggested to result from the absence of the corniculate cartilage (Haynes et al,1984; Speirs,1986). The pathogenesis of the observed dysphagia following partial arytenoidectomy may result from the inability of the arytenoids to contribute to glottal closure during swallowing (Speirs,1986; 1987). However, the real need to retain any portion of the corniculate cartilage is still uncertain, and if epiglottic function is normal it is questionable whether the rima glottidis needs to be completely sealed on adduction (McIlwraith and Turner,1987).

Subjective evaluation, based on performance of intended activity and complications following subtotal and partial arytenoidectomy have been reported. Reports of successful outcome following arytenoidectomy vary greatly depending on the criteria used by the author to define "success". In addition, accurate interpretation of studies evaluating arytenoidectomies is difficult as the underlying disease process may be either arytenoid chondropathy (AC), LLH, or a combination of both. Improved athletic performance and reduction in respiratory noise following subtotal arytenoidectomy has been reported in 50% of horses with AC and 83% with

LLH (Haynes et al,1984). Coughing and evidence of dysphagia was reported in 25% of horses in this study, but were not considered to effect performance.

Improved athletic ability following unilateral partial arytenoidectomy is reported in 56% of horses treated for either LLH or failed PL (Speirs,1986) and 63% to 80% of horses with AC (Speirs,1986, and Tulleners et al,1988:I). Complications such as dysphagia and coughing following this procedure have been reported as high as 45% (Speirs,1986) and more recently as low as 10% (Tulleners et al,1988:I). The reason for the disparity between the complication rates reported by Speirs and Tulleners may reflect minor differences in surgical procedure or may be influenced by the nature of the condition being treated.

In 1990, quantitative evaluation of subtotal arytenoidectomy for the treatment of surgically-induced LLH, unequivocally demonstrated the failure of this technique to improve upper airway function in exercising horses (Belknap et al,1990). Similarly, evaluation of tracheal pressures (as an indicator of upper airway resistance) revealed that, in horses with surgically-induced LLH, and in horses with arytenoid chondropathy, subtotal arytenoidectomy did not significantly decrease tracheal pressures (Williams et al,1990:I,II). These findings are in direct contrast to that of Haynes et al,(1984), who reported improved exercise tolerance following subtotal arytenoidectomy, based on subjective assessment. Differences between these authors may be explained by the subjective method of evaluation used by Haynes (1984) compared to quantitation of airway function (Belknap et al,1990; Williams et al,1990:II). Differences in the outcome reported following subtotal arytenoidectomy may

also reflect the varied athletic requirements of the horses evaluated and differences in the amount of corniculate cartilage removed.

D. Laryngeal Reinnervation

From the above review of treatments for LLH, their varied degrees of "success", result from either a less than adequate airway cross sectional area or post-operative complications. As stated by Goulden and Anderson in 1982, optimal airway cross sectional area and minimal post-operative complications, may be achieved by using more physiologically compatible techniques, such as reinnervation of the abductor muscle of the larynx.

Treatment of laryngeal paralysis in people by laryngeal reinnervation using a nerve muscle pedicle (NMP) graft has been described and is considered a valuable procedure (Lyons and Tucker,1974; Tucker,1976). The mechanism by which denervated muscle is reinnervated using either direct nerve implantation or NMP transposition is not completely understood. It has been proposed that the NMP graft technique transplants motor end plates (the synapse of a nerve and a muscle fiber) in the NMP to the recipient paralysed muscle. Subsequently, contraction of the recipient muscle is caused by propagation of depolarization from the NMP graft (Johnson and Tucker,1987). An alternative theory is that axons transplanted either in the NMP or the transected nerve, sprout and form junctions with the recipient muscle fibers (Hall et al,1988).

For NMP transplantation to be successful the recipient muscle must be able to be reinnervated despite the underlying disease process and the extent of neurogenic atrophy of the muscle. As the pathogenesis of equine LLH is considered a distal axonopathy and not a primary myopathy, laryngeal reinnervation may have potential value in the treatment of LLH. Clinical signs of LLH typically occur in horses from 2-5 years (Goulden and Anderson, 1981:II). Therefore, the duration of neurogenic atrophy of the CAD muscle is unlikely to preclude the muscles ability reinnervate, as reinnervation is commonly successful after 3 years and up to 22 years of denervation atrophy in humans (Tucker,1976).

Following successful reinnervation, the muscle must assume the functional and biological characteristics of the muscle originally innervated by the transferred nerve (Tucker,1976). As the pathophysiology of equine LLH involves the inability of the CAD muscle to abduct the arytenoid cartilage during inspiration, donor nerves supplying accessary muscles of respiration which contract during inspiration have been used.

In 1989, Ducharme and co-workers reported results of the efficacy of CAD muscle reinnervation in ponies with induced laryngeal hemiplegia. The second cervical nerve (with and without NMP grafts from the omohyoideus muscle) was used to reinnervate the equine larynx (Ducharme et al,1989:I-III).

The surgical technique described here is as reported by Fulton (1990) using a NMP graft. Other techniques of reinnervation are reported elsewhere (Ducharme et al,1989:I-III; Harrison et al,1992). Using similar patient

positioning and surgical approach to that for PL, a branch of the first cervical nerve is identified as it travels caudal to the cricopharyngeus muscle to insert in the omohyoideus muscle. The cricopharyngeus muscle is retracted cranially to expose the CAD muscle in which a 1-cm opening is created parallel to its muscle fibers. An omohyoideus muscle pedicle (5 x 5 mm) is created containing the insertion of the first cervical nerve and is transposed into the previously created opening in the CAD muscle. The NMP graft is anchored by 2 simple interrupted 4-0 absorbable sutures, and the wound is then closed routinely.

Since the initial description of this procedure, modifications to surgical technique have included, electrical stimulation for identification of nerves (Harrison et al,1992), local anesthetic induced desensitization of the first cervical nerve prior to excision of the muscle pedicle, and implantation of multiple NMP grafts at various locations in the CAD muscle (Fulton,1990).

Success of laryngeal reinnervation techniques has been evaluated using endoscopic appearance of the larynx at rest (Ducharme et al,1989:I; Fulton et al,1992; Harrison et al,1992) and during treadmill exercise (Fulton et al,1991). The ability to reinnervate the CAD muscle has also been evaluated using histologic evidence of reinnervation (Ducharme et al,1989; Fulton et al,1992; Harrison et al,1992) and objective measurement of upper airway function during exercise (Fulton et al,1991).

Using a NMP graft harvested from the second cervical nerve (C2) and the omohyoideus muscle, Ducharme et al.(1989:I) found that 30 weeks after

surgery, the endoscopic appearance of the larynx at rest, showed only slight arytenoid abduction in 1 of 4 ponies. Despite these findings, histologic evidence of reinnervation after NMP graft technique, seen as muscle fiber grouping (Eisele et al,1988), was observed in 3 of 4 ponies. Subsequent to this report, the same researchers, using a direct nerve (C2) implantation technique, observed partial arytenoid abduction in 4 of 6 ponies, though convincing histological evidence of reinnervation in the CAD muscles was not found (Ducharme et al,1989:II). In a third study reinnervation was attempted by anastomosing a sectioned branch of C2 with the abductor branch of a distally sectioned left RLN (Ducharme et al,1989:III). Endoscopic examination, while horses were breathing 10% CO_2, revealed clonic abductor movement of the arytenoid cartilage which was synchronous with inspiration in 5 of 6 horses. Histologic evidence for reinnervation supported the observed abductor muscle function in these horses. Despite the fact that physiologically, the reinnervation was successful, the partial restoration of function did not appear to be sufficient for racing. In addition, the technical difficulty of the nerve anastomosis technique, and the questionable viability of the distal RLN in cases of LLH, render this procedure of questionable value (Fulton,1990).

Following the initial findings of Ducharme et al.(1989), Fulton et al.(1991) reported the successful use of a NMP graft in restoring upper airway function in horses with induced LLH. Measurements of upper airway function in 5 horses receiving a NMP graft, and 2 horses undergoing a sham procedure, provided objective data that laryngeal reinnervation significantly improves upper

airway function in horses with LLH during exercise. Substantial abduction of the arytenoid cartilage was observed endoscopically following electrical stimulation of a proximal segment of C1, during nasal occlusion (Fulton et al,1992), and strenuous exercise (Fulton pers comm.) though not during quiet breathing at rest (Fulton et al,1991). Although reinnervation studies by Ducharme and Fulton report histological evidence of CAD muscle reinnervation, the lack of observed abduction of the arytenoid cartilage in the studies of Ducharme et al,(1989:I-II), may be explained by insufficient stimulation of the accessary muscles of respiration during the resting endoscopic examination. Despite the encouraging findings of Fulton's study, of improved upper airway function and lack of significant post-operative complications, the duration for reinnervation to allow significant improvement in upper airway function took up to 52 weeks. Thus, the clinical application of this technique may be limited by the economic feasibility of the time taken to return athletes to competitive levels of performance. Following these findings, it has been proposed that multiple NMP grafts may potentially reduced the time for reinnervation, though to date preliminary findings have not supported this hypothesis (Derksen et al,unpublished data).

Recently, the ability of a right CAD muscle pedicle graft to innervate the contralateral denervated CAD muscle was evaluated. Results from this study suggested that muscle-to-muscle neurotization of the paralyzed muscle did not occur, and that this technique appeared to be of limited clinical value in the

treatment of LLH in horses (Harrison et al,1992). Continued investigation and refinement of laryngeal reinnervation techniques is clearly warranted.

Conclusion

The development of videoendoscopic and upper airway function measurement techniques to document the effect of LLH during exercise, represents a major advancement in our understanding of the pathophysiology of LLH in the horse. As discussed previously, the objective techniques currently available have limited clinical application. Therefore, the first goal in my study is to evaluate the usefulness of flow-volume loop analysis in providing measurement of airway function that may be a useful clinical diagnostic test. Evaluation of this technique in documenting the effect of LLH in resting and exercising horses is presented in chapter V.

As revealed in the preceding review of the various treatments for LLH, as yet none is considered ideal. The treatment of choice when performing arytenoidectomy remains controversial between advocates of subtotal and partial arytenoidectomy techniques. To date the efficacy of partial arytenoidectomy in treating LLH has not been objectively evaluated. Therefore, the second objective of this study, presented in chapter VI, is to determine the efficacy of partial arytenoidectomy for treatment of LLH using previously documented techniques (calculation of impedance) and flow-volume loop analysis.

V. USE OF FLOW-VOLUME LOOPS TO EVALUATE UPPER AIRWAY OBSTRUCTION IN EXERCISING STANDARDBRED HORSES

A. Summary

Flow-volume loops generated from 6 Standardbred horses at rest and during treadmill exercise were evaluated for their use in detecting upper airway obstruction. Tidal breathing flow-volume loops (TBFVL) were obtained from horses at rest and exercising at speeds corresponding to 75% of maximal heart rate and at maximal heart rate. The TBFVL were evaluated, using a pulmonary function computer; calculated indices describing airflow rate and expiratory-to-inspiratory airflow ratio for individual loops were determined. In addition to TBFVL indices, standard variables of upper airway function also were measured: peak airflow, peak pressure, and calculated inspiratory and expiratory impedances. Measurements were recorded before left recurrent laryngeal neurectomy (LRLN; baseline) and 14 days after surgically induced left laryngeal hemiplegia.

When horses were at rest, TBFVL shape and the indices describing the loop were highly variable. In contrast, in exercising horses, TBFVL shape was consistent and coefficients of variation of loop indices were less during exercise than at rest. After LRLN, TBFVL from exercising horses indicated marked inspiratory airflow limitation, while the expiratory airflow curve was preserved. Peak inspiratory flow rate and inspiratory flow at 50 and 25% of tidal volume decreased, and the ratio of peak expiratory to inspiratory airflow (PEF/PIF) and

that of mid-tidal volume expiratory and inspiratory airflow rates (EF_{50}/IF_{50}) increased significantly ($P = 0.05$). Inspiratory impedance also increased after LRLN.

Although in resting horses TBFVL were not a useful indicator of upper airway obstruction, examination of TBFVL from exercising horses allowed objective, specific, and repeatable detection of upper airway obstruction. The technique was non-invasive, rapid, and well tolerated by horses; thus, it is a potentially valuable clinical diagnostic test.

B. Introduction

Upper airway obstruction is a common cause of reduced exercise tolerance in performance horses (Raphel,1982; Sweeney et al,1991; Morris and Seeherman,1991) and is frequently associated with inspiratory noise (Fleming,1882; Haynes,1984). Lesions of the upper airway resulting in airflow obstruction include laryngeal hemiplegia, subepiglottic cysts, arytenoid chondropathy, and aryepiglottic entrapment. Of these, left laryngeal hemiplegia (LLH) is most commonly diagnosed (Morris and Seeherman,1990; 1991). The inspiratory flow limitation caused by axial displacement of the left arytenoid cartilage is the direct result of paralysis of its abductor muscle (Robinson and Sorenson,1978; Derksen et al,1986). Endoscopic examination of the larynx and pharynx in resting horses permits descriptive evaluation of upper airway lesions (Cook,1974). However, some upper airway lesions, such as dorsal displacement of the soft palate, may be inapparent in the resting horses and are

best identified by videoendoscopy during exercise (Derksen,1988; Morris and Seeherman,1988). The limitation of this technique is that it requires subjective interpretation of airway function. Upper airway impedance has been measured experimentally in horses to objectively evaluate the efficacy of prosthetic laryngoplasty (Derksen et al,1986), ventriculectomy (Shappell et al,1988), subtotal arytenoidectomy (Belknap et al, 1990), and laryngeal reinnervation (Fulton et al,1991) as treatments for LLH. The clinical use of objective measurement techniques of upper airway function has been limited (Stick and Derksen,1989; Williams et al,1990:II), primarily because of the inconvenient and invasive nature of the technique (Derksen et al,1986).

Flow-volume loop analysis is a common test of respiratory tract function in human medicine, because it is non-invasive, convenient, and sensitive. Airflow rate is continuously plotted against volume during a single maximal inspiratory and expiratory effort (FVL). Initially used in the clinical evaluation of lower airway disease (Hyatt et al,1958), FVL analysis remains one of the most widely used pulmonary function tests in human medicine. Determination of FVL has been used for the clinical diagnosis of upper airway obstruction in human beings since 1968 (Jordanoglou and Pride,1968. The sensitivity, specificity, and repeatability of this test rely on patient co-operation to perform maximal inhalation and exhalation. In doing so, flow rates approach maximal and are associated with significant intraluminal pressure changes allowing detection of subtle airway obstruction (Fry and Hyatt,1960). In veterinary

medicine, the non-cooperative nature of our patients has prevented clinical use of maximal FVL.

Clinical evaluation of upper airway function, using a tidal breathing flow-volume loop (TBFVL) has been attempted in human neonates and infants who are incapable of performing a maximal voluntary respiratory effort on demand (Abramson et al,1982). When breathing with less than maximal effort, such non-cooperative subjects have low airflow rates that are associated with lack of sensitivity of the TBFVL to detect airway obstruction (Abramson et al,1982; Wise et al,1980). The great flow variability associated with TBFVL prevents strict numerical interpretation of loop indices, therefore limiting its usefulness in evaluating airway obstruction (Abramson et al,1982). Tidal breathing flow-volume loop analysis performed in dogs with upper airway obstruction also lacks sensitivity and cannot reliably quantitate less than severe obstruction (Amis and Kurpershoek,1986; Amis et al,1986).

The sensitivity of the TBFVL in detecting airway obstruction may improve as flow rates approach maximal (Fry and Hyatt,1960). In horses, high-speed treadmill exercise results in near-maximal airflow rates (Belknap et al,1990; Fulton et al,1991). Therefore, the objective of the study reported here was to evaluate the ability of TBFVL, generated during exercise, to detect upper airway obstruction induced by left recurrent laryngeal neurectomy (LRLN).

C. Materials and Methods

Horses—Six adult Standardbreds (3 male and 3 female) 5.2 ± 2.0 (mean ± sd; range 3 to 8) years old and weighing 437.8 ± 40.2 kg (range, 390.0 to 490) were studied. All horses were maintained on pasture for at least 30 days before experiments, treated with anthelmintics, and vaccinated against tetanus, equine influenza, and rhinopneumonitis. Prior to measurements or surgical procedures, clinical examination and endoscopic evaluation of the upper airway at rest indicated no abnormalities. Horses were kept at pasture between surgical procedures and measurement protocols.

Measurement techniques—Techniques for measurement of airflow, tidal volume, and transupper airway pressure have been described (Derksen et al,1986). Briefly, horses were fitted with a 15.2-cm diameter pneumotachograph (Laminar flow straightener element, Merriam Instruments, Grand Rapids, Mich.) mounted on a face mask. The mask covered mouth and nostrils and allowed complete nostril dilatation. The combined dead space of the mask and pneumotachograph was approximately 3.5 L. A wire mesh (Mesh SS Screen, McMaster Carr, Chicago, Ill.) located between the muzzle and pneumotachograph, prevented contamination of the pneumotachograph with secretions and functioned as a flow straightener element. The resistance of the pneumotachograph was 0.04 cm of H_2O/L/s, up to an airflow of 90 L/s. The combined resistance of the facemask, wire mesh, and pneumotachograph was 0.05 cm of H_2O/L/s at the peak airflows recorded in this study. Pressure changes across the pneumotachograph were measured by use of a differential

pressure transducer (Model DP45-22, Validyne Sales, Northbridge, Calif.) which produced a signal proportional to flow. The pneumotachograph was calibrated using a rotameter flow meter (Model FP-2-37-P-10/77, Fisher & Porter Co, Warminster, Pa.) capable of measuring airflow rate up to 90 L/s.

Inspiratory and expiratory transupper airway pressure (P_{UI} and P_{UE}) was measured as the pressure difference between tracheal and mask pressure. Tracheal pressure was measured via a lateral tracheal catheter placed percutaneously at the mid-cervical level. A second catheter was connected to measure pressure within the face mask. Catheters were connected to each side of a second differential pressure transducer, which was calibrated by use of a water manometer. Flow and pressure signals were phase-matched up to 10 Hz, as described (Derksen and Robinson,1980).

Airflow and pressure signals were passed through 4-and 8-Hz low-pass filters, respectively, and were fed into a respiratory function computer (Buxco LS-14, Buxco Electronics, Inc., Sharon, Conn.). Selection of filters was derived from preliminary studies. To obtain tidal volume (V_T) the flow signal was digitally integrated with respect to time. Inspiratory and expiratory impedances (Z_I and Z_E) were calculated as the ratio of peak transupper airway pressure and peak airflow over 10 consecutive breaths. Minute ventilation ($\dot{V}_E$) was calculated as the product of respiratory rate (f) and V_T. Heart rate (HR) was recorded, using a telemetry system (Digital UHF Telemetry System, M1403A, Hewlett Packard, Palo Alto, Calif.).

Ten representative TBFVL were selected from each exercise period and were analyzed, using computer software (Buxco LS-14, Buxco Electronics Inc, Sharon, Conn.) specifically designed to analyze FVL. Criteria for selection of FVL included adequate loop closure (< 5% difference between inspiratory and expiratory volumes) and lack of artifact (snorting and swallowing), as outlined by Amis et al,(1986).

The shape of the TBFVL was qualitatively evaluated. For quantitative analysis of TBFVL, V_T, inspiratory and expiratory times (T_I and T_E), total breath time (T_{TOT}), f, peak inspiratory and expiratory airflow rates (PIF and PEF), flow rates at 50%, 25%, and 12.5% of tidal volume (IF_{50}, EF_{50}, IF_{25}, EF_{25}, $IF_{12.5}$, and $EF_{12.5}$), ratios of these flow rates, T_I/T_E, V_T/T_I, $T_I/_{TOT}$, and volume at PIF and PEF were calculated. The mean ± SEM and coefficient of variation of measured values and derived indices were obtained.

Experimental design— Over a 3 day period, prior to any measurement procedures, all horses were acclimatized to work on the treadmill while wearing the breathing apparatus. Maximal HR (HR_{max}) during exercise was determined prior to upper airway function tests. All horses underwent a single rapid incremental exercise test (RIET) to estimate the relation between HR and treadmill speed for each individual horse. The RIET was performed as reported by Rose et al,(1990), except that horses wore the mask previously described and a 3-degree treadmill incline was used. Horses were first exercised at a treadmill speed of 4 m/s for 3 minutes. Subsequently, treadmill speed was increased to 6 m/s for 90 seconds. Treadmill speed was then increased at

intervals of 60 seconds to 8, 10, 11, and 12 m/s, respectively. The RIET was terminated when horses could no longer maintain position on the treadmill. Heart rate was recorded in the last 15 seconds of each exercise period. From these measurements, the treadmill speed at which further increase failed to substantially increase HR, speed at HR_{max} was determined. The treadmill speed at which 75% of maximal HR ($HR_{0.75max}$) was observed was also calculated.

Experimental protocol—Measurements were initially made with horses at rest, standing adjacent to the treadmill (period A) throughout the last minute of a 2-minute interval. Subsequently, horses were exercised on the treadmill with a 3-degree incline at 4 m/s for a 2-minute period, then at the treadmill speed corresponding to their $HR_{0.75max}$ for 2 minutes (period B). All horses rested for 1 minute, then exercised at a treadmill speed corresponding to HR_{max} (period C) for a 2-minute period. Data were collected in the last minute of each 2-minute exercise period. On the day after each TBFVL measurement, the larynx was examined by use of videoendoscopy when the horse was at rest and exercising at HR_{max}.

Measurements were obtained before LRLN (baseline) and 14 days after LRLN. Left laryngeal neurectomy was performed through a 10-cm skin incision over the left jugular vein in the mid-cervical region (Derksen et al. 1986). The recurrent laryngeal nerve was isolated by blunt dissection and transected. Subcutaneous tissues and skin were then apposed in routine manner.

Statistical analysis—Data obtained from individual RIET were analyzed using linear regression analysis to determine predicted treadmill velocities

corresponding to $HR_{0.75max}$. Significant differences between mean HR were determined by use of two-way ANOVA. When F values were significant at $p < 0.05$, means were compared, using Fischer's least significant difference test.

A three-way ANOVA was used to analyze the effect of exercise and surgical treatment according to the model Yijk = Ai + Bj + ABij + Ck + ACik + BCjk + error (Gill 1978), where Ai was the fixed effect of exercise (3 levels), Bj was the fixed effect of surgical procedure (2 levels), and Ck was the random effect of 6 horses. When F values were significant at $p < 0.05$, treatment means were compared by use of the Tukey test.

D. Results

The HR_{max} determined from the RIET for the 6 horses was 225.5 ± 4.92 beats/min. This rate was achieved at a treadmill speed of 11.0 ± 0.2 m/s and was significantly different from mean HR at 10.0 m/s but not from that at 12.0 m/s. The $HR_{0.75max}$ was 166.8 ± 3.9 beats/min and corresponded to a treadmill speed of 6.2 ± 0.7 m/s (Figure 4).

At period B, trotting and pacing gaits were observed, whereas at period C all horses galloped prior to LRLN, except for 1 that paced. After LRLN at period B, 3 horses galloped and 3 trotted or paced. After LRLN at period C, all horses galloped. Because of the severity of upper airway obstruction after LRLN, 1 horse was unable to work at the required treadmill speed at period C.

Qualitative evaluation—A variety of different TBFVL shapes was recorded at rest (period A). On the basis of variation of the inspiratory flow curve and

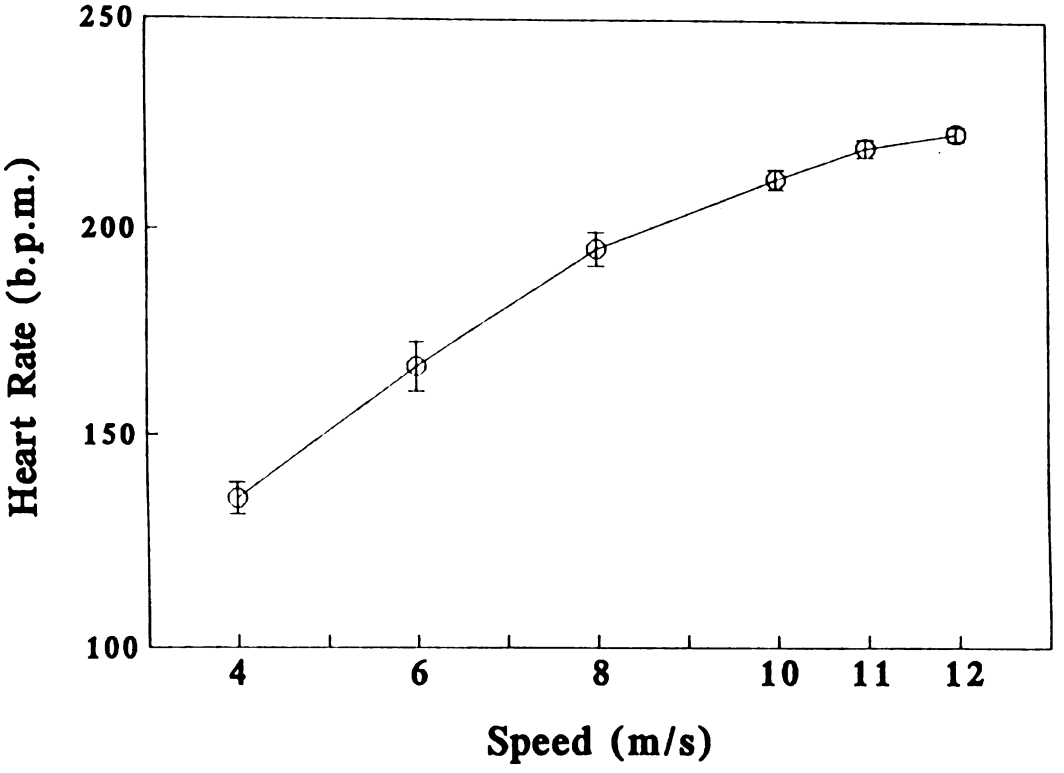

Figure 4. Mean (± SEM) heart rate (beats/min;bpm) in 6 horses performing an incremental treadmill exercise test prior to left recurrent laryngeal neurectomy (LRLN). The treadmill had a 3-degree slope.

PIF location, 4 basic shapes predominated within and between horses. The inspiratory curve was monophasic, biphasic, or less frequently, triphasic. The PIF was either early or late in inspiration. The expiratory flow curve was typically biphasic, with peak flow observed early in expiration (Figure 5).

When airflow rates and tidal volume increased in response to exercise, TBFVL shape was markedly modified (Figure 6). At period C, before LRLN, 3

of the 6 horses (2 galloping and 1 pacing) had a regular biphasic breathing pattern (Figure 7A), 2 had a combination of biphasic and monophasic breathing patterns (Figure 7B), and 1 had a monophasic breathing pattern throughout the gallop (Figure 7C). Of these 3 TBFVL shapes observed during exercise prior to LRLN, predominantly biphasic, and less frequently, monophasic expiratory limb shapes were observed during periods B and C. A biphasic expiratory limb shape was always associated with biphasic inspiratory limb shape (Figure 7A), whereas monophasic expiratory limb shape was associated with monophasic and biphasic inspiratory limb shapes (Figures 7B and C). In the biphasic inspiratory flow curves, peak flow was observed at approximately 30% of tidal volume. The smaller second inspiratory flow peak was observed late in inspiration and was preceded by a more pronounced reduction in flow rate than that seen in the biphasic expiratory flow curve. Although a clear and consistent relation between gait and loop shape was not evident, the monophasic loop shape illustrated in Figure 7C was only seen in galloping horses during period C. This loop shape was associated with smaller tidal volume and higher respiratory rate than those associated with the other loop shapes.

After LRLN, videoendoscopy confirmed the presence of LLH at rest and during exercise in all 6 horses. No changes in TBFVL shape were seen at period A. In contrast, marked changes were observed in the shape of the inspiratory limb of the TBFVL at periods B and C; similar shapes were seen in all 6 horses. Although the shape of the expiratory limb of the TBFVL was approximately the same as that seen prior to LRLN, the inspiratory flow curve

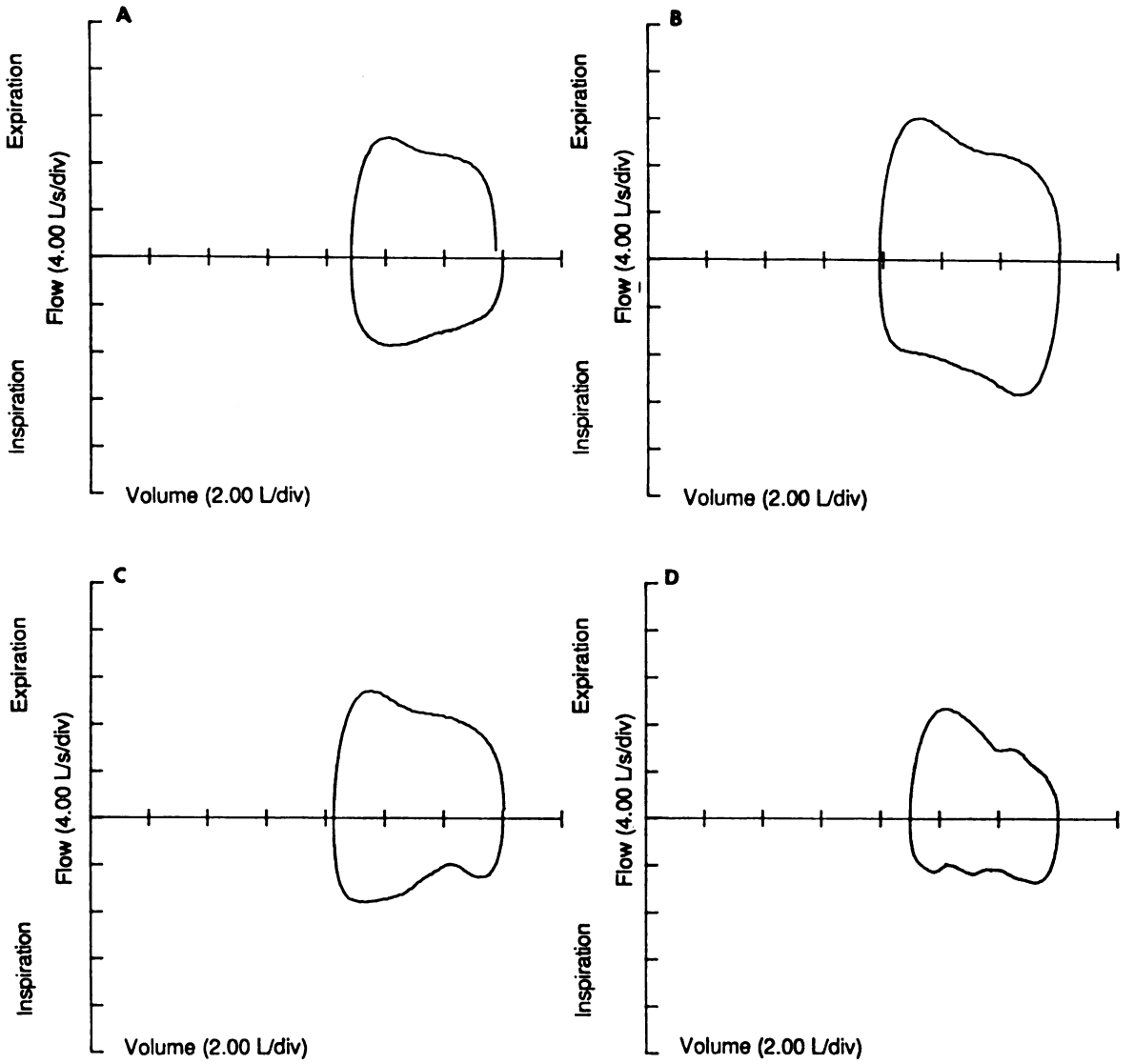

Figure 5. Representative tidal breathing flow-volume loops (TBFVL) from 4 horses at rest. Variation in TBFVL shape was seen within and between horses. Tidal volume at peak inspiratory flow was variable. The TBFVL indicate peak inspiratory flow near the end of inspiration (A) and early in inspiration (B). Variations in the inspiratory limb of TBFVL included monophasic (A and B), biphasic (C), and triphasic (D) patterns.

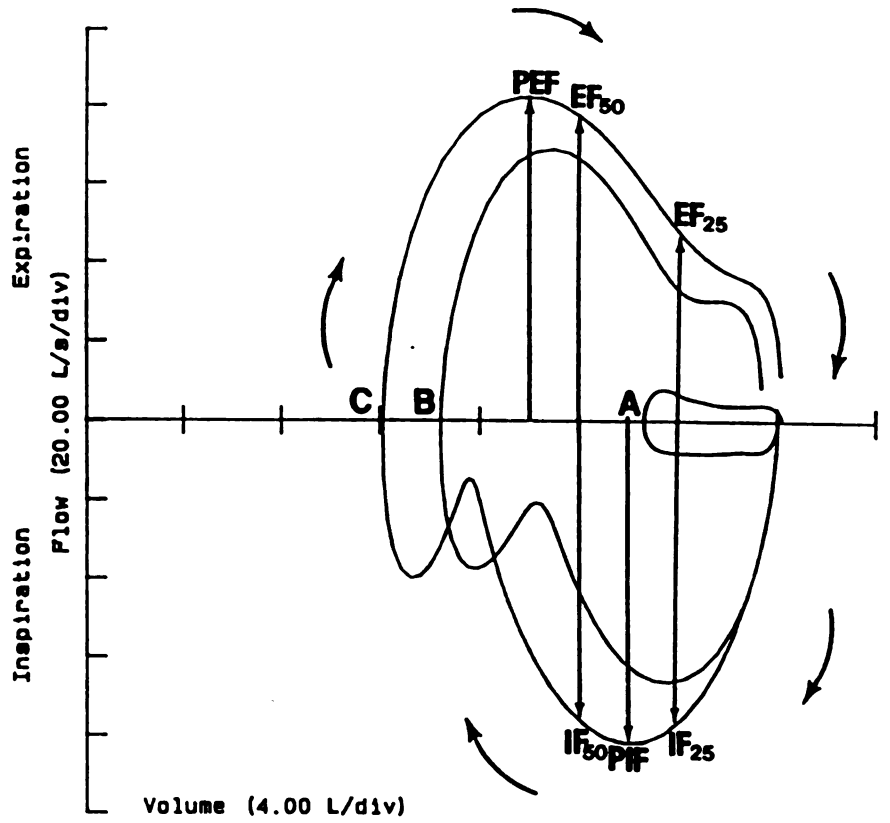

Figure 6. Representative TBFVL from a horse at rest (period A), exercising at 75% of maximal heart rate (period B), and at maximal heart rate (period C). The effect of increasing exercise on shape, airflow rate, and tidal volume is shown. The representative TBFVL (C) at period C shows the flow measurements used to calculate TBFVL indices. Curved arrows indicate the direction of the respiratory cycle.

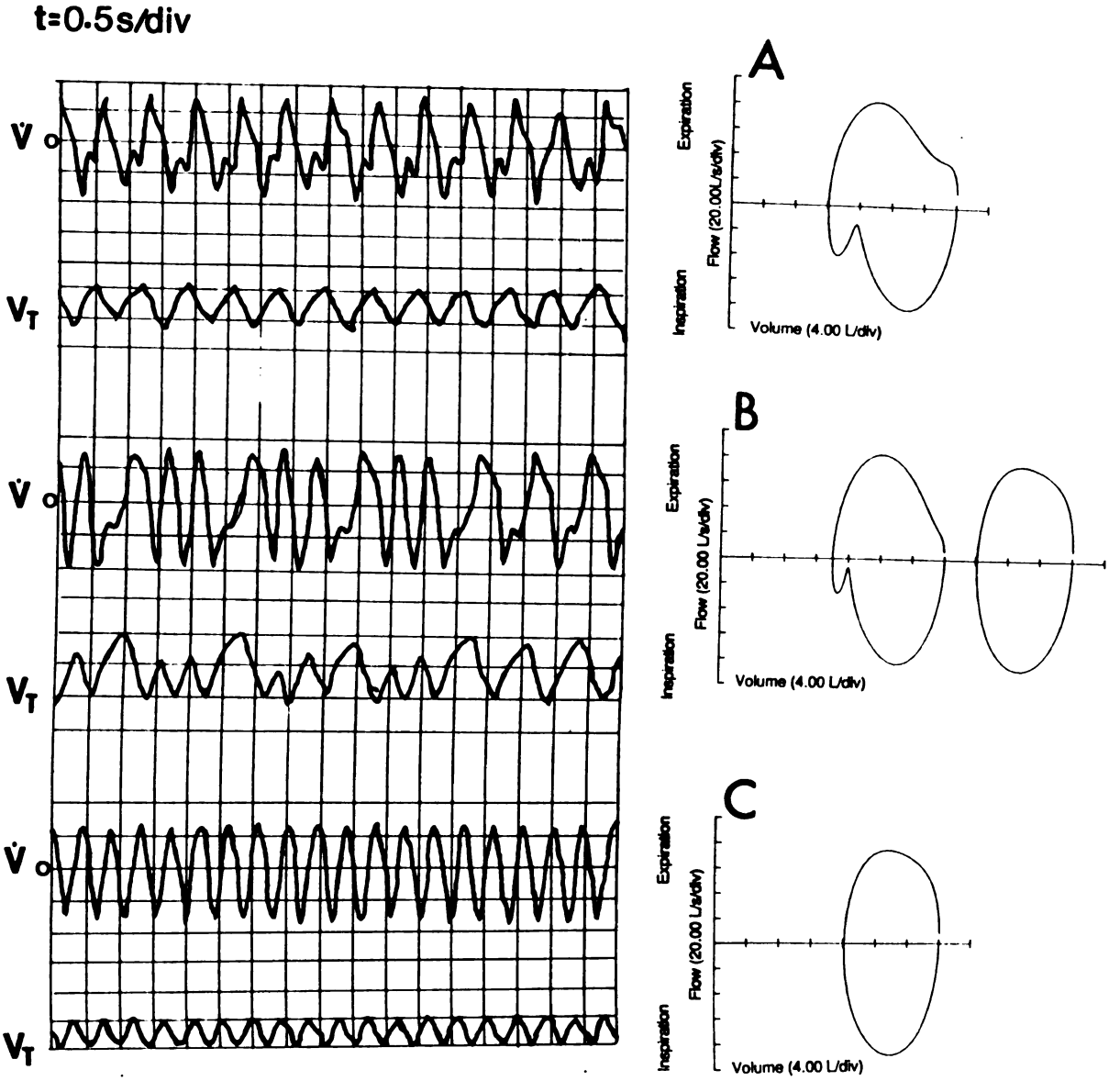

Figure 7. Airflow curves from different horses before LRLN exercising at maximal heart rate (period C). Horses had a constant biphasic breathing pattern (A), a combination of biphasic and monophasic patterns (B), or a constant monophasic pattern (C). The TBFVL derived from flow and volume tracings are at the right of the tracing. A typical biphasic TBFVL shape is shown in A, composed of biphasic expiratory and inspiratory airflow curves. Monophasic expiratory airflow curves were seen with a biphasic (B) or monophasic (C) inspiratory airflow curve. $\dot{V}$ = airflow (50 L/s/division), V_T = tidal volume (10 L/division) and, t = time (0.5 sec/division).

was typified by a flow peak that occurred early in inspiration and was followed by a pronounced reduction in airflow (Fig 8). This reduction in inspiratory flow rate was accentuated with increasing treadmill speed. After LRLN, all horses adopted either a biphasic or triphasic inspiratory breathing pattern at exercise period C; monophasic inspiratory shapes were not observed.

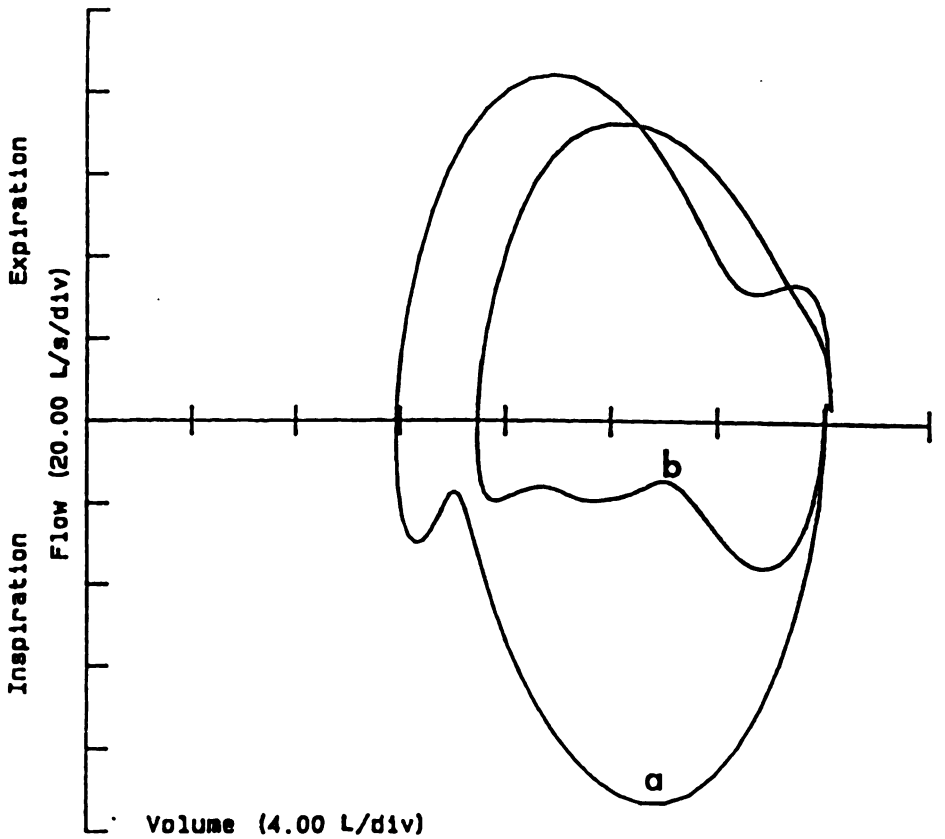

Figure 8. Typical TBFVL from a horse exercising at maximal heart rate (period C) before LRLN (a) and after LRLN (b). Preservation of the expiratory flow curve and inspiratory flow limitation are seen after LRLN.

Quantitative evaluation—Prior to LRLN, increasing intensity of exercise resulted in a progressive increase in HR, V_T, $\dot{V}_E$, P_{UI}, PIF, and PEF. Although f and P_{UE} increased with treadmill speed, significant differences between the

exercise periods B and C were not documented. Significant differences were not observed in either Z_I and Z_E between rest and exercise (Table 1).

With regard to the TBFVL indices determined before LRLN (Table 2), increasing treadmill speed progressively decreased T_I and T_E, and increased V_T, V_T/T_I, lung volume at PIF and PEF, and all airflow rates during inspiration and expiration. Other indices were not affected by exercise.

After LRLN, P_{UI} and Z_I increased significantly at exercise periods B and C (Table 1), whereas PIF was decreased, compared to baseline (pre-LRLN) measurements. The LRLN procedure did not have significant effect on f, V_T, Z_E, P_{UE}, and PEF at any exercise level. After LRLN at period B, HR was significantly greater than the baseline value, and at period C, $\dot{V}_E$ significantly decreased. After LRLN, PEF/PIF and EF_{50}/IF_{50} increased significantly, compared with baseline values at exercise periods B and C (Figure 9), inspiratory flow rate at 50 and 25% of tidal volume and lung volume at PIF decreased at period C, and PIF decreased at periods B and C (Table 2;Figure 10). The LRLN procedure had no effect on indices describing the expiratory limb of the TBFVL (Table 2).

After LRLN at period C, T_E/T_I was significantly decreased, whereas at period B and C, T_I/T_{TOT} was significantly increased. The V_T/T_I value was also significantly decreased at periods B and C after LRLN (Table 2). Some coefficients of variation of TBFVL indices which changed significantly after LRLN are shown in Table 3.

Table 1 - Effect of exercise on the measured and calculated variables in the 6 horses before (baseline) and after left recurrent laryngeal neurectomy (LRLN).

Variable	Surgical Status	Exercise level		
		A‡	B‡	C‡
HR (beats/min)	baseline	40.17 ± 4.18	173.67 ± 2.79*	217.17 ± 2.37*†
	LRLN	40.00 ± 1.98	189.00 ± 2.53§	222.80 ± 3.72
f (breaths/min)	baseline	27.83 ± 2.07	77.33 ± 6.21*	92.67 ± 15.16*
	LRLN	23.66 ± 1.43	68.50 ± 3.96	70.80 ± 3.00
V_T (L)	baseline	5.39 ± 0.39	12.50 ± 0.78*	14.80 ± 1.18*†
	LRLN	5.98 ± 0.29	11.78 ± 0.68	14.51 ± 0.08
$\dot{V}_E$ (L/min)	baseline	151.41 ± 15.01	950.23 ± 59.02*	1295.97 ± 127.52*†
	LRLN	140.75 ± 7.69	808.40 ± 68.29	1027.60 ± 71.17§
P_{UI} (cm of H_2O)	baseline	1.94 ± 0.22	22.29 ± 1.15*	38.57 ± 3.93*†
	LRLN	2.16 ± 0.32	49.40 ± 4.08§	62.73 ± 6.70§
P_{UE} (cm of H_2O)	baseline	1.10 ± 0.40	14.16 ± 3.15*	11.86 ± 3.41*
	LRLN	2.08 ± 0.91	9.65 ± 0.73	11.61 ± 2.49
PIF (L/sec)	baseline	5.09 ± 0.34	51.19 ± 4.05*	75.52 ± 9.35*†
	LRLN	5.84 ± 0.39	36.58 ± 2.74§	40.87 ± 3.23§
PEF (L/sec)	baseline	7.71 ± 0.36	56.94 ± 4.39	66.05 ± 5.58*†
	LRLN	7.16 ± 0.64	56.89 ± 4.98	65.76 ± 4.59
Z_I (cm H_2O/L/sec)	baseline	0.39 ± 0.03	0.46 ± 0.06	0.53 ± 0.04
	LRLN	0.38 ± 0.06	1.41 ± 0.20§	1.63 ± 0.28§
Z_E (cm H_2O/L/sec)	baseline	0.14 ± 0.03	0.25 ± 0.06	0.19 ± 0.06
	LRLN	0.26 ± 0.09	0.18 ± 0.02	0.19 ± 0.06

HR = heart rate, *f* = respiratory frequency, V_T = tidal volume, $\dot{V}_E$ = minute ventilation, P_{UI} = inspiratory pressure, P_{UE} = expiratory pressure, PIF = peak inspiratory flow, PEF = peak expiratory flow, Z_I = inspiratory impedance, Z_E = expiratory impedance.

* Data significantly different ($P < 0.05$) from period A.
† Data significantly different ($P < 0.05$) from period B.
§ Data significantly different ($P < 0.05$) from baseline measurement at same speed.
‡ Values represent means and SEM.

Table 2 - Effect of exercise on selected tidal breathing flow-volume loop values from the 6 horses before (baseline) and after left recurrent laryngeal neurectomy (LRLN).

Variable	Surgical Status	Exercise level A‡	B‡	C‡
T_I (ms)	baseline	1234.12 ± 105.28	420.67 ± 33.52*	387.50 ± 65.70*
	LRLN	1426.80 ± 115.28	540.83 ± 26.00	536.51 ± 17.82
T_E (ms)	baseline	1196.87 ± 86.67	396.00 ± 37.14*	366.17 ± 57.62*
	LRLN	1398.61 ± 122.44	373.50 ± 9.8	351.19 ± 8.4
T_E/T_I	baseline	0.99 ± 0.05	0.94 ± 0.03	0.98 ± 0.05
	LRLN	0.97 ± 0.05	0.70 ± 0.02	0.65 ± 0.01§
T_I/T_{TOT}	baseline	0.51 ± 0.01	0.51 ± 0.01	0.51 ± 0.01
	LRLN	0.52 ± 0.01	0.59 ± 0.01§	0.61 ± 0.01§
V_T(L)	baseline	6.02 ± 0.92	13.11 ± 0.80*	15.73 ± 1.27*
	LRLN	6.39 ± 0.35	12.47 ± 0.44	14.07 ± 0.53
V_T/T_I	baseline	4.84 ± 0.34	31.77 ± 2.08*	44.78 ± 5.03*†
	LRLN	4.40 ± 0.14	23.87 ± 1.70§	25.70 ± 1.02§
PIF (L/s)	baseline	7.02 ± 0.40	50.42 ± 3.97*	77.02 ± 8.43*†
	LRLN	6.03 ± 0.26	36.21 ± 2.09§	38.22 ± 1.36§
IF_{50} (L/s)	baseline	5.24 ± 0.31	49.23 ± 4.08*	70.77 ± 8.47*†
	LRLN	4.84 ± 0.18	23.77 ± 1.61	24.09 ± 1.03§
IF_{25} (L/s)	baseline	6.17 ± 0.56	43.57 ± 2.70*	59.48 ± 5.04*†
	LRLN	5.17 ± 0.38	34.34 ± 2.14	35.53 ± 1.64§
PEF (L/s)	baseline	9.25 ± 0.94	56.68 ± 5.24*	71.71 ± 5.86*†
	LRLN	8.06 ± 0.53	56.54 ± 3.25	65.22 ± 2.19
EF_{50} (L/s)	baseline	6.15 ± 0.35	47.02 ± 7.38*	65.76 ± 8.09*†
	LRLN	5.27 ± 0.65	50.35 ± 3.67	61.40 ± 1.81
EF_{25} (L/s)	baseline	5.25 ± 0.54	36.61 ± 3.38*	53.15 ± 5.50*†
	LRLN	4.88 ± 0.49	34.75 ± 2.58	45.02 ± 1.14
PEF/PIF	baseline	1.33 ± 0.07	1.13 ± 0.06	0.97 ± 0.07
	LRLN	1.35 ± 0.10	1.58 ± 0.05§	1.70 ± 0.03§
EF_{50}/IF_{50}	baseline	1.25 ± 0.11	1.19 ± 0.11	1.08 ± 0.17
	LRLN	1.11 ± 0.15	2.15 ± 0.12§	2.56 ± 0.04§
Vol PIF (L)	baseline	1.87 ± 0.41	3.56 ± 0.32*	5.79 ± 0.33*†
	LRLN	2.74 ± 0.42	2.52 ± 0.17	2.74 ± 0.17§
Vol PEF (L)	baseline	5.07 ± 0.90	8.94 ± 0.80*	10.15 ± 1.31*
	LRLN	5.61 ± 0.34	8.15 ± 0.26	8.59 ± 0.40

T_I = inspiratory time, T_E = expiratory time, V_T = tidal volume, PIF = peak inspiratory flow, IF_{50} = inspiratory flow at 50% of V_T, IF_{25} = inspiratory flow at 25% of V_T, PEF = peak expiratory flow, EF_{50} = expiratory flow at 50% of V_T, EF_{25} = expiratory flow at 25% of V_T, Vol PIF = volume at peak inspiratory flow, Vol PEF = volume at peak expiratory flow.

* Data significantly different ($P < 0.05$) from period A.
† Data significantly different ($P < 0.05$) from period B.
§ Data significantly different ($P < 0.05$) from baseline measurement at same speed.
‡ Values represent means and SEM.

Table 3 - Coefficients of variation for various tidal breathing flow-volume loop indices from the 6 horses before (baseline) and after left recurrent laryngeal neurectomy (LRLN).

Variable	Surgical Status	Exercise level		
		A	B	C
		$\bar{x}$CV(CV)	$\bar{x}$CV(CV)	$\bar{x}$CV(CV)
T_E/T_I	baseline	19.8 (0.5)	4.78 (0.5)	4.35 (0.4)
	LRLN	12.8 (0.5)	4.2 (0.3)	5.0 (0.7)
T_I/T_{TOT}	baseline	9.82 (0.5)	2.35 (0.5)	2.115 (0.4)
	LRLN	6.0 (0.3)	1.3 (0.4)	1.8 (0.7)
V_T/T_I	baseline	16.32 (0.3)	3.96 (0.6)	3.255 (0.5)
	LRLN	12.7 (0.4)	2.7 (0.8)	3.2 (1.2)
PIF (L/s)	baseline	19.93 (0.3)	6.57 (0.4)	3.16 (0.8)
	LRLN	12.3 (0.4)	3.5 (0.7)	3.6 (0.7)
IF_{50} (L/s)	baseline	24.14 (0.2)	9.04 (0.5)	5.83 (0.7)
	LRLN	13.5 (0.3)	5.7 (0.3)	6.2 (0.8)
IF_{25} (L/s)	baseline	21.9 (0.5)	6.69 (0.4)	5.28 (0.7)
	LRLN	15.0 (0.4)	5.0 (0.6)	6.6 (1.2)
PEF/PIF	baseline	20.80 (0.5)	7.38 (0.4)	5.1 (0.6)
	LRLN	12.2 (0.3)	5.5 (0.6)	3.8 (0.8)
EF_{50}/IF_{50}	baseline	31.86 (0.5)	11.81 (0.3)	7.44 (0.5)
	LRLN	16.0 (0.4)	8.0 (0.3)	7.2 (0.7)
Vol PIF (L)	baseline	66.1 (0.5)	10.37 (0.4)	16.42 (1.4)
	LRLN	68.0 (0.6)	5.2 (0.4)	7.2 (0.4)

$\bar{x}$CV = Mean coefficients of variation calculated from the coefficient of variation for the 10 flow-volume loops analyzed for each horse at each exercise period.

(CV) = Coefficient of variation of the calculated mean coefficient of variation of the 6 horses.

See Table 2 for key.

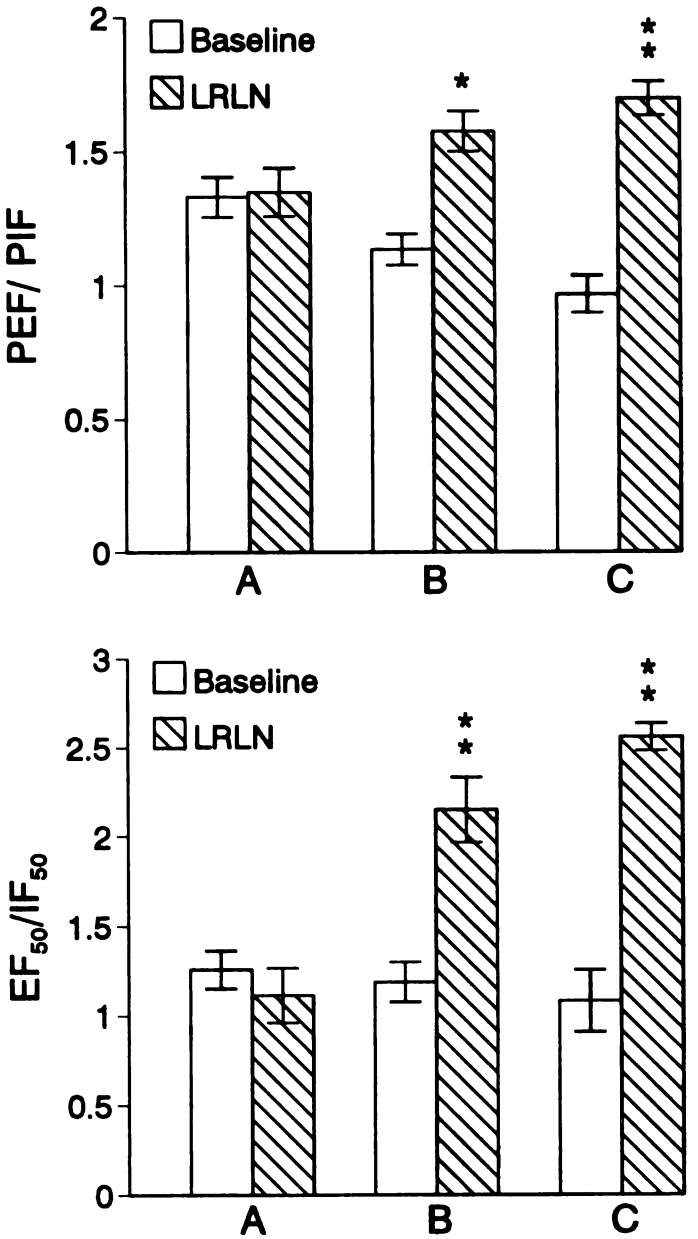

Figure 9. Peak expiratory flow-to-peak inspiratory flow ratio (PEF/PIF) and expiratory-to-inspiratory flow ratio at mid-tidal volume (EF_{50}/IF_{50}) before and after LRLN at rest and exercise. Baseline = prior to LRLN; LRLN = 14 days after LRLN; * = data significantly ($P < 0.05$) different from baseline measurement at same speed; ** = data significantly ($P < 0.01$) different from baseline measurement at same speed.

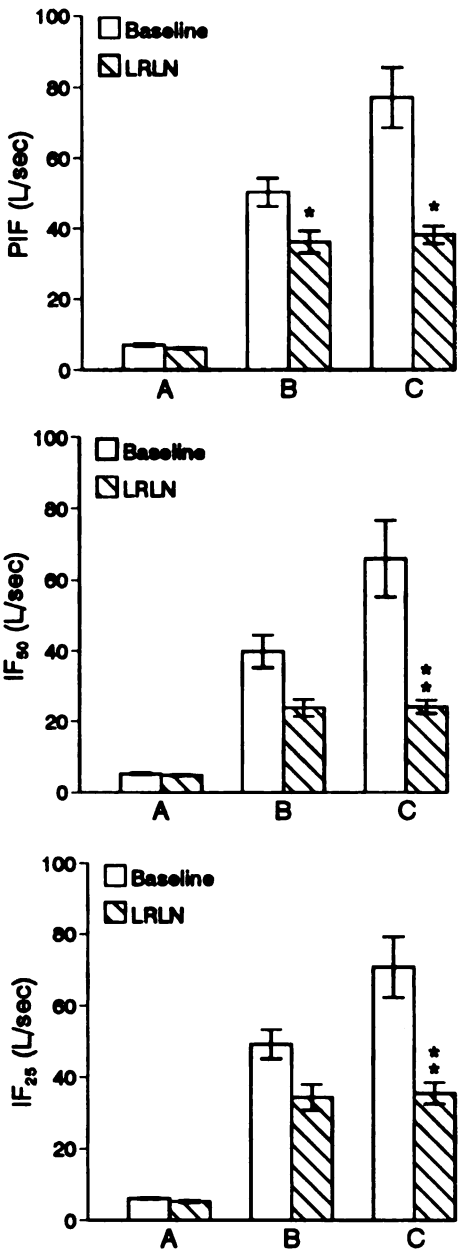

Figure 10. Peak inspiratory flow (PIF), inspiratory flow at mid-tidal volume (IF_{50}), and inspiratory flow at end tidal volume plus 25% tidal volume (IF_{25}) before and after LRLN at rest and exercise. Baseline = prior to LRLN; LRLN = 14 days after LRLN; * = data significantly ($P < 0.05$) different from baseline measurement at same speed; ** = data significantly ($P < 0.01$) different from baseline measurement at same speed.

E. Discussion

Quantitative evaluation of upper airway function during exercise has been repeatedly performed by measurement of peak airflow rates, peak pressure changes, and the calculation of impedance in clinically normal horses and horses with upper airway obstruction induced by LRLN (Derksen et al,1986; Shappell et al,1988; Belknap et al,1990; Fulton et al,1991; Mangseth,1984; Funkquist et al,1988). This standard technique of measuring upper airway flow mechanics necessitates the invasive and time-consuming placement of a transtracheal catheter. Furthermore, the time required for calculation of inspiratory and expiratory impedances makes the technique inconvenient. Measurement of tracheal pressures via a nasotracheal catheter provides a less invasive alternative to percutaneous placement (Williams et al,1990:I). Such measurement of tracheal pressures has been advocated as a clinically useful test of upper airway function (Williams et al,1990:I; II). However, tracheal pressure is not only influenced by upper airway geometry, but also by the pattern of breathing and airflow rates (Fry and Hyatt,1960). Therefore, changes in tracheal pressure in exercising horses are difficult to interpret.

In contrast, the measurement of TBFVL in horses at rest and during exercise was non-invasive and easily performed. As noted, horses adapted easily to the treadmill and tolerated the face mask well (Morris and Seeherman,1991; Shappell et al,1988; Belknap et al,1990; Fulton et al,1991). Furthermore, with the aid of recently developed computer software, analysis

of TBFVL was convenient and rapid, and was completed immediately after the measurement period.

Qualitative analysis in resting horses—Tidal breathing flow-volume loops recorded from horses at rest indicated inter- and intrahorse variability in shape, tidal volume, and airflow rates. Interestingly, the inspiratory limb of the TBFVL was uniphasic in some horses and polyphasic in others (Figure 5). Similar variations in TBFVL shape were reported in resting ponies by Art and Lekeux (1988). In contrast, TBFVL in resting dogs have uniphasic inspiratory and expiratory limbs (Amis and Kurpershoek,1986). In dogs, Amis and Kurpershoek described 4 distinct TBFVL shapes, which differed principally on the basis of location of the peak inspiratory flow. Similar variations in the location of peak inspiratory flow were found in our horses. Differences in TBFVL shapes between these 2 species are probably a reflection of differing breathing strategies known to exist between dogs and horses (Kosch,1985).

Coefficients of variation of TBFVL indices ranged from 9.82 to 66.1% in horses at rest and were much higher than those seen at exercise. This reflects the greater variability in breathing strategy adopted by resting horses, compared with exercising horses. This large coefficient of variation limits the clinical usefulness of TBFVL obtained in standing horses. Similar large coefficients of variation (1 to 46%) have been reported in dogs (Amis and Kupershoek,1986).

Effect of LRLN in resting horses—After LRLN, horses at rest did not have significant changes in TBFVL indices or in Z_I and Z_E. At rest, during quiet

breathing, airway pressures are insufficient to cause dynamic collapse of the arytenoid cartilage in horses with LLH (Robinson and Sorenson,1978; Derksen et al,1986). Likewise, no differences in loop shapes were appreciable before and after LRLN in horses at rest. The TBFVL are also insensitive in detection of upper airway obstruction in conscious dogs; thus, the clinical usefulness of the technique is limited to patients with advanced upper airway obstruction (Amis and Kurpershoek 1986; Amis et al,1986). From the aforementioned discussion, it is clear that determination of TBFVL does not enable detection of LLH in standing horses.

Qualitative evaluation in exercising horses—In human medicine, determination of maximal FVL is considered to be a non-invasive, rapid, sensitive, and specific clinical diagnostic tool, aiding in the detection and evaluation of upper airway obstruction (Miller and Hyatt,1969; Miller and Hyatt,1973; Kashima,1984). However, to achieve a maximal FVL, the technique requires patient cooperation and maximal respiratory effort, resulting in high airflow rates (Miller and Hyatt,1969).

In exercising horses, airflow rate is greatly increased whereas variability in breathing strategy is reduced (Hörnicke et al,1983; Hörnicke et al,1987). Therefore, we hypothesized that the sensitivity of TBFVL in detecting upper airway obstruction in non-cooperative patients, like our horses, may be markedly enhanced during strenuous treadmill exercise. The TBFVL obtained in healthy, non-athletic people during exercise only impinge on their maximal FVL near end expiration (Olafsson and Hyatt,1969; Babb et al,1991).

However, in well-trained young men, TBFVL obtained during maximal exercise approach much of the maximal expiratory flow curve of their maximal FVL (Grimby et al, 1971). These exercising TBFVL in people are associated with near-maximal airflow rate and tidal volume that approximates 50% of vital capacity. Similarly, in our study, airflow rate approached maximal flow rate (Leith,1976) and tidal volume was approximately 50% of predicted vital capacity (Davidson et al,1986). We reasoned that if a similar ventilatory response to exercise is also true in performance horses, TBFVL obtained during maximal exercise may be as sensitive as maximal FVL for detection of airway obstruction. In this study, the ability of TBFVL determination to detect upper airway obstruction in horses at rest and during exercise, using TBFVL analysis, was compared with the standard technique that involves measurement of peak driving pressure, airflow change, and calculation of inspiratory and expiratory impedances.

To standardize the exercise protocol, maximal heart rate was first determined in each individual horse. In subsequent measurement protocols, horses were exercised at treadmill speeds correlating to $HR_{0.75max}$ and HR_{max}. Exercise was standardized in this way in an attempt to minimize variability in airflow rates between horses at each measurement period. Indeed, coefficients of variation for TBFVL indices obtained during exercise in our horses were smaller than those obtained in resting horses. The progressive decrease in coefficients of variation for TBFVL indices, with increasing exercise level (Table 3), indicates that respiratory patterns became less variable during exercise. The

greater consistency of TBFVL seen during exercise, compared with that of TBFVL at rest is likely attributable to the high ventilatory requirements imposed. Furthermore, breathing pattern is imposed by a coupling of respiratory rate and stride frequency (Hörnicke et al,1983); thus the observed decrease in coefficients of variation for TBFVL indices may, in part, reflect the decreased variation in gait between horses at exercise period C. The shape of the TBFVL during exercise is likely influenced by gait, stride frequency, and the mechanical events related to locomotion, such as acceleration, deceleration, and weight bearing (Attenburrow,1983). Because we did not measure aspects of locomotion such as stride frequency and length and because we did not standardize gait, the effects of locomotion on shape of the TBFVL cannot be determined.

Different gaits observed between horses within exercise periods may potentially influence values for various respiratory variables; including f, V_T, airflow, and airway pressures. Although, differences in V_T and f in apparently normal horses, using trotting/pacing and galloping gaits, has been reported (Hörnicke et al,1983) in our horses the different gaits observed at period B after LRLN did not result in large interhorse variability of values for the respiratory variables measured. This is most likely attributable to the uncoupling of the 1:1 ratio between respiratory rate and stride frequency, allowing galloping horses to use a higher V_T after LRLN.

The observed ventilatory patterns and TBFVL shapes seen at rest and during exercise may reflect influences of rebreathing of gases, the added

impedance imposed by the mask-pneumotachograph breathing system, or a combination of these 2 factors. Previous studies indicated that various types of breathing apparatuses worn during exercise reduces respiratory frequency, may change stride frequency-to-ventilation ratios, and alter arterial blood gas tensions (Bisgard et al,1978; Bayley et al,1987). As neither arterial blood gas nor end-tidal CO_2 evaluation was measured in this study the extent of rebreathing CO_2 and its effects on TBFVL shapes observed is unknown. The pressure change across the mask-pneumotachograph at peak inspiratory airflow rates in this study was approximately 10% of peak inspiratory transupper airway pressures and, therefore, is likely to minimally effect ventilatory response to exercise.

Quantitative evaluation in exercising horses—The increases in peak flow rates, peak transupper airway pressures, and the minimal change in peak impedance associated with increased exercise prior to LRLN have been reported (Table 1) (Shappell et al,1988; Belknap et al,1990; Fulton et al,1991). This study extended those observations and documented that a progressive increase in exercise intensity was associated with an increase in airflow rates throughout the respiratory cycle. Indeed, because flow ratios were not significantly affected by increasing exercise, these data indicate that inspiratory and expiratory flows may be increased equally.

Effect of LRLN in exercising horses—After LRLN, P_{UI}, Z_I, and T_I/T_{TOT} increased and PIF, T_E/T_I, and V_T/T_I decreased in exercising horses, whereas P_{UE}, PEF, and Z_E remained unaffected (Tables 1 and 2). These data indicate that

LRLN causes upper airway obstruction on inhalation as a result of dynamic collapse of the left arytenoid cartilage. The validity of LRLN as a model of naturally acquired LLH was confirmed by a recent report (Williams et al,1990:II). The tracheal pressure changes measured after experimentally induced LLH were comparable to those measured in horses with naturally acquired LLH.

Flow-volume loop shapes obtained from exercising horses after LRLN were easily distinguished from those recorded prior to LRLN at the same level of exercise. The TBFVL shape was typified by a pronounced flattening of the inspiratory flow curve. After the initial PIF, inspiratory flow decreased markedly and remained constant until immediately before the onset of exhalation. This flow profile indicates flow limitation during the last two-thirds of the inspiratory portion of the tidal volume. Videoendoscopy during exercise in horses with induced LLH indicates that, on exhalation, the affected arytenoid cartilage is moved abaxially, probably as a result of intraluminal pressures that are positive with respect to atmospheric pressure. Immediately after the onset of inhalation, the affected arytenoid cartilage moves axially to almost completely obstruct the rima glottidis. This cartilage remains in this axial position throughout inhalation. The initial PIF observed in TBFVL obtained from exercising horses after LRLN probably develops before the axial movement of the affected cartilage has been completed. The period of flow limitation apparently corresponds to the period during which the affected arytenoid cartilage is in the maximally displaced position.

The expiratory limb of the TBFVL in exercising horses was unaffected by LRLN. The shape of the inspiratory portion of the TBFVL, coupled with the preservation of the shape of the pre-LRLN expiratory flow curve, is characteristic of dynamic upper airway lesions (Miller and Hyatt,1969). The effects of upper airway obstruction on FVL depends on size and location of the lesion and the fixed or variable nature of the lesion (Miller and Hyatt,1969). Miller and Hyatt,(1969) proposed a classification of upper airway obstruction and described how these abnormalities affect the FVL. They classified obstructions into 3 functional groups on the basis of pressure-flow relations around the lesion site: fixed obstruction; variable extrathoracic obstruction; and variable intrathoracic obstruction. Variable obstructions are substantially affected by changes in transmural pressure and subsequently may result in dynamic collapse. Thus, intrathoracic lesions result in predominantly expiratory flow limitation, whereas extrathoracic lesions cause a reduction in inspiratory gas flow. Fixed obstructions exert flow-limiting effects on both phases of respiration. The changes in the shape of TBFVL induced by LRLN in exercising horses were characteristic of variable extrathoracic obstruction.

The observed changes in TBFVL shape are supported by the numerical data (Table 2). The TBFVL indices describing exhalation were unaffected by LRLN. In contrast, in exercising horses, LRLN resulted in significant reduction of PIF, IF_{50}, and IF_{25}, and an increase in PEF/PIF and EF_{50}/IF_{50}. The largest percentage change was observed in the IF_{50}, which decreased by 40.4 and 63.5% at periods B and C, respectively. The change in the EF_{50}/IF_{50} after LRLN

was highly significant ($P < 0.01$) even at measurement period B. This indicates that these 2 loop indices may be most useful in the detection of dynamic upper airway obstruction in exercising horses. Originally identified as a potential sensitive indicator of variable extrathoracic obstruction in human beings (Jordanoglou and Pride,1968), the IF_{50} and EF_{50}/IF_{50} may reflect near-maximal inspiratory airflow limitation associated with the point of complete dynamic collapse of the left arytenoid cartilage (Derksen,1988). This earlier prediction was recently confirmed by a large study in people that concluded that the IF_{50} is the most reliable indicator of dynamic upper airway obstruction (Polverino et al,1990). The mean value of 2.56 for EF_{50}/IF_{50} in our study was similar to values reported in a series of clinical cases involving human patients with dynamic extrathoracic lesions (Kashima,1984; Miller and Hyatt,1969). However, in such adult human studies, maximal FVL are achieved, whereas in our study, TBFVL were obtained through exercise. Comparison of these data therefore indicates that TBFVL obtained during high-speed exercise may be as sensitive for detection of upper airway obstruction as is maximal FVL.

In conclusion, results of this study indicate that analysis of TBFVL in exercising horses allows detection of upper airway obstruction induced by LRLN. After LRLN in exercising horses, the shape of the TBFVL was characteristic for a variable extrathoracic obstruction. Indices of mid-tidal inspiratory flow (IF_{50} and EF_{50}/IF_{50}) were most sensitive for detection of upper airway obstruction. Because the technique was quantitative, rapid, non-invasive, and well tolerated by horses, TBFVL analysis may become a useful

diagnostic tool in conjunction with upper airway endoscopy during exercise for evaluation of naturally acquired upper airway obstruction in horses.

VI. EVALUATION OF PARTIAL ARYTENOIDECTOMY AS A TREATMENT FOR EQUINE LARYNGEAL HEMIPLEGIA

A. Summary

The efficacy of partial arytenoidectomy was assessed in 6 Standardbred horses, with surgically-induced laryngeal hemiplegia, at rest (period A) and during exercise at speeds corresponding to maximum heart rate (period C) and 75% of maximum heart rate (period B). Peak expiratory and inspiratory airflow rate (PEF and PIF), and expiratory and inspiratory transupper airway pressure (P_{UE} and P_{UI}) were measured and, expiratory and inspiratory impedance (Z_E and Z_I) were calculated. Simultaneously, tidal breathing flow-volume loops (TBFVL) were acquired using a respiratory function computer. Indices derived from TBFVL included, airflow rates at 50 and 25% of tidal volume (EF_{50}, IF_{50}, EF_{25}, and IF_{25}) and the ratios of expiratory to inspiratory flows. Measurements were made before left recurrent laryngeal neurectomy (baseline), 2 weeks after left recurrent laryngeal neurectomy (LRLN), and 16 weeks after left partial arytenoidectomy coupled with bilateral ventriculectomy (ARYT).

After LRLN, during exercise periods B and C, Z_I and the ratio of EF_{50}/IF_{50} significantly increased and PIF, IF_{50} and IF_{25} significantly decreased from baseline values. Sixteen weeks after ARYT, Z_I returned to baseline values at exercise periods B and C. Although PIF, IF_{50}, IF_{25}, PEF/PIF, and EF_{50}/IF_{50} returned to baseline values at exercise period B, these indices remained significantly less than baseline measurements during exercise period C. After

ARYT, TBFVL shapes from horses at exercise period C approached that seen at the baseline evaluation.

Partial arytenoidectomy improves upper airway function in exercising horses with surgically-induced left laryngeal hemiplegia, though qualitative and quantitative evaluation of TBFVL's suggest that some flow limitation remains at near maximal airflow rates. These results suggest that, although the procedure does not completely restore the upper airway to normal, partial arytenoidectomy is a viable treatment option for failed laryngoplasty and arytenoid chondropathy in the horse.

B. Introduction

Partial arytenoidectomy, the removal of the arytenoid and corniculate cartilages while leaving the muscular process in situ, was first introduced as a treatment for left laryngeal hemiplegia (LLH) in 1845 (Liautard,1892). This procedure was considered unsatisfactory because it was associated with a high rate of post-operative complications. With the development of the ventriculectomy (Williams,1911) and later prosthetic laryngoplasty (Marks et al,1970:II), the low morbidity and mortality of these procedures obviated the use of arytenoidectomy as a treatment for LLH. Subtotal arytenoidectomy, the removal of the arytenoid body leaving the muscular process and corniculate cartilage intact, and partial arytenoidectomy have been recommended as treatments for arytenoid chondropathy (Haynes et al,1980; Tulleners et al,1988:I), arytenoid malformations and failed prosthetic laryngoplasty (White

and Blackwell,1980; Haynes et al,1984). The merits of these two techniques have been evaluated subjectively based on assessment of performance and post-operative complications (Haynes et al,1984; Speirs,1986; Tulleners et al,1988:I).

In 1990, Belknap et al, quantitatively evaluated subtotal arytenoidectomy and demonstrated that subtotal arytenoidectomy failed to improve upper airway function in horses with surgically-induced LLH exercising submaximally. To date, there has been no objective evaluation of the efficacy of partial arytenoidectomy.

Upper airway function in exercising horses has been quantitated by measurement of transupper airway pressure and airflow, and calculation of inspiratory and expiratory impedance (Derksen et al, 1986). As reported in chapter V, analysis of tidal breathing flow-volume loops (TBFVL), is a useful, sensitive, convenient and non-invasive technique, for quantitation of upper airway obstruction in exercising horses. In the present study, the effect of partial arytenoidectomy on upper airway function was evaluated by TBFVL analysis, measurement of upper airway impedance and videoendoscopic examination of the larynx in strenuously exercising horses with surgically-induced LLH.

C. Materials and Methods

Horses—As outlined in chapter V, the 6 adult Standardbred horses used in this project were maintained on pasture between surgical procedures and measurement protocols.

Measurement techniques—Airflow rates, tidal volume and transupper airway pressure were recorded as described in chapter V. Simultaneous with measurements of airflow and airway pressure, TBFVL were obtained for horses at rest and during exercise as outlined in chapter V. The shape of TBFVL generated and the mean ± SEM of measured values and derived indices were also obtained.

Experimental design—As described in the preliminary study (chapter V), treadmill speeds at which maximum heart rate (HR_{max}) and 75% of maximum heart rate ($HR_{0.75max}$) occurred were estimated.

All data were recorded during the last minute of each 2-min measurement period. Measurements were made while horses were at rest, standing adjacent the treadmill (period A). Subsequently, horses were exercised on the treadmill with a 3-degree incline at 4 m/sec for 2 min, then at the treadmill speed corresponding to $HR_{0.75max}$ for 2 min (period B). Horses rested for 1 min and then exercised at a treadmill speed corresponding to HR_{max} (period C) for 2 min.

Measurements obtained before left recurrent laryngeal neurectomy (baseline) and 2 weeks after LRLN (LRLN) reported in Chapter V were designed to evaluate the usefulness of TBFVL indices for detection of upper airway

obstruction. Sixteen weeks after left partial arytenoidectomy and bilateral ventriculectomy (ARYT), horses underwent the same measurement protocol as for baseline and LRLN measurements. On the day following each measurement of upper airway function, the larynx of each horse was examined using videoendoscopy at rest and during exercise at HR_{max}.

Surgical Procedures

Induction of laryngeal hemiplegia was performed by transection of the left recurrent laryngeal nerve (Derksen et al,1986). Left partial arytenoidectomy was performed as follows. Anaesthesia was induced with guiafenesin (Aceto Chemical Co, Flushing, NY.) and thiamylal (Biotal, Bioceutic Division, Boehringer Ingelheim Animal Health Inc, St Joseph, Mo.). The animals were intubated via a mid-cervical tracheotomy and anaesthesia was maintained with halothane (Fluothane, Ayerst Laboratories Inc, New York, NY.) in oxygen. Partial arytenoidectomy was performed as previously described by McIlwraith and Turner (1987), except that the corniculate cartilage and its mucosa were removed en bloc, and a bilateral ventriculectomy was performed. Via a ventral laryngotomy a fiberoptic retractor (Shea fiberoptic retractor, Stryker Corp, Kalamazoo, Mich.) was used to illuminate the lumen of the larynx. The mucosa was incised beginning at the ventral aspect of the junction of the corniculate and arytenoid cartilages and extending caudad along the ventral border of the arytenoid cartilage. This incision was continued along two-thirds of the caudal border of the arytenoid cartilage. The cranial aspect of the incision was extended along the entire junction of the corniculate and arytenoid cartilages.

The laryngeal mucosa was elevated from the luminal side of the arytenoid cartilage using a blunt Asheim knife. A separate incision was then made extending from the left laryngeal ventricle dorsally along the rostral border of the corniculate cartilage. The arytenoid and corniculate cartilages were then separated. The corniculate cartilage and attached luminal mucosa was removed en bloc, after dissecting the laryngeal musculature from its lateral aspect. The body of the arytenoid cartilage was similarly dissected from its lateral musculature and transected from its muscular process and removed, leaving the muscular process and intact luminal mucosa. Bilateral ventriculectomy was then performed, and all free mucosal edges were apposed with 2-0 polydioxanone (PDS, Ethicon Inc, Somerville, NJ.) in a simple continuous pattern. Horses were treated preoperatively and postoperatively with procaine penicillin (Procaine penicillin G, Pfizer Inc, New York, NY) (10,000 IU/kg IM BID for 5 days), and phenylbutazone paste (Butazolidin paste, Coopers Animal Health Inc, Kansas City, Mo.) (3 mg/kg PO BID for 5 days). Food was withheld for 48 hours after surgery and tracheotomy tubes (Dyson self-retaining tracheal tubes, Coopers Animal Health Inc, Mishawaka, Ind.) were removed following endoscopic confirmation of an adequate airway at 24 hours. The larynx of each horse was endoscopically examined at rest 1, 4, 8 and 16 weeks postoperatively.

Statistical analysis of data obtained from this study were analyzed in the same manner as described in the preliminary study in chapter V.

D. Results

The HR_{max} and $HR_{0.75max}$ averaged 225.5 ± 4.92 bpm (mean +/- SEM) and 166.8 ± 3.9 bpm at treadmill speeds of 11.0 ± 0.2 m/s and 6.2 ± 0.7 m/s, respectively. The effect of exercise on all physiological parameters is shown in Table 1 and discussed in chapter V.

The effect of LRLN and partial arytenoidectomy on TBFVL shape is shown in Figure 11. The flattened shape of the inspiratory flow curve after LRLN (b) was altered after partial arytenoidectomy (c), to a shape that approached the inspiratory flow curve (a) generated at baseline evaluation. The effects of LRLN on the indices of upper airway function are shown in Table 4 and Figures 12-16.

Sixteen weeks after partial arytenoidectomy and bilateral ventriculectomy, P_{UI} and Z_I were not significantly different from baseline values during exercise periods B and C (Table 4;Figure 12). Furthermore, all indices describing TBFVL returned to baseline (pre-LRLN) values at period B (Table 4;Figures 14-16). However, PIF, IF_{50}, IF_{25}, PEF/PIF, EF_{50}/IF_{50}, T_E/T_I, T_I/T_{TOT}, and V_T/T_I remained significantly different from the baseline value at exercise period C (Table 4;Figures 12,14,15). Expiratory flow rates were unaffected by either LRLN or ARYT at all exercise levels (Figures 13,16).

Left laryngeal hemiplegia was confirmed using videoendoscopic evaluation of the larynx at rest and during exercise in all horses. Following partial arytenoidectomy and bilateral ventriculectomy, no post-operative complications were encountered other than minor dehiscence of the sutured

mucosa in two horses. Evidence of dysphagia or coughing was not noted either at rest or during exercise. Endoscopic examination in the resting horse at 16 weeks showed complete mucosal healing. The right corniculate cartilage appeared rotated toward the left side in all horses at rest and during exercise.

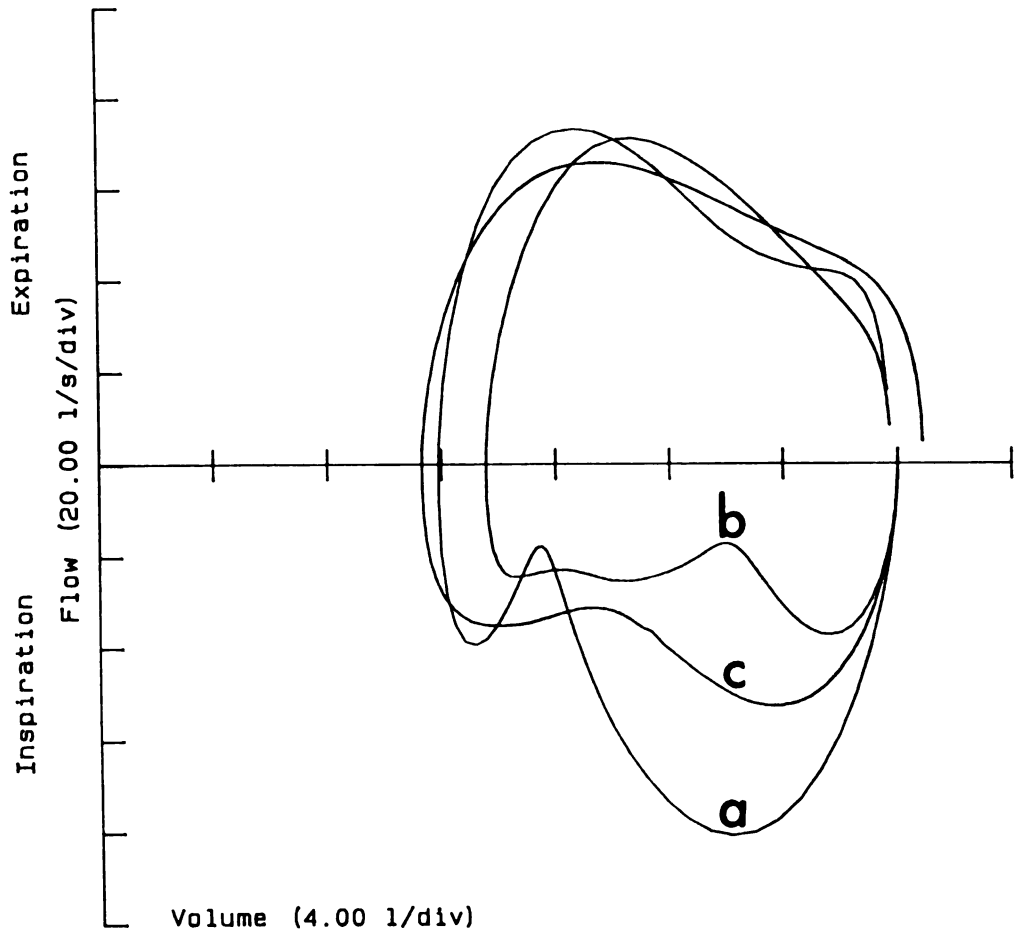

Figure 11. TBFVL's from a horse at baseline (a), after LRLN (b), and following partial arytenoidectomy and bilateral ventriculectomy (c). TBFVL were generated at a speed corresponding to maximal heart rate.

Table 4 - Effect of surgery on measured and calculated variables from 6 horses with surgically induced left laryngeal hemiplegia before (pre-operative) and after (post-operative) left partial arytenoidectomy and bilateral ventriculectomy.

Variable	Exercise Period	Baseline‡	Pre-operative‡	Post-operative‡
$\dot{V}_E$ (litre/min)	A	151.41 ± 15.01	140.75 ± 7.69	138.40 ± 12.12
	B	950.23 ± 59.02	808.40 ± 68.29	963.80 ± 39.60
	C	1,295.97 ± 127.52	1,027.60 ± 71.17*	1178.50 ± 38.58
P_{UI} (cm of H_2O)	A	1.94 ± 0.22	2.16 ± 0.32	1.87 ± 0.23
	B	22.29 ± 1.15	49.40 ± 4.08*	26.12 ± 3.20†
	C	38.57 ± 3.93	62.73 ± 6.70*	39.99 ± 4.39†
PIF (litre/sec)	A	5.09 ± 0.34	5.84 ± 0.39	6.49 ± 0.55
	B	51.19 ± 4.05	36.58 ± 2.74*	43.28 ± 1.82
	C	75.52 ± 9.35	40.87 ± 3.23*	50.09 ± 2.16*
Z_I (cm of H_2O/litre/sec)	A	0.39 ± 0.03	0.38 ± 0.06	0.30 ± 0.04
	B	0.46 ± 0.06	1.41 ± 0.20*	0.62 ± 0.10†
	C	0.53 ± 0.04	1.63 ± 0.28*	0.81 ± 0.10†
IF_{50} (litre/sec)	A	5.24 ± 0.31	4.84 ± 0.18	5.82 ± 0.31
	B	39.86 ± 4.08	23.77 ± 1.61*	37.87 ± 1.95
	C	65.98 ± 8.47	24.09 ± 1.03*	36.24 ± 1.30*
IF_{25} (litre/sec)	A	6.17 ± 0.56	5.17 ± 0.38	5.90 ± 0.31
	B	49.77 ± 2.70	34.34 ± 2.14*	42.03 ± 1.92
	C	70.78 ± 5.04	35.53 ± 1.64*	47.89 ± 2.17*
PEF/PIF	A	1.33 ± 0.07	1.35 ± 0.10	1.25 ± 0.07
	B	1.13 ± 0.06	1.58 ± 0.05*	1.19 ± 0.02†
	C	0.97 ± 0.07	1.70 ± 0.03*	1.36 ± 0.02*†
EF_{50}/IF_{50}	A	1.25 ± 0.11	1.11 ± 0.15	1.13 ± 0.12
	B	1.19 ± 0.11	2.15 ± 0.12*	1.27 ± 0.02†
	C	1.08 ± 1.07	2.56 ± 0.04*	1.72 ± 0.08*†
T_E/T_I	A	0.99 ± 0.05	0.97 ± 0.05	0.95 ± 0.06
	B	0.94 ± 0.03	0.70 ± 0.02*	0.83 ± 0.01
	C	0.98 ± 0.05	0.65 ± 0.01	0.73 ± 0.01*
T_I/T_{TOT}	A	0.51 ± 0.01	0.52 ± 0.01	0.52 ± 0.02
	B	0.51 ± 0.01	0.59 ± 0.01*	0.55 ± 0.004
	C	0.51 ± 0.01	0.61 ± 0.01*	0.58 ± 0.004*
V_T/T_I	A	4.84 ± 0.34	4.40 ± 0.14	5.19 ± 0.27
	B	31.77 ± 2.08	23.87 ± 1.70*	29.98 ± 1.03
	C	44.78 ± 5.03	25.70 ± 1.02*	34.47 ± 1.38*

* Data significantly ($P < 0.05$) different from baseline (before left recurrent laryngeal neurectomy) measurement at same speed. † Data significantly different from pre-operative measurement at same speed. ‡ Values represent mean and sem. V_T = tidal volume, $\dot{V}_E$ = minute ventilation, P_{UI} = peak inspiratory pressure, PIF = peak inspiratory flow, Z_I = peak inspiratory impedance, IF_{50} = inspiratory flow at 50% of V_T, IF_{25} = inspiratory flow at 25% of V_T, T_E = expiratory time, T_I = inspiratory time, T_{TOT} = total breath time

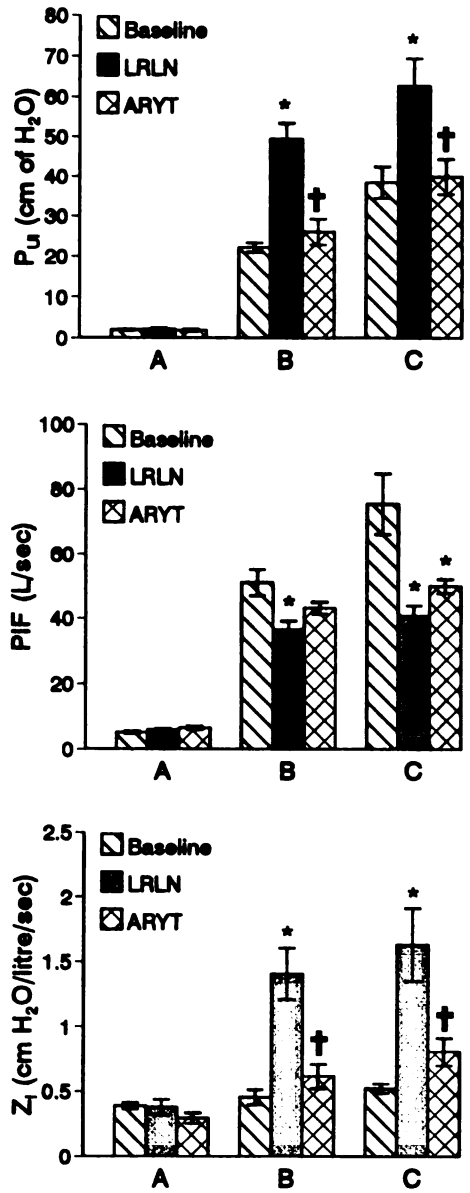

Figure 12. Peak inspiratory pressure (P_{UI}), peak inspiratory flow (PIF), and inspiratory impedance (Z_I) before and after LRLN, and after partial arytenoidectomy at rest (A) and during moderate (B) and strenuous (C) exercise. Baseline = prior to LRLN; LRLN = 2 weeks after LRLN; ARYT = 16 weeks after partial arytenoidectomy * = data significantly different from baseline measurement at same speed ($p < 0.05$). † = data significantly different from LRLN measurement at same speed ($p < 0.05$).

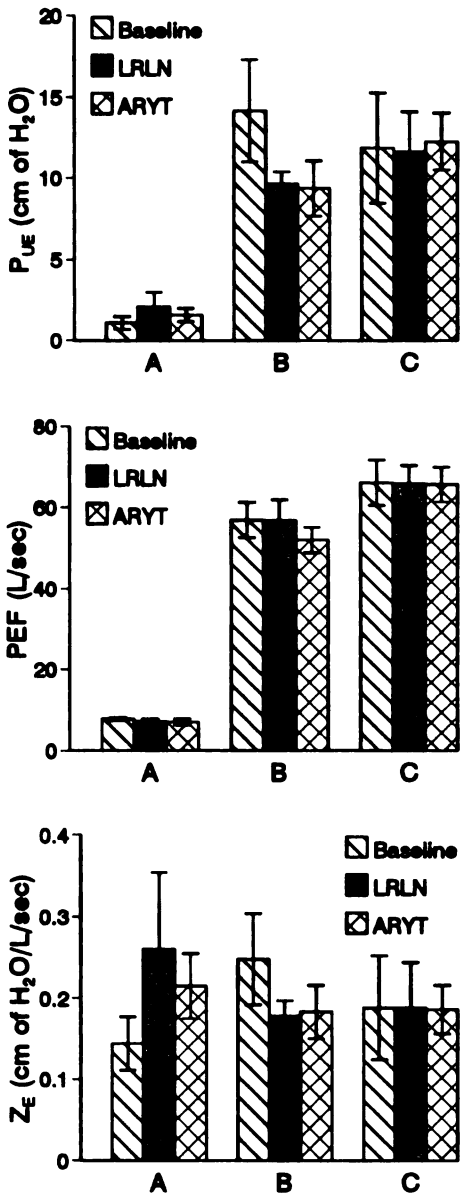

Figure 13. Peak expiratory pressure (P_{UE}), peak expiratory flow (PEF), and expiratory impedance (Z_E) before and after LRLN, and after partial arytenoidectomy at rest (A) and during moderate (B) and strenuous (C) exercise. Baseline = prior to LRLN; LRLN = 2 weeks after LRLN; ARYT = 16 weeks after partial arytenoidectomy.

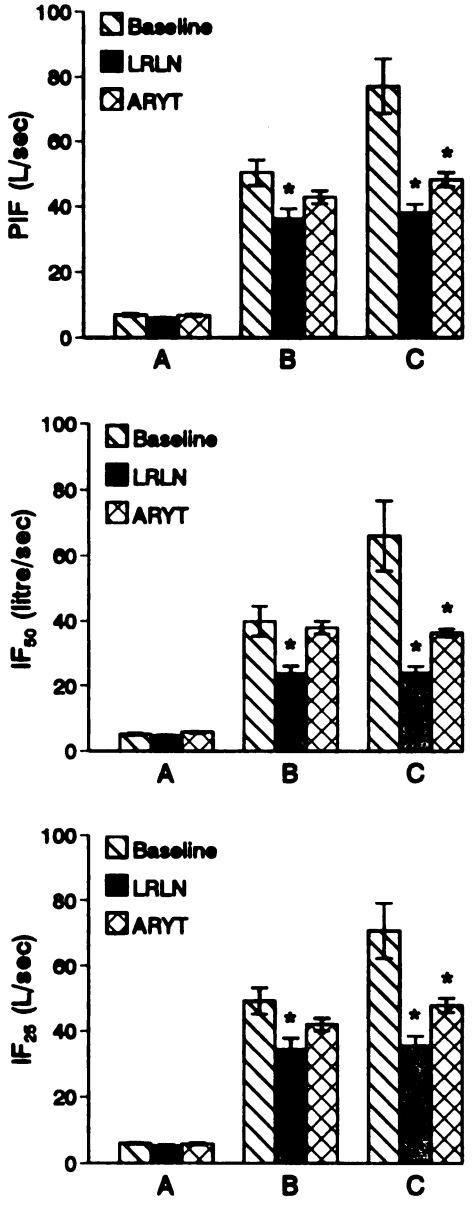

Figure 14. Peak inspiratory flow (PIF), inspiratory flow at mid-tidal volume (IF_{50}), and inspiratory flow at 25% tidal volume (IF_{25}) before and after LRLN, and after partial arytenoidectomy at rest (A) and moderate (B) and strenuous (C) exercise. Baseline = prior to LRLN; LRLN = 2 weeks after LRLN; ARYT = 16 weeks after partial arytenoidectomy. * = data significantly different from baseline measurement at same speed ($p < 0.05$).

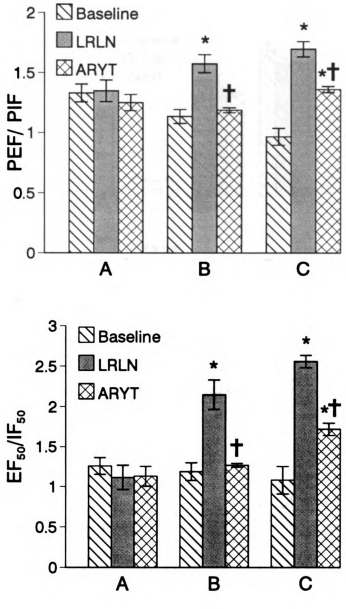

Figure 15. Peak expiratory flow / peak inspiratory flow ratio (PEF/PIF) and expiratory/ inspiratory flow ratio at mid-tidal volume (EF_{50}/IF_{50}) before and after LRLN, and after partial arytenoidectomy at rest (A) and moderate (B) and strenuous (C) exercise. Baseline = prior to LRLN; LRLN = 2 weeks after LRLN; ARYT = 16 weeks after partial arytenoidectomy * = data significantly different from baseline measurement at same speed ($p < 0.05$).† = data significantly different from LRLN measurement at same speed ($p < 0.05$).

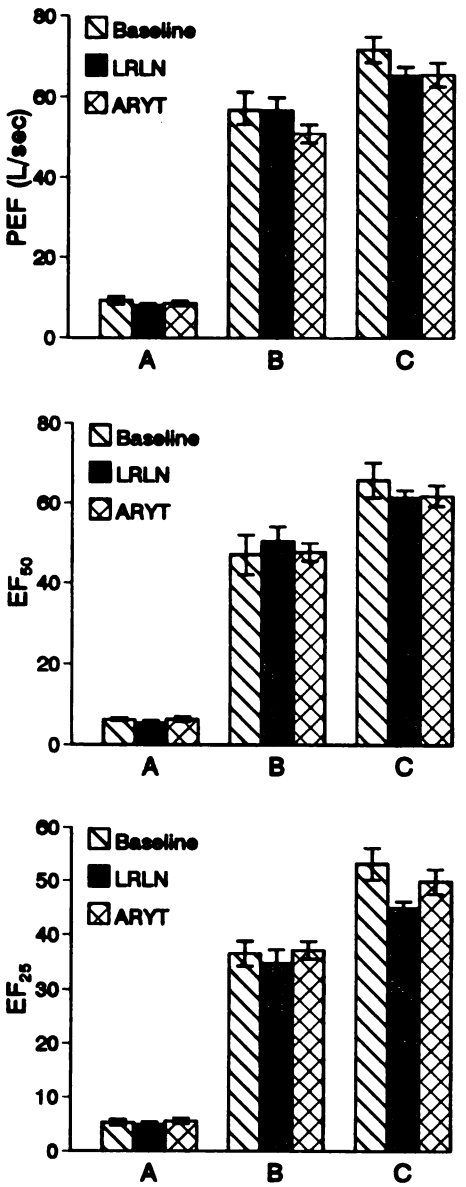

Figure 16. Peak expiratory flow (PEF), expiratory flow at mid-tidal volume (EF_{50}), and expiratory flow at 25% tidal volume (EF_{25}) before and after LRLN, and after partial arytenoidectomy at rest (A) and moderate (B) and strenuous (C) exercise. Baseline = prior to LRLN; LRLN = 2 weeks after LRLN; ARYT = 16 weeks after partial arytenoidectomy.

Sixteen weeks post-operatively, videoendoscopy during exercise at HR_{max} revealed an apparently adequate airway in all horses. Slow motion playback of the video recording made during exercise revealed minor centripetal movement of the left side of the larynx on inspiration in 4 horses with more pronounced inward movement observed in 2 horses. The latter two horses had the highest Z_l values during exercise period C.

E. Discussion

The aim of arytenoidectomy is to provide an airway of maximal cross-sectional area during exercise while preserving normal swallowing (Speirs,1986). Although Haynes et al,1984 suggested that these objectives can best be achieved using subtotal arytenoidectomy, dynamic inspiratory collapse of the remaining corniculate cartilage, may result in continued airway obstruction during exercise (Stick and Derksen,1989; Belknap et al,1990). Partial arytenoidectomy reportedly eliminates the collapsing corniculate cartilage (Stick and Derksen,1989) and may allow return to racing in approximately 50-75% of cases (Speirs,1986; Tulleners et al,1988:I). The technique has been associated with an unacceptably high incidence (36%) of dysphagia and/or coughing (Speirs,1986), but a large recent study found a much lower incidence of these complications (Tulleners et al,1988:I). Therefore, partial arytenoidectomy may be the preferred treatment for arytenoid chondritis and failed prosthetic laryngoplasty in performance horses, and was chosen for evaluation in the present study. We evaluated our horses 16 weeks after

surgery, because preliminary studies, using endoscopic examination of the larynx with horses standing, confirmed that the diameter of the rima glottidis appeared to continued to enlarge for up to 4 months after partial arytenoidectomy (Speirs,1986).

During moderate and strenuous exercise (Periods B and C, respectively), after partial arytenoidectomy, the airflow-generating transupper airway inspiratory pressures and inspiratory impedance did not differ from baseline values (Table 4; Figure 12), suggesting that partial arytenoidectomy restored upper airway function in horses with induced LLH. Additionally, during Period C, partial arytenoidectomy reversed the decrease in $\dot{V}_E$ observed after LRLN (Table 4). However, although Z_I and P_{UI} returned to baseline values after partial arytenoidectomy, PIF remained significantly reduced suggesting that this operation did not completely restore upper airway geometry. This became apparent only at the higher exercise level (Period C). Lack of tissue support may have allowed partial dynamic collapse of the left side of the larynx after partial arytenoidectomy.

Further information regarding the effects of partial arytenoidectomy on upper airway function was obtained using TBFVL analysis. After partial arytenoidectomy, measurements of inspiratory airflow during Period B did not differ significantly from baseline measurements (Table 4; Figures 14,15). In contrast, during more strenuous exercise (Period C), PIF and the TBFVL indices describing airflow throughout inspiration (IF_{50} and IF_{25}) remained significantly less than baseline values. Although PEF/PIF and EF_{50}/IF_{50} (Table 4; Figure 15),

were less than values obtained after LRLN, they remained significantly greater than baseline values.

The TBFVL in Figure 11 illustrates the reduced airflow throughout inspiration and preservation of airflow during expiration after LRLN. After partial arytenoidectomy, the TBFVL shape at Period C was characterized by an inspiratory curve intermediate between those observed post-LRLN and at baseline. Therefore, TBFVL evaluation suggests that partial arytenoidectomy eliminated the LLH-induced dynamic upper airway obstruction at submaximal exercise (Period B), but that some inspiratory flow limitation persisted during more strenuous exercise. When extending these findings to racing conditions it may be concluded that partial arytenoidectomy does not completely restore upper airway function in horses with LLH.

The leftward displacement of the right corniculate cartilage observed at rest and during exercise may have resulted from caudal retraction of rostral mucosa of the left side of the larynx, while leaving the transverse arytenoid ligament intact (Speirs,1986). The varied degrees of centripetal movement of the left side of the larynx during inspiration was probably the result of the semi-rigid nature of the tissue of the left side of the larynx after partial arytenoidectomy and the lack of left side abductor function. This centripetal movement, which appeared more pronounced in horses with more abundant mucosa, in conjunction with an airway of less than normal cross-sectional area, may explain the partial inspiratory flow limitation. The results of the present study support previous observations by others (Stick and Derksen,1989;

Belknap et al,1990) that unsupported structures, such as the corniculate cartilage, are a significant cause of upper airway obstruction after subtotal arytenoidectomy. Therefore, we recommend, removal of as much laryngeal mucosal as practical during surgery while permitting primary closure under minimal tension.

Although the decrease in Z_l that followed partial arytenoidectomy parallelled the decrease in Z_l after prosthetic laryngoplasty (Shappell et al,1988), accurate comparison of the efficacy of these two techniques in improving upper airway function in horses with LLH is impossible due to the higher treadmill speeds, higher peak airflows and lower treadmill incline reported in the present study. Despite these differences in exercise conditions, comparisons of upper airway impedance between these two studies would suggest that the two different surgical techniques have similar efficacy. In the present study, there were obvious discrepancies in the results from TBFVL and the calculation of Z_l during period C. Detection of persistent partial inspiratory obstruction after partial arytenoidectomy using TBFVL analysis, but not by evaluation of Z_l, indicates that the former technique is a more sensitive measure of upper airway function. Re-evaluation of prosthetic laryngoplasty for the treatment of LLH using TBFVL analysis may provide more detailed assessment of the ability of this surgical technique to restore upper airway function.

The horses in our study showed no evidence of coughing or dysphagia. However, in clinical cases, pre-existing laryngeal and peri-laryngeal pathology associated with arytenoid chondropathies and failed prosthetic laryngoplasty

may influence the incidence of serious post-operative complications and the efficacy of partial arytenoidectomy in restoring upper airway function (Speirs,1986; Tulleners et al,1988:I). Based on studies of upper airway flow mechanics, videoendoscopy in exercising horses and minimal post-operative complications, we recommend partial arytenoidectomy as the treatment of choice for arytenoid chondropathy and failed prosthetic laryngoplasty.

VII. CONCLUSIONS AND RECOMMENDATIONS

The results of this project provide important preliminary evidence for the usefulness of flow-volume loop analysis in the evaluation of upper airway obstructions in horses during exercise. The instantaneous generation of TBFVL and their flow indices by specifically programmed computer software facilitates the clinical use of this objective diagnostic tool. The significant change in TBFVL indices, seen with airway obstruction, in conjunction with the non-invasive nature of this test are a testimony for the use of this respiratory function test in a clinical setting.

The TBFVL acquired during exercise, following LRLN, are in agreement with laryngeal function observed videoendoscopically after induced and naturally occurring cases of LLH. Our understanding of the pathophysiology of various other upper airway obstructions, such as dorsal displacement of the soft palate, arytenoid chondropathy and epiglottic entrapment, may allow prediction of the shape of TBFVL acquired from such horses during exercise. Thus TBFVL analysis of these other causes of reduced exercise tolerance and poor performance may provide objective information as to nature and severity of the airway obstruction.

Although induced LLH, used in this project, represents a severe form of airway obstruction, it appears that TBFVL analysis may be a relatively sensitive indicator of airway obstruction. Following partial arytenoidectomy, Z_l returned to baseline values, but TBFVL indices improved only partially. This suggests

that TBFVL analysis is more sensitive than the measurement of Z_l in detection of upper airway obstruction. The clinical use of this technique may be of value in the detecting the effect of upper airway lesions such as recurrent laryngeal neuropathy, arytenoid chondropathy, dorsal displacement of the soft palate, epiglottic entrapment and pharyngeal lymphoid hyperplasia. The use of TBFVL analysis to evaluate these clinical entities may provide insight as to there significance as causes of airway obstruction.

Further studies evaluating the variability of TBFVL indices in a larger population of horses would provide an important step toward establishing a "normal" range of values for the upper airway. Investigation into the effect of the number of representative TBFVL evaluated and the effect of using varied levels of signal filtering may also provide important information to allow valid evaluations of clinical cases of airway obstruction.

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