



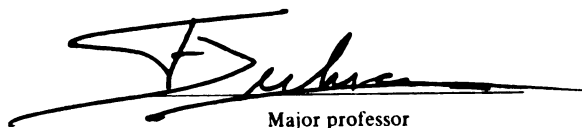
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Joanne Tetens

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**THE EFFICACY OF PROSTHETIC LARYNGOPLASTY
WITH AND WITHOUT BILATERAL VENTRICULOCORDECTOMY
AS TREATMENTS FOR LARYNGEAL HEMIPLEGIA IN HORSES**

By

Joanne Tetens

A THESIS

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ABSTRACT

THE EFFICACY OF PROSTHETIC LARYNGOPLASTY WITH AND WITHOUT BILATERAL VENTRICULOCORDECTOMY AS TREATMENTS FOR LARYNGEAL HEMIPLEGIA IN HORSES

By

Joanne Tetens

The objective was to evaluate the efficacy of prosthetic laryngoplasty with and without bilateral ventriculocordecotomy in the treatment of left laryngeal hemiplegia (LLH).

Fifteen adult Standardbred horses were divided into three groups. Sham operation, prosthetic laryngoplasty, and prosthetic laryngoplasty with bilateral ventriculocordecotomy were performed after induction of LLH. Measurements of upper airway function were obtained prior to left recurrent laryngeal neurectomy (LRLN), 14 days after LRLN, and 60 and 180 days after surgical treatment.

Left recurrent laryngeal neurectomy induced airway obstruction. In sham-operated horses, this obstruction was unaffected by time. In contrast, airway obstruction was reversed in the other groups with no difference between the 2 groups.

We conclude that 60 and 180 days after prosthetic laryngoplasty, upper airway function returns to pre-LRLN values in horses exercising at maximum heart rate. Also, combining ventriculocordecotomy with prosthetic laryngoplasty does not further improve upper airway function.

**In dedication to all the horses
who made this project possible**

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KEY TO ABBREVIATIONS

AT	arytenoideus transversus
bpm	beats per minute
CAD	cricoarytenoideus dorsalis
CAL	cricoarytenoideus lateralis
CR	crown-rump
EF ₂₅	expiratory flow at 25% of tidal volume
EF ₅₀	expiratory flow at 50% of tidal volume
f	respiratory frequency
FVL	flow-volume loop
HR	heart rate
HR _{0.75max}	75% of maximal heart rate
HR _{max}	maximal heart rate
IF ₂₅	inspiratory flow at 25% of tidal volume
IF ₅₀	inspiratory flow at 50% of tidal volume
ILH	idiopathic laryngeal hemiplegia
L/s	liters per second
L:R	left:right
LH	laryngeal hemiplegia
LRLN	left recurrent laryngeal neurectomy
LRLNv	left recurrent laryngeal nerve
MEFVC	maximum expiratory flow-volume curve
m/s	meters per second
PEF	peak expiratory flow
PIF	peak inspiratory flow
P _{uE}	peak expiratory pressure
P _{uI}	peak inspiratory pressure
RIET	rapid incremental exercise test
RRLNv	right recurrent laryngeal nerve
TBFVL	tidal breathing flow-volume loop
T _e	expiratory time
T _i	inspiratory time
T _{tot}	total breathing time
$\dot{V}_{min}$	minute ventilation
V _T	tidal volume
Z _E	expiratory impedance
Z _I	inspiratory impedance

Chapter 1

THE EQUINE LARYNX

The following section will present information regarding the evolution, embryology, development, structure, and function of the larynx. These topics are vital to the understanding of how the larynx functions in both health and disease; and how we, as veterinarians, may intervene to help re-establish normality in the diseased equine larynx.

Laryngeal Evolution

The larynx first evolved as a muscular sphincter in the wall of the alimentary canal. This sphincter encircled the proximal end of a tube leading into the air bladder or the lungs of lung fish. At this stage, there was no mechanism for active opening of the larynx (Getty, 1975).

The next evolutionary stage involved the development of muscle fibers which would dilate the larynx. Lateral cartilaginous plates (future arytenoid cartilages and part of the cricoid cartilage) developed for insertion of dilator muscle fibers so that a dilatory action in the margin of the glottis could be facilitated. These cartilaginous plates are present in newts and salamanders (Getty, 1975).

As the larynx continued to evolve, a fused cricothyroid cartilage developed from which the dilator muscle fibers would take origin and into which sphincter muscle fibers would insert (Getty, 1975).

Finally, in mammals, a joint appeared between the cricoid and thyroid components of the cricothyroid cartilage. This facilitated opening and closing of the laryngeal aperture. At the same time, the arytenoid cartilages became reduced in length, and the sphincteric muscles became divided to form the thyroarytenoideus, cricoarytenoideus lateralis (CAL), and arytenoideus transversus (AT) (Getty, 1975).

Embryology and Development

Since laryngeal development is essentially uniform in all mammals (Henick, 1993) and no detailed descriptions of equine laryngeal development are available, human, murine, and ovine laryngeal embryogenesis will be described.

Embryology and development can be divided into two periods: the embryonic period proper and the fetal period. The first 8 weeks of human intrauterine life constitute the embryonic period, which corresponds to an embryo with a crown-rump (CR) length of approximately 30 mm. The fetal period represents the last 7 months of gestation. The embryonic period proper has been described in terms of the Carnegie system of embryonic staging. This staging system utilizes morphologic criteria which are employed in a scheme of 23 stages. Since this system is not based on factors such as embryonic age and length, which do not necessarily coincide with morphological development, it allows greater precision in establishing the sequence and timing of developmental events (Tucker & O'Rahilly, 1972).

To simplify the discussion, laryngeal development will be divided into three anatomical divisions: laryngeal vestibule, laryngeal skeleton, and laryngeal musculature.

Prior to stage 8 (18 days of human intrauterine life) of the Carnegie system, no signs of foregut development are present. During stage 9 (20 days of human intrauterine life), the foregut begins to form. A median groove develops in the foregut which represents the first indication of the respiratory system (Tucker & O'Rahilly, 1972).

The respiratory primordium forms as an epithelial thickening along the ventral medial aspect of the developing foregut during Stage 11 (24 days of human intrauterine life). It is located caudal to the level of the developing fourth pharyngeal pouch (Hast, 1970; Bryden et al., 1973; Henick, 1993).

During stage 12 (26 days of human intrauterine life), the foregut lumen expands into the respiratory primordium to form the respiratory diverticulum. The cranial end of the diverticulum is called the primitive pharyngeal floor. The foregut segment between the primitive pharyngeal floor and the fourth pharyngeal pouch is called the primitive laryngopharynx, which will develop into the adult supraglottis (adult laryngeal vestibule) (Henick, 1993).

Previous research in humans describes the development of an "ascending tracheoesophageal septum" which forms from the fusion of the margins of the laryngotracheal groove (Hast, 1970; Tucker & O'Rahilly, 1972; Tucker & Tucker, 1975; Wilson, 1979). This septum was believed to separate the respiratory diverticulum from the ventral pharynx and foregut (Wilson, 1979). Current research in mice using three-dimensional computer generated reconstructions dispute this theory (Henick, 1993). Murine studies demonstrate that the supraglottis forms in the region of the primitive

laryngopharynx, and the trachea results from continued caudal descent of the bronchopulmonary buds and carina from the cranial end of the respiratory diverticulum or infraglottis (Henick, 1993).

During stages 13 and 14 (28 and 32 days of human intrauterine life, respectively), the respiratory diverticulum gives rise to the glottis, infraglottis, carina, and tracheobronchial system. The rima glottidis develops from the entrance into the respiratory diverticulum or the primitive pharyngeal floor. The infraglottis develops from the cranial aspect of the respiratory diverticulum. Bilateral compression of the caudal aspect of the primitive laryngopharynx contributes to the characteristic shape of the infraglottic lumen. Compression of the primitive laryngopharynx occurs due to the rapidly enlarging laryngeal mesodermal anlagen. The laryngeal mesodermal anlagen is a wedge-shape condensation of mesoderm that will give rise to the laryngeal cartilages and musculature. The lateral walls are brought together in a ventrodorsal direction. Fusion of the lateral walls of primitive laryngopharynx give rise to the epithelial lamina. The enlarging fourth branchial arch artery compresses the ventral aspect of the pharyngeal floor of the foregut and gives rise to the arytenoid swellings. The enlarging third branchial arch artery participates in the formation of the hypobranchial eminence (Henick, 1993).

The epithelial lamina, during stages 16–18 (5–6.5 weeks of human intrauterine life), completely obliterates the lumen of the primitive laryngopharynx except for a narrow pharyngoglottic duct along its dorsal aspect (Tucker & O’Rahilly, 1972; Henick, 1993). The pharyngoglottic duct bridges the hypopharynx with the infraglottic region (Henick, 1993). The laryngeal cecum develops along the cranioventral aspect of the

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epithelial lamina and is bounded by the arytenoid swellings dorsally and the epiglottic swelling ventrally (Henick, 1993). The epiglottic swelling is derived from the dorsal aspect of the hypobranchial eminence (Bryden et al., 1973; Henick, 1993). The laryngeal cecum descends caudally along the ventral aspect of the epithelial lamina until it reaches the level of the glottis (Henick, 1993). The infraglottis replaces the primitive pharyngeal floor as the ventral limit of the primitive laryngopharynx. The arytenoid swellings replace the fourth pharyngeal pouch as the dorsal limit of the primitive laryngopharynx (Henick, 1993).

During stages 19–23 (6.5–8 weeks of human intrauterine life), recanalization of the epithelial lamina begins. This brings the pharyngoglottic duct into communication with the laryngeal cecum thus forming the laryngeal vestibule (supraglottis). The last region to recanalize is the ventral aspect of the glottis. Bilateral lateral expansions from the distal aspect of the laryngeal cecum form the vestibular outgrowths, which will become the adult laryngeal ventricles (Henick, 1993). The aryepiglottic folds are formed by the elongated portions of the lateral fourth arch mass, which runs from the hypobranchial eminence (epiglottis) to the upper prominence of the sixth branchial arch (arytenoid eminence) (Hast, 1970).

In mice, laryngeal skeletal development begins during stage 14 (34–36 somite pairs [a somite represents one of the paired, block-like masses of mesoderm, arranged segmentally alongside the neural tube of the embryo, forming the vertebral column and segmental musculature [Taylor, 1988]], where the laryngeal mesodermal anlagen appears flanking the primitive laryngopharynx (Henick, 1993). Further differentiation of the laryngeal mesodermal anlagen during stage 16 (45–51 somite pairs) gives rise to 2

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distinct regions: a hyoid region and a cricothyroid region. The thyroid anlagen gives rise ventrally to 3 distinct regions of the cricoid anlagen: two dorsolaterally and one ventromedially. Chondrification centers of the laryngeal mesodermal anlagen first appear along the ventral aspect of the hyoid and cricoid anlagen during stages 17 and 18 (52–64 somite pairs). Lateral and dorsal fusion of the cricoid anlage occur during the same stages. During stages 19–23, complete chondrification of the laryngeal cartilages occurs (Henick, 1993).

In contrast to mice, the presence of bilateral chondrification centers with regards to the development of the cricoid cartilage has been described in humans (Kallius, 1897). Other studies indicate that there is a single, ventral chondrification center (Zaw-Tun & Burdi, 1985).

Based on histologic examination of human embryos, development of the laryngeal musculature can be divided into 6 stages. During stage I and II (CR length 4–6 mm and 7–9 mm), the primitive glottic slit is surrounded by condensations of undifferentiated mesenchymal cells. Two planes of cells can be identified: the inner constrictor, which is a fifth branchial arch derivative; and the outer constrictor, which is a fourth branchial arch derivative (Hast, 1972). The inner constrictor gives rise to all of the intrinsic muscles of the larynx except the cricothyroid muscle, which is a fourth branchial arch derivative (Frazer, 1910; Hast, 1972). All of the intrinsic muscles, except the cricothyroid, are supplied by a nerve from the sixth branchial arch, the recurrent laryngeal nerve (Hast, 1972). The cricothyroid muscle is supplied by the cranial laryngeal nerve, which is a fourth branchial arch derivative (Hast, 1970).

As the ventral part of the thyroid cartilages grow caudally and the inferior cornu develops during the second month of gestation, fibers of the inferior constrictor are cut through by the inferior thyroid cornu articulating with the cricoid cartilage. This results in separation of a bundle of outer constrictor muscle fibers which form from the cricoid to the thyroid cartilage. This will become the cricothyroid muscle in the adult (Hast, 1970).

During stage III (CR 10–12.5 mm), the primordium of the laryngeal muscles appear first as an intrinsic sphincter lying within the anlage of the thyroid cartilage and at the level of the cricoid cartilage. Myoblasts are strung in the form of a ring or sphincter. As development continues, the sphincter separates into individual muscle masses: the constrictors of the glottis and epiglottic sphincter (interarytenoid, aryepiglottic, and CAL muscle) and the abductor of the glottis (cricoarytenoideus dorsalis [CAD] muscle) (Hast, 1972). Other authors believe that the muscles develop not as a sphincter but independently (Lisser, 1911).

During stage IV and V (CR 13–15 mm and 16–18 mm), the intrinsic laryngeal muscles are recognizable, and by stage VI (CR 19–23 mm), all are identifiable (Hast, 1972).

The extrinsic muscles form from an epicardial ridge as part of the primitive infrahyoid muscle mass. The mass divides into superficial and deep layers. The sternohyoid and omohyoid muscles result from a split of the superficial layer into medial and lateral parts. The sternothyroid and thyrohyoid muscles form from the deep layer which separates into upper and lower parts (Hast, 1970).

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After the embryonic period proper, the fetal period begins. During human laryngeal development, the corniculate and arytenoid cartilages chondrify during the third month of gestation (Hast, 1970). Also, the laryngeal ventricles are sharply outlined, but no glandular development is evident (Tucker & Tucker, 1975). The laryngeal saccules begin to become evident, and ventral fusion of the thyroid laminae occurs (Tucker & Tucker, 1975).

During the fifth month of gestation, fibrocartilage forms in the epiglottis (Hast, 1970). Definitive glandular formation in the ventricles and saccules occurs during the sixth month (Tucker & Tucker, 1975). The cuneiform cartilage develops in the blastoma of the plica aryepiglottica late during the seventh month (Hast, 1970). Finally, the epiglottic contours become well defined during the eighth month of gestation (Tucker & Tucker, 1975).

In summary, laryngeal development can be divided into 3 anatomical divisions: laryngeal vestibule, laryngeal skeleton, and laryngeal musculature. The respiratory system develops from the embryonic foregut. The adult laryngeal vestibule (supraglottis) develops from the primitive laryngopharynx, which is the foregut segment between the primitive pharyngeal floor and the fourth pharyngeal pouch. The respiratory diverticulum gives rise to the glottis, infraglottis, carina, and tracheobronchial system. The arytenoid swellings originate from the enlarging fourth branchial arch artery. The epiglottic swelling is derived from the hypobranchial eminence, which forms from the third branchial arch artery. The laryngeal ventricles form from bilateral expansions of the laryngeal cecum. The elongated portions of the lateral fourth arch mass form the aryepiglottic folds.

Differentiation of the laryngeal mesodermal anlagen gives rise to 2 distinct regions: a hyoid region and a cricothyroid region. The thyroid anlagen gives rise to the cricoid anlagen.

Finally, the laryngeal musculature originates from condensations of undifferentiated mesenchymal cells surrounding the primitive glottic slit. The inner constrictor plane of mesenchymal cells gives rise to all of the intrinsic muscles of the larynx except the cricothyroid muscle. The outer constrictor plane, which is a fourth branchial arch derivative, gives rise to the cricothyroid muscle. The extrinsic muscles of the larynx form from an epicardial ridge as part of the primitive infrahyoid muscle mass.

Structure

For the surgeon, knowledge of structure is essential. Therefore, I will now describe the structure of the equine larynx in detail.

In most animals, the glottis is the narrowest part of the airway (Cook, 1966; Marks et al., 1970b; Cook, 1981). In man, the length of the arytenoid cartilage is $\frac{1}{2}$ the diameter of the glottis (Marks et al., 1970b). Therefore, the glottis is only 50% that of the tracheal cross-sectional diameter. In horses, however, the cross-section of the glottis on inspiration is 14% larger than the tracheal cross-sectional area. This is because the length of the arytenoid cartilage is $\frac{7}{10}$ the diameter of the glottis which results in maximal cross-sectional area with arytenoid cartilage abduction. Based on these observations, Marks hypothesized that horses can have a 14% reduction in glottal airway with little, if any, reduction in airflow. However, airflow was not quantitatively

measured. Nevertheless, small changes in arytenoid cartilage position greatly affects cross-sectional area (Marks et al., 1970b).

Cartilages

The larynx consists of 3 unpaired and 2 paired cartilages. The thyroid cartilage is the largest of the unpaired cartilages (Lohse, 1984). It consists of two lateral laminae which are fused rostroventrally (Sack & Habel, 1988). Each lamina presents a rostral cornu, which articulates with the thyrohyoid bone, and a caudal cornu, which articulates with the cricoid cartilage. A foramen, which lies ventral to the rostral cornu, contains the cranial laryngeal nerve. The thyroid cartilage is notched along its ventral aspect just caudal to the union of the thyroid laminae (Sack & Habel, 1988). The thyroid cartilage is composed of hyaline cartilage surrounded by connective tissue (Lohse, 1984). With age, ossification occurs. Running from the border of the thyroid notch to the ventral arch of the cricoid cartilage is the cricothyroid ligament (Lohse, 1984). The cricothyroid joint allows rotation as well as cranial-caudal sliding (Proctor, 1977). The cranial part of the thyroid cartilage can move up and down, and the entire cartilage can move backward and forward (Proctor, 1977).

The epiglottis is the second unpaired cartilage. It fuses with the 2 cuneiform cartilages rostral to the thyroid cartilage. The epiglottis is composed of elastic connective tissue and does not ossify with age. The aryepiglottic folds extend from the lateral borders of the epiglottis to the arytenoid cartilage on the ipsilateral side. The thyroepiglottic ligament is composed of elastic fibers which course from the base of the epiglottis to the medial surface of the thyroid laminae (Lohse, 1984).

The cricoid cartilage, the third unpaired cartilage, lies between the thyroid laminae and first cartilaginous tracheal ring (Lohse, 1984). It is shaped like a signet ring with a broad dorsal lamina and a curved lateroventral arch (Sack & Habel, 1988). The dorsal surface of the lamina is divided by a median ridge. The rostral border of the lamina articulates with the arytenoid cartilage, and the lateral border of the lamina articulates with the caudal cornu of the thyroid cartilage (Sack & Habel, 1988). Caudally, the cricoid cartilage is attached to the first tracheal ring by the cricotracheal membrane (Proctor, 1977; Lohse, 1984). The cricoid cartilage, like the thyroid cartilage, is composed of hyaline cartilage (Sack & Habel, 1988). The inner surface of the cricoid cartilage is covered by a mucous membrane (Lohse, 1984). With age, the cricoid cartilage may ossify (Sack & Habel, 1988).

The paired arytenoid cartilage has 3 significant projections. The corniculate process is elastic and originates from the rostral arytenoid border. The rostral and caudal borders converge ventrally to form the elastic vocal process. The muscular process projects from the dorsal part of the lateral surface and, with its medial surface, articulates with the cricoid lamina. The muscular process and body of the arytenoid are composed of hyaline cartilage (Sack & Habel, 1988). The cricoarytenoid ligament supports the ventromedial aspect of the cricoarytenoid joint (Lohse, 1984). The transverse arytenoid ligament connects the dorsomedial angles of the opposing arytenoid cartilages (Lohse, 1984).

The other paired cartilage is the cuneiform cartilage. It articulates with the lateral border of the epiglottic base and projects caudodorsad. The vestibular ligament attaches to the free extremity of the cuneiform cartilage (Getty, 1975).

Epithelial Lining

In rodents, the larynx is lined with stratified squamous and pseudostratified ciliated columnar epithelium in a highly specific, regional distribution pattern. At the cranial base of the epiglottis, the epithelium is interrupted by excretory ducts of subepithelial glands. The dorsolateral vestibule contains stratified squamous epithelium, while the ventrolateral aspect contains pseudostratified ciliated columnar epithelium. The vestibular folds are lined with stratified columnar epithelium, while the vocal folds contain stratified squamous epithelium. The laryngeal ventricles contain pseudostratified ciliated columnar epithelium with areas of stratified squamous epithelium. The floor of the vestibule and the lateral and upper medial surface of the vocal folds contain pseudostratified, nonciliated columnar epithelium that lacks goblet cells. Caudal to the vocal folds, 2 layers of ciliated columnar epithelium extend to the trachea (Reznick, 1990). There does not appear to be any significant differences in the epithelial lining of the larynx of the horse when compared to that of the rodent (Getty, 1975).

Muscles

There are three extrinsic muscles of the larynx. The thyrohyoideus runs rostrally from the thyroid lamina to the basihyoid and thyrohyoid bones (Sack & Habel, 1988). If the hyoid bone is fixed, the muscle draws the larynx rostrad (Getty, 1975). If the hyoid bone is not fixed, the muscle acts in conjunction with the sternothyroideus, omohyoideus, and sternohyoideus to draw the hyoid bone and the root of the tongue caudad (Getty, 1975). The hyoepiglotticus runs from the basihyoid to the rostral surface of the epiglottis (Sack & Habel, 1988). It functions to approximate the basihyoid bone

with the base of the epiglottis (Getty, 1975). The sternothyroideus inserts onto the thyroid lamina (Sack & Habel, 1988). It functions to draw the larynx caudad (Getty, 1975).

The intrinsic laryngeal muscles function to open, close, tense, and lengthen the glottis (Proctor, 1977). The cricothyroideus muscle arises from the lateral surface and caudal edge of the cricoid cartilage and passes dorsorostrally to the caudal edge and lateral surface of the thyroid lamina (Sack & Habel, 1988). This muscle draws the rostral portion of the thyroid and cricoid cartilages together and pulls the thyroid cartilage rostrally with respect to the cricoid and arytenoid cartilages, thus lengthening the vocal folds (Proctor, 1977).

The CAD arises from the lamina and median ridge of the cricoid cartilage and inserts on the muscular process of the arytenoid cartilage (Sack & Habel, 1988). This muscle functions to abduct the arytenoid cartilages, thereby opening the glottis (Proctor, 1977). It also keeps the vocal folds in a straight line during all degrees of glottic opening (Proctor, 1977).

The AT originates from the muscular process of the arytenoid cartilage and inserts on the contralateral muscular process (Sack & Habel, 1988). This muscle functions to close the glottis (Proctor, 1977).

The thyroarytenoid muscle originates primarily from the dorsal surface of the body and adjoining part of the lamina of the thyroid cartilage and inserts onto the lateral surface and muscular process of the arytenoid cartilage (Getty, 1975). In the horse, this muscle is divided into two parts. The ventricularis muscle arises from the cricothyroid ligament and ventral border of the thyroid lamina and inserts on the muscular process of

the arytenoid cartilage (Sack & Habel, 1988). The vocalis muscle arises from the cricothyroid ligament and inserts on the lateral surface of the arytenoid cartilage, just below the muscular process (Sack & Habel, 1988). The thyroarytenoid muscle functions in glottic closure and also helps control tension in the vocal folds (Proctor, 1977).

The CAL arises from the rostral border of the cricoid arch and inserts on the muscular process of the arytenoid cartilage (Sack & Habel, 1988). This muscle functions to close the glottis (Proctor, 1977).

Innervation

Brainstem nuclei that contain neurons responsible for laryngeal innervation are the nucleus ambiguus and retrofacial nucleus (Gacek et al., 1977; Davis & Nail, 1984). Neurons located in the dorsal division of the nucleus ambiguus send adductor motor neurons to the larynx while the ventral division contains motor neurons destined for the abductor of the larynx, the CAD (Gacek et al., 1977).

The retrofacial nucleus contains motor neurons to the adductors in its peripheral portion while motor neurons to the abductors are centrally located. Axons from the 2 nuclei converge and exit the brainstem in the rostral 1 or 2 rootlets of the vagus nerve (Gacek et al., 1977).

Motor fibers destined for the recurrent laryngeal nerve are contained in a discrete portion of the vagus nerve rather than as a separate nerve bundle. The motor neurons are mixed throughout the central and peripheral portion of the vagus nerve. Prior to entering the larynx, they collect into abductor and adductor halves (Gacek et al., 1977).

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The right recurrent laryngeal nerve (RRLNv) branches from the vagus nerve at the level of the first intercostal space, passes medially around either the right subclavian or costocervical artery, and comes to lie on the lateral wall of the trachea (Rooney & Delaney, 1970; Quinlan et al., 1982). It passes cranially with the trachea and becomes related to its dorsolateral surface in the midcervical region (Quinlan et al., 1982).

The left recurrent laryngeal nerve (LRLNv) branches from the vagus nerve at the level of the heart base, which is located 25–30 mm caudal to the RRLNv branching point (Rooney & Delaney, 1970; Quinlan et al., 1982). It divides into 2 branches which curve medially around the aorta and ligamentum arteriosum to lie on the trachea (Quinlan et al., 1982). A small branch lies in close association with the sympathetic nerve for a short distance before rejoining the larger main branch. The LRLNv then travels a similar course as the RRLNv (Quinlan et al., 1982).

At the level of the caudal border of the cricoid cartilage, the recurrent laryngeal nerve splits into 2 branches. The small branch passes between the cricoid cartilage and CAD to enter the CAD through its ventral surface. The large branch passes rostrally over the cricoid lamina at the lateral extremity of the CAD and proceeds along the caudal edge of the thyroid cartilage. A branch splits off and passes medially under the cranioventral surface of the CAD to insert onto the caudal border of the AT. The other branch passes cranioventrally and medially to the thyroid lamina. As it passes over the lateral surface of the CAL, it divides into 3 branches. The caudal branch enters the lateral surface of the CAL. The middle branch passes over the lateral surface of the CAL and divides. One branch passes caudally and enters the medial aspect of the CAL. One or 2 branches pass ventral to the vocalis muscle. Another branch passes rostrally



over the lateral ventricle and enters the ventricularis muscle. The dorsal branch passes over the lateral ventricle medial to the thyroid lamina and joins with the internal branch of the cranial laryngeal nerve (Quinlan et al., 1982).

The cranial laryngeal nerve arises from the vagus nerve and passes rostroventrally medial to the origin of the internal carotid and occipital arteries. It supplies a muscular branch to the cricothyroid muscle and is sensory to the mucous membrane of the larynx (Sack & Habel, 1988).

In the cat and rabbit, each laryngeal muscle is innervated by a single, ipsilateral pool of motoneurons originating from the nucleus ambiguus. The CAD pool is located in the ventral part of the recurrent laryngeal nerve representation and does not extend as far caudally as the AT or CAL. The CAL pool is located in the caudal and dorsomedial part of the recurrent laryngeal nerve pool. The AT pool overlaps the CAD and CAL pool, and its motor neurons are more numerous than the CAD and CAL (Davis & Nail, 1984).

In summary, the equine larynx consists of 3 unpaired cartilages (thyroid, epiglottis, and cricoid) and 2 paired cartilages (arytenoid and cuneiform). The mucous membrane of the larynx is lined by stratified squamous epithelium cranially and pseudostratified ciliated columnar epithelium caudally, including the laryngeal saccules. There are 3 extrinsic muscles of the larynx: thyrohyoideus, hyoepiglotticus, and sternothyroideus. The intrinsic muscles include the: cricothyroideus, CAD, AT, thyroarytenoid, and CAL. They function to open, close, tense, and lengthen the glottis. The nucleus ambiguus and retrofacial nucleus contain neurons responsible for laryngeal

innervation. The recurrent laryngeal nerve innervates all of the intrinsic muscles of the larynx except the cricothyroid muscle, which is supplied by the cranial laryngeal nerve.

Function

The larynx developed phylogenetically purely as a valve to protect the lungs from aspiration during swallowing. Its role in phonation was a later evolutionary development (Proctor, 1977).

The larynx participates in swallowing, coughing, laughing, hiccuping, vomiting, postural adjustments, and expulsive efforts, as well as in airway protection, vocalization, and breathing (Bartlett, 1989). All of these functions require both arytenoid and vocal cord movement; and, therefore, I will now describe the mechanisms responsible for these cartilage movements.

The most consistent mechanism underlying arytenoid and vocal cord movement in resting animals is contraction of the CAD during inspiration and CAD relaxation, permitting passive recoil, during expiration (Bartlett, 1989). Complete glottic closure is aided by firing of the adductor muscles during expiration (Bartlett et al., 1973; Duncan & Baker, 1987; Bartlett, 1989). Initially it was thought that change in glottic size was due to sideways sliding of the arytenoid cartilages (Fink et al., 1956). However, medial or lateral rotation of the arytenoid cartilages has been shown to be the primary mechanism that results in adduction or abduction of the vocal folds, respectively (Bartlett, 1989).

The abductor (CAD) fires in a phasic burst during inspiration, and the adductors (CAL, AT, thyroarytenoid) fire during expiration (Bartlett et al., 1973; Duncan & Baker,

1987; Bartlett, 1989). In the horse, the CAD has considerable tonic activity during the resting phase of the respiratory cycle (Duncan & Baker, 1987). Laryngeal reflexes modify ventilatory efforts (Bartlett, 1989). During exercise, negative pressure in the upper respiratory tract results in a challenge to the abductors to maintain airway patency (Woodall & Mathew, 1986). Changes in pressure, flow, and temperature activate laryngeal mechanoreceptors which then result in regulation of the size of the glottic aperture (Woodall & Mathew, 1986; Bartlett, 1989).

In the dog, laryngeal mechanoreceptors are classified as pressure receptors (stimulated by collapsing or distending pressure), flow receptors (stimulated by airflow across the larynx), or "drive" receptors (stimulated by respiratory activity of upper airway muscles). Pressure receptors are the most prevalent receptor, followed by "drive" receptors and flow receptors, respectively (Sant'Ambrogio et al., 1983). Pressure receptors can be divided into 2 populations: those that respond to distending pressure and those that respond to collapsing pressure (Mathew et al., 1984). Collapsing pressure receptors are more numerous (Mathew et al., 1984). Even though these 3 receptor types differ in sensory modality, they are similar in that they are predominantly active during inspiration (Sant'Ambrogio et al., 1983). The activity of the 3 receptors to stimulate dilator muscles is markedly increased during upper airway obstruction in order to maintain airway patency (Sant'Ambrogio et al., 1983).

In summary, the larynx serves many functions, all of which require arytenoid and vocal fold movement. Contraction and relaxation of the CAD, in conjunction with the adductors, during the respiratory cycle is the most consistent mechanism underlying

arytenoid and vocal fold movement. Rotation, rather than sliding, of the arytenoid cartilages results in abduction and adduction of the vocal folds.

Several laryngeal mechanoreceptors have been identified which are responsible for changes in airway patency. They include receptors which respond to collapsing and distending pressure (pressure receptors), receptors which respond to changes in airflow (flow receptors), and receptors which respond to changes in the activity of upper airway muscles ("drive" receptors). In the dog, pressure receptors are the most numerous, followed by "drive" and flow receptors, respectively.

Chapter 2

PATHOPHYSIOLOGY OF IDIOPATHIC LARYNGEAL HEMIPLEGIA

The following section will present information regarding the pathophysiology and incidence of idiopathic laryngeal hemiplegia (ILH). I will describe in detail the muscle, nerve, and brain lesions associated with the disease process. Also, the relevance of arytenoid asymmetry will be discussed.

Pathology

Horses affected with subclinical and clinical ILH show evidence of neurogenic atrophy of the intrinsic muscles of the larynx (Cole, 1946; Duncan et al., 1974; Anderson et al., 1980; Cahill & Goulden, 1986IV; Duncan et al., 1991I; Lopez-Plana et al., 1993b). Characteristic features of neurogenic atrophy include fiber-type grouping, variation in fiber size, presence of both atrophic and hypertrophic fibers, centrally placed nuclei, fascicular atrophy, increased connective tissue and fat within and between fascicles, and loss of myelinated fibers in the intramuscular nerves (Cahill & Goulden, 1986IV). Single, scattered, angular fibers are present in the earliest form of neurogenic atrophy and are the hallmark of muscle denervation (Duncan et al., 1991I). Muscle denervation is usually partial with changes occurring in the muscle fibers belonging to the motor unit innervated by the damaged motor axon (Cahill & Goulden, 1986 IV). The

affected muscle fibers shrink and, thus, sarcolemmal nuclei appear more numerous. The adjacent muscles are normal or hypertrophied. Denervated muscle fibers stimulate neighboring, healthy nerve fibers to send out fine axonal sprouts to reinnervate denervated muscle fibers. This process, known as collateral sprouting, results in fiber type grouping, where the reinnervated muscle fibers will assume the same metabolic type as determined by the innervating nerve fibers (Cahill & Goulden, 1986IV).

To determine whether a muscle has been denervated, histochemical typing of muscle is performed (accomplished by staining for different enzymes). Myosin ATPase activity is related to the intrinsic speed of muscle contraction (Davies & Gunn, 1972). Normal muscle exhibits a mosaic pattern where denervated muscle exhibits fiber type grouping (Cahill & Goulden, 1986IV; Duncan et al., 1991I). Equine laryngeal muscles primarily consists of fast-twitch combined aerobic and anaerobic fibers, some slow-twitch combined aerobic and anaerobic fibers, and a few slow-twitch predominantly aerobic fibers (Gunn, 1973). Late fetal laryngeal muscles contain the same fiber types as adults. An abnormal pattern of fiber type distribution has been found in the left CAD of fetal horses with ILH, suggesting the neurogenic disturbance occurs before birth. There is also evidence that preferential atrophy of myosin ATPase high reacting fibers occurs in horses affected with ILH (Gunn, 1973).

The muscles affected in horses with ILH include all of the intrinsic muscles of the larynx supplied by the recurrent laryngeal nerve (Duncan et al., 1977; Anderson et al., 1980). The adductors, CAL and AT, are more severely affected at an earlier stage than the primary abductor, the CAD (Duncan et al., 1977; Anderson et al., 1980; Cahill & Goulden, 1986I; Duncan et al., 1991I; Lopez-Plana et al., 1993b). The degree of muscle

pathology directly correlates with the extent and location of nerve fiber damage (Cahill & Goulden, 1986IV) and endoscopic appearance of the larynx (Duncan et. al, 1991I). The muscles on the left side of the larynx are primarily affected, though denervation of the adductors on the right side has also been documented (Duncan et al., 1991I; Lopez-Plana et al., 1993b).

Arytenoid Asymmetry

Investigators have found a high frequency of both subclinical laryngeal muscle pathology and endoscopic findings of arytenoid trembling, asynchrony, and asymmetry in what were previously thought to be normal horses (Duncan & Baker, 1987). Up to 50 % of clinically normal horses have asynchronous abductor function of the glottis (Baker, 1983a; Hillidge, 1985; Lopez-Plana et al., 1993a). This may be considered normal because of an apparent absence of progression to clinical disease (Baker, 1983a; Lopez-Plana et al., 1993a). In contrast to man and dogs, the nerve fibers in the motor nerves to the equine larynx do not cross the midline to the contralateral side (Quinlan et al., 1982). Therefore, supplementary innervation when unilateral laryngeal nerve damage occurs is not possible in the horse (Quinlan et al., 1982). Since there is independent innervation of the left and right sides and different lengths of its motor neurons, the existence of small differences in movements of the left and right arytenoid cartilages are considered normal (Goulden & Anderson, 1981II).

Arytenoid and vocal cord movement is controlled by laryngeal muscles, which act as a finely balanced system of agonists and antagonists. Abnormal arytenoid and vocal fold function results from an imbalance between adductor and abductor muscles.

Preferential denervation of one, or several, of these muscles could, theoretically, lead to loss of balance which might result in abnormal arytenoid and vocal fold movements (Duncan & Baker, 1987). Aberrant reinnervation could also be responsible for trembling (Duncan et al., 1977). Alternatively, asynchrony may be due to differences in conduction velocities, differences in the trajectory of the left and RRLNv, or a decrease in the thickest myelinated fibers in the LLRNv (Duncan et al., 1977; Lopez-Plana et al., 1993a).

Nerve Pathology and Proposed Mechanisms

Idiopathic laryngeal hemiplegia in horses is classified as a distal axonopathy (dying-back neuropathy), where axonal degeneration with a slow proximal spread of nerve fiber breakdown occurs over time (Cole, 1946; Duncan et al., 1991II). The dying-back disorder has also been documented in people with inherited, metabolic, toxic, and deficiency neuropathies, in numerous breeds of dogs, and in Birman cats (Braund et al., 1994; Burbidge, 1995). Some mechanisms proposed to explain the dying-back neuropathy include primary toxicity of nerve cell bodies, Schwann cell abnormalities, primary axonal changes, and disrupted axonal flow (Braund et al., 1994).

In horses with ILH, there is preferential denervation of the LRLNv with a majority of the changes occurring in the branch supplying the adductor muscles (Duncan et al., 1991II). The most obvious changes are in the distal part of the LRLNv, but lesions are also present in other areas of the left and RRLNv (Cahill & Goulden, 1986II).

The exact reason for the differential involvement of adductor versus abductor muscle atrophy seen in horses with ILH is unknown, but several hypotheses have been

proposed. Distal axonopathies are characterized by changes occurring in large diameter fibers, therefore, preferential denervation in horses with ILH could be due to differences in fiber diameter (Duncan et al., 1991II). Duncan and colleagues found no difference in fiber diameter between adductors and abductors in normal ponies (Duncan et al., 1977). However, other investigators have demonstrated an increase in large diameter fibers in the branch of the recurrent laryngeal nerve innervating the CAL (an adductor) (Cahill & Goulden, 1986I). In horses with ILH, there appears to be a greater depletion in the large diameter fibers to the adductors (Duncan et al., 1977).

Nerve conduction velocity is closely related to the diameter of myelinated nerve fibers. In man, dogs, and giraffes, the LRLNv contains more large, fast-conducting fibers. However, a significant difference between left and right sides, in both diameter of myelinated fibers and velocity of conduction, has not been found in the dog and rat (Lopez-Plana et al., 1993a).

In a teased fiber study of laryngeal nerves from horses with ILH, short, thinly myelinated internodes are interspersed among normally myelinated internodes. This is indicative of remyelination of previously demyelinated areas of nerve fibers. The abnormal internodes are grouped along particular nerve fibers rather than being randomly distributed between all nerve fibers. Despite the prominence of demyelination and remyelination, the grouping of abnormal internodes on particular nerve fibers indicates an underlying axonal pathology resulting in secondary changes in the myelin sheath (Cahill & Goulden, 1986III). The theory of primary axonal degeneration has been disputed by other investigators (Duncan et al., 1977).

The LRLNv is longer than the right. It loops around the aortic arch and may be considered fixed at the aortic arch and the larynx. The RRLNv loops around the costocervical artery and is fixed at this point and the larynx (Rooney & Delaney, 1970). Therefore, the left nerve may be tensed more by movements of the head and neck up and/or to the right (Marks et al., 1970a; Rooney & Delaney, 1970). Above a critical tension, degenerative changes identical to those observed in horses with ILH take place (Marks et al., 1970a). There may be greater tension on the nerve in long-necked, large breed horses (Rooney & Delaney, 1970). The tension forces may cause vascular insufficiency and nerve damage (Rooney & Delaney, 1970).

The presence of longer nerve fibers in the adductor branch of the recurrent laryngeal may be the cause of preferential denervation (Loew, 1973; Mason, 1973; Duncan et al., 1991II). The nerve fibers to the adductor muscles extend more distad than the abductor nerve fibers by approximately 5–6 cm (Duncan & Baker, 1987). Therefore, the adductors may be the first to be affected by a distal axonopathy process (Duncan & Baker, 1987). However, fiber length contributing to preferential denervation is unlikely, since the ventricularis muscle has the longest fiber length but is the least affected (Lopez-Plana et al., 1993a).

Another proposed mechanism for the distal axonopathy seen in horses with ILH is altered axonal transport. Some pathologic changes seen in horses, man, and dogs with distal axonopathies are paranodal organelle accumulation in fibers with axonal outpouchings and elongated axonal swellings which contain a variety of accumulated organelles. Accumulation of organelles which are normally being transported in either an anterograde or retrograde direction could result from an abnormality of axonal

transport. The motor nerve fibers of the equine LRLNv are the longest motor nerve fibers in the horse. Also, the LRLNv is approximately 20–30 cm longer than the right. Therefore, a failure or disturbance of axonal flow over such a long distance could result from a lack or diminution in the necessary energy requirements for transport. Changes in transport and subsequent organelle accumulation may be due to ischemia. Alternatively, the organelles may represent the proximal portions of nerve fibers undergoing distal axonal degeneration (Duncan & Hammang, 1987).

Compression by enlarged thoracic lymph nodes, the aorta, or between the aorta and trachea may lead to denervation (Dyer & Duncan, 1987). A distal site of compression is unlikely to result in selective damage, since the fibers are intermingled within the parent nerve (Dyer & Duncan, 1987; Griffiths, 1991). Also, investigators have been unable to demonstrate nerve pathology at sites of aortic pulsations (Cook, 1970). Compression as the nerve fibers pass between the thyroid and cricoid cartilages may cause preferential denervation (Duncan et al., 1991II).

Fiber position may play a role in the differential involvement of the adductor nerve fibers. If the nerve fibers to the adductors are located in one specific segment of the parent nerve, they may be susceptible to differential involvement (Dyer & Duncan, 1987). Laryngeal motor neurons are separated into abductor and adductor groups within the brainstem nuclei, but axons of these groups of motor neurons are mixed throughout the central and peripheral course of the vagus nerve (Gacek et al., 1977). The motor fibers collect into abductor and adductor halves of the recurrent laryngeal nerve before entering the larynx. Therefore, theories based on a vulnerable position of a particular

group of motor neurons are not tenable in the vagus nerve but may be in the recurrent laryngeal nerve (Gacek et al., 1977).

In man, partial loss of function of the vocal folds has been suggested to be due to selective susceptibility of the abductor muscle to denervation. In the horse, however, the adductor muscles appear to be selectively susceptible. Following partial suturing of the recurrent laryngeal nerve, there appears to be an even mixing of both types of fibers at the branching point, with the abductor and adductor branches containing intact and degenerating fibers. Further evidence to support nerve fiber mixing is the constant changing of fascicular architecture within the recurrent laryngeal nerve. The propensity of adductor muscle fibers to denervate may relate to the overall length of the nerve supply or the size of fibers to the individual laryngeal muscles. In the nerve suture study, there was a clear separation of intact and degenerating fibers just distal to the suture, but mixing occurred close to the point of innervation of laryngeal muscles. The numbers of intact myelinated fibers remained similar along the partially denervated nerve segment. Therefore, focal lesions of the recurrent laryngeal nerve should not result in denervation of individual laryngeal muscles (Dyer & Duncan, 1987).

Other possible explanations for preferential denervation include nerve destruction secondary to neurotoxin production by *Streptococcus equi*, thiamine deficiency, and hereditary predispositions (Loew, 1973; Mason, 1973, Duncan et al., 1991II). Quinlan and Morton did not find an increased incidence of ILH in horses with a history of *Streptococcus equi* infection (Quinlan & Morton, 1957). A hereditary predisposition has been confirmed in several studies (Quinlan & Morton, 1957; Cook, 1988; Poncet et al., 1989).

Laryngeal paralysis-polyneuropathy complex has been documented in horses with ILH, in Birman cats, in German Shepherds with hereditary giant axonal neuropathy, and in Long-Haired Dachshunds with hereditary sensory neuropathy (Griffiths, 1991; Braund et al., 1994). In horses with ILH, there is evidence to support a central nervous system component (Cahill & Goulden, 1989) as well as a peripheral nerve component (Cahill & Goulden, 1986II). Cahill and Goulden found neurogenic changes in the extensor digitorum longus muscle which is supplied by another long peripheral nerve (Cahill & Goulden, 1986II).

Brain Lesions

Histologic examination of the recurrent laryngeal nerves and vagus trunk from horses with ILH reveals abnormalities in both the recurrent laryngeal nerves and nucleus ambiguus, in spite of the lesions being distributed so specifically to the muscles of one nerve branch of the vagus. Whether the nuclear changes are primary or secondary as a result of extension back to the nerve cell from axonal degeneration is unknown (Cook, 1970).

In horses with ILH, there is evidence of an increase in the number of axonal spheroids present in the lateral cuneate nucleus. The lateral cuneate nucleus contains distal regions of long central nerve fibers. Spheroids represent swollen, degenerating/regenerating axons. They are found in normal humans and animals with an increasing frequency of occurrence with age and some neurologic diseases (Cahill & Goulden, 1989).

In summary, neurogenic atrophy of the intrinsic laryngeal muscles is found in horses with both subclinical and clinical ILH. All of the intrinsic muscles of the larynx innervated by the recurrent laryngeal nerve are affected. The adductors, the CAL and the AT, are more severely affected at an earlier stage than the primary abductor, the CAD. The muscles on the left side are primarily affected, though denervation of the adductors on the right side has also been documented. Endoscopic findings of trembling, asynchrony, and asymmetry should be considered normal, in my opinion, and not evidence of early ILH.

The exact reason for the differential involvement of the abductor and adductor muscle atrophy seen in horses with ILH is unknown, but several hypotheses have been proposed. They include differences in fiber diameter, fiber length, fiber position, axonal transport, hereditary predispositions, focal areas of compression, thiamine deficiency, and destruction by neurotoxins from *Streptococcus equi*. Based on the scientific data accumulated to date, alterations in axonal transport appears to be the most likely explanation for the differential involvement of the 2 muscle groups. However, there may be more than one reason why differential involvement occurs.

Incidence

Approximately 14% of horses with exercise intolerance have upper airway disorders (Rehder et al., 1995). Idiopathic laryngeal hemiplegia is the most common cause of respiratory unsoundness in horses (Duncan & Griffith, 1973; Raphael, 1982) with an incidence of 2.6 to 8.3% (Hillidge, 1986; Lane et al., 1987).

The incidence of ILH appears to correlate with adult body size (Cook, 1965; Goulden & Anderson, 1981I; Cook, 1988). Cross-bred horses (heavy weight type) have an increased incidence of ILH (Goulden & Anderson, 1981I), while horses less than 15 hands tall are rarely affected (Cook, 1965; Dornblaser, 1967; Bohanon et al., 1990). Laryngeal asynchrony, which does not appear to progress to clinical disease, is found in approximately 40% of large-breed horses (Baker, 1983b; Hillidge, 1985). A study in Clydesdales indicated that approximately 50% of animals greater than 1 year of age have some evidence of CAD disease based on endoscopic examination during quiet breathing and after swallowing (Goulden et al., 1985).

The incidence of ILH also appears to be gender related. In most studies, the incidence is greater in males than females (Cook, 1965; Goulden & Anderson, 1981O; Hillidge, 1985; Bohanon et al., 1990). Also, left-sided paresis is most common (95%) (Cook, 1965).

The relative incidence rate in Standardbreds and Thoroughbreds is controversial (Goulden & Anderson, 1981I; Cook, 1988). Some investigators have demonstrated that there is an equal incidence in the disease between the 2 breeds (Goulden & Anderson, 1981I). In other studies, there has been a greater incidence of ILH in thoroughbreds, but these findings were based solely on laryngeal palpation (Cook, 1988).

Respiratory noise during exercise is a common finding in horses with ILH (Hillidge, 1986). Indeed, approximately 80% of ILH horses have an associated respiratory noise (Hillidge, 1985). Also, 50% of horses who make a respiratory noise during exercise are diagnosed with ILH (Hillidge, 1986).

The majority of thoroughbreds with ILH exhibit clinical signs between the age of 3 and 5 years while cold bloods are affected later in life (4–7 years) (Marks et al., 1969). In my view, the earlier detection of ILH in thoroughbreds is related to the age at which intensive exercise is begun in these animals. Approximately 80% of affected horses will show clinical signs by 6 years of age (Cole, 1943).

Idiopathic laryngeal hemiplegia appears to have a slightly different clinical presentation in draft horses. The mean age for diagnosis of ILH is 6.9 years, with clinical signs first being recognized at 5.6 years (Bohanon et al., 1990). Respiratory noise alone is observed in 48%, exercise intolerance and respiratory noise is observed in 30%, and exercise intolerance alone is observed in 19% (Bohanon et al., 1990). The different clinical presentation in draft horses most likely is a reflection of the age they begin work and the type of work they perform (non-speed work).

Chapter 3

ASSESSMENT OF EQUINE UPPER AIRWAY FUNCTION

A working knowledge of the clinical and research tools available to assess equine upper respiratory tract function in health and disease is essential to our understanding of how laryngeal disorders produce respiratory impairment. In this section, I will present an overview of several techniques used to assess equine upper airway function.

Endoscopy

Endoscopic evaluation can result in definitive diagnoses of intermittent and persistent airway dysfunctions as well as the anatomic characterization of obstruction during high inspiratory and expiratory airflow rates. As important, routine use of endoscopy helps to rule out upper respiratory tract dysfunction as a cause of exercise intolerance, thereby decreasing unnecessary surgery for presumed upper respiratory tract dysfunction (Morris & Seeherman, 1990).

Upper airway endoscopy is used to diagnose aryepiglottic fold entrapment, dorsal displacement of the soft palate, ILH, pharyngeal cysts, pharyngeal lymphoid hyperplasia, subepiglottic cysts, arytenoid cysts, arytenoid chondritis, polyps of the vocal folds, ethmoid hematomas, rostral displacement of the palatopharyngeal arch, and deformities of other laryngeal cartilages (Raker, 1975; Lane, 1987; Morris & Seeherman, 1990).

At rest, the paired arytenoid cartilages are in a median position between abduction and adduction. During exercise, arytenoid abduction occurs. When the nostrils are occluded and inhalation occurs (in normal horses), the upper airway maintains patency, and full abduction of the arytenoid cartilages occurs (Raker, 1975).

The slap test is one diagnostic aid that has been used to assess arytenoid cartilage function (Cook, 1974). In normal horses, the slap test produces a flickering axial movement of the contralateral arytenoid cartilage (Cook, 1974; Greet et al., 1980). The reflex involves a slap on the left withers which results in the generation of an impulse which travels up the thoracic spinal nerve (Greet et al., 1980). The impulse crosses in the thoracic spinal cord to the contralateral side and travels to the nucleus ambiguus via the cervical spinal cord. The impulse then travels down the RRLNv, activates the adductor muscles, causing right arytenoid cartilage adduction (Greet et al., 1980). The most likely reason why adduction rather than abduction is observed is because the adductor muscles are the dominant muscle group of the larynx. In tense or excited horses, the response is abolished, because the arytenoid cartilages become fixed in an abducted position (Greet et al., 1980). In horses with ILH, the test is insensitive and may produce false negatives (Greet et al., 1980; Newton-Clarke et al., 1994). The false negative response may be explained by axonal sprouting and reinnervation of muscle fibers in the face of persistent denervation (Greet et al., 1980; Newton-Clarke et al., 1994).

The effects of sedatives on laryngeal function has been evaluated (Gaughan et al., 1990; Archer et al., 1991). Xylazine hydrochloride does not appear to alter the adduction response of the arytenoid cartilages to tactile stimulation (Gaughan et al.,

1990). At rest and following nasal occlusion, xylazine hydrochloride does decrease the area of the rima glottidis and degree of abduction without changing the amount of asynchrony or trembling (Archer et al., 1991). Other investigators report that xylazine hydrochloride results in more synchronous arytenoid cartilage movement (Ducharme et al., 1991). However, these observations should be interpreted with caution because of their subjective nature (Archer et al., 1991; Ducharme et al., 1991). Xylazine hydrochloride does not appear to influence computer-assisted laryngeal measurements (Ducharme et al., 1991).

During routine endoscopic examination, the application of a nose twitch for restraint is common practice. Twitch application does not appear to change the degree of abduction, adduction, asynchrony, or trembling (Archer et al., 1991).

The degree of abduction present after swallowing is found to be more accurate than nasal occlusion as an assessment of laryngeal cartilage movement. Many horses that are unable to symmetrically abduct the arytenoid cartilages after nasal occlusion are able to fully abduct after swallowing or exercise. Also, horses that cannot symmetrically abduct after swallowing show evidence of dynamic collapse during exercise (Parente & Martin, 1995).

The sensitivity, specificity, and repeatability of laryngeal cartilage movement based on endoscopic examination has been evaluated. Movement compromise can occur due to examiner-generated errors, excitement, and physical and chemical restraint. Good intra-observer agreement rates have been documented with higher agreement in unsedated horses undergoing an ipsilateral examination (endoscope passed up the nostril of the affected side). The intra-observer repeatability is better with left-sided examination,

because abduction or lack thereof of the left arytenoid cartilage may appear more distinct when viewed from the left side (Ducharme et al., 1991).

A final endoscopic method used to assess laryngeal cartilage function is the calculation of the left:right (L:R) cross-sectional area of the rima glottidis. Absolute areas calculated from computer-assisted images varies with distance and obliquity. Since the left and right surface areas are equally affected by varying distances and obliquity in the dorsoventral plane, the L:R ratio is a more reliable parameter than absolute area (Rakestraw et al., 1991). However, L:R ratios do not compensate for obliquity in the transverse plane (Ducharme et al., 1991). This system only assesses the symmetry of abduction, not synchrony (Ducharme et al., 1991). Morphometric evaluation of laryngeal images can be used as an adjunct to visual assessment of laryngeal cartilage movement (Hackett et al., 1991).

Laryngeal cartilage movement at rest is categorized into 4 grades: Grade I—normal; Grade II—asynchronous but full abduction occurs with nasal occlusion or swallowing; Grade III—similar to Grade II but full abduction is not achieved; Grade IV—marked asymmetry with no substantial movement. The mean L:R ratio for Grade I is 0.84, for Grade II is 0.82, for Grade III is 0.59, and for Grade IV is 0.24. The L:R ratio of approximately 0.80 for Grades I and II reflect the fact that the larynx cannot be centered in front of the endoscope (Hackett et al., 1991). Grade IV ILH can be detected using L:R ratios (Rakestraw et al., 1991; Hackett et al., 1991). However, L:R ratios cannot distinguish Grade III from Grade I or II (Rakestraw et al., 1991; Hackett et al., 1991). Since Grade IV ILH can be definitively diagnosed by means of endoscopy in the

resting horse and L:R ratios cannot distinguish Grade III from Grade I or II, the clinical usefulness of morphometric evaluation of laryngeal images is limited.

In one study, horses diagnosed with Grade III ILH (at rest) were evaluated for maximum abduction and collapse during exercise by use of morphometric evaluation of laryngeal images. Grade IIIA had a L:R ratio of 0.80 at maximal abduction and 0.79 at maximal collapse. Horses with Grade IIIB had L:R ratios of 0.69 and 0.57 for maximum abduction and collapse, respectively. Horses with Grade IIIC had L:R ratios of 0.61 and 0.18 for maximum abduction and collapse, respectively. The maximal collapse Grade IIIB ratio was significantly larger than the maximal collapse Grade IIIC ratio. Horses with Grade IIIB and IIIC may benefit from a prosthetic laryngoplasty. However, horses with Grade IIIA ILH do not require surgical correction, since they are able to achieve and maintain full abduction during exercise (Hammer et al., 1995).

In summary, endoscopic evaluation of the upper respiratory tract at rest and during exercise is the most useful diagnostic tool currently available to assess upper airway function in horses. The slap test is useful in assessing arytenoid cartilage function, but the results must be interpreted with caution. The use of sedatives should be avoided when evaluating the equine upper respiratory tract because of their effects on arytenoid cartilage abduction. The degree of abduction after swallowing correlates well with the degree of abduction achieved with exercise. Finally, morphometric evaluation of laryngeal images can be used as an adjunct to routine endoscopy but adds little new information.

Pressure-Flow Relationships

Pressure

Static pressure in moving air equals the pressure exerted on a surface moving with the velocity of air. During exercise, high air flow velocities are achieved which results in errors in measuring static pressure. Small flow disturbances at the site of measurement result in large errors which under or overestimate the actual pressure (Nielan et al., 1992).

With transcutaneous tracheal catheters, there is little to no airway obstruction and nearly unaltered flow (Nielan et al., 1992). There appears to be no significant differences in tracheal pressure measurements between nasotracheal and transtracheal catheter systems (Williams et al., 1990b; Nielan et al., 1992). Also, proximal airway pressure measurements are unaffected by the presence of an endoscope (Ducharme et al., 1994).

Nasotracheal and transtracheal catheters can modify tracheal airflow patterns and cause significant repeatable error if they are designed incorrectly. The size and shape of the ports and their location affect static pressure measurements (Nielan et al., 1992). Static pressure measurements are influenced by length and diameter of the conduit, air flow, and velocity (Blake, 1983).

Design conditions of pressure catheters should include the ability to: 1) transmit the pressure accurately from flow to measurement site; 2) record accurately; 3) be positioned easily; 4) not alter normal ventilation; 5) be well-tolerated and non-irritating; 6) maintain position during exercise (Nielan et al., 1992).

During respiration, air flow accelerates to move around the end of the tracheal catheter resulting in altered static pressures (Bernoulli's principle). Ports too near the nose of the catheter underestimate pressure measurements by an amount that increases with increasing flow rates. Downstream from these edge effects (eddies), flow smooths out and coalesces with unaltered flow away from the probe. Properly sized ports in this downstream region yield accurate static pressure measurements. Therefore, the ports should be positioned at least 7 catheter diameters away from the nose (Nielan et al., 1992).

With high turbulence, there is some spatial and temporal unsteadiness in pressure. Therefore, several ports should be placed around the circumference of the catheter to minimize this effect. Multiple holes help to average the irregularities and make the system insensitive (± 0.5 cm of H₂O) to misalignment of less than 10 degrees with the long axis of the trachea. The static pressure at the larynx and carina is difficult to measure accurately due to diverging, converging, bifurcating flow (Nielan et al., 1992).

The repeatability of tracheal and pharyngeal pressure measurements has been evaluated in exercising horses. Ninety-six percent of mean pressure measurements were found to be within 5 cm of H₂O of the mean value for any horse. Seventy-five percent of peak pressure measurements were also within 5 cm of H₂O of the mean value for any given horse. Ninety-six percent of peak pressure measurements were within 10 cm of H₂O of the mean peak measurements for any horse. The greatest variability was in tracheal inspiratory pressure, and, hence, translaryngeal pressure. With horses traveling at 14 meters/second, tracheal inspiratory pressure ranged between -40 to -50 cm of H₂O and expiratory pressure ranged from 15 to 28 cm of H₂O. The mean pressure

measurement is more repeatable than the peak pressure measurement, but peak pressure is more clinically appropriate since it results in collapse or vibration of the airway (Ducharme et al., 1994).

Various types of breathing apparatuses worn during exercise decrease respiratory frequency, may change stride frequency-to-ventilation ratios, and alter blood gas tension (Lumsden et al., 1993). In a study by Lumsden and colleagues (1993), pressure changes across a pneumotachograph at peak inspiratory flow rates (PIF) was 10% of peak inspiratory pressure. Therefore, the pneumotachograph may affect the ventilatory response to exercise (Lumsden et al., 1993). This was supported in a recent study where the effect of a face mask and pneumotachograph on tracheal and nasopharyngeal pressures in exercising horses was investigated (Holcombe et al., 1996). Peak tracheal and pharyngeal inspiratory pressures were significantly more negative and expiratory pressures were significantly more positive in horses wearing the mask system. However, the effect of the mask-pneumotachograph assembly in studies designed to detect effects of surgical manipulations may be less important, because the effect of the system is constant during an experimental study (Holcombe et al., 1996).

Respiratory disease can significantly change the phase relationship between respiratory and stride frequency (Attenburrow, 1983). Upper airway pressure measurements do not appear to be significantly affected by uncoupling of respiratory and stride frequency in galloping horses (Palmer et al., 1995). However, uncoupling significantly affects respiratory time and frequency. Gait appears to significantly affect upper airway pressure measurements, with trotters being different from pacers and gallopers (Palmer et al., 1995).

Resistance

Resistance is the opposition to motion (Ingram & Pedley, 1986). Resistance is the ratio of the pressure difference driving the flow to the flow rate when flow and pressure signals are in phase (Derksen et al., 1986; Ingram & Pedley, 1986). However, resistance is not the only factor opposing air movement (Young & Hall, 1989). Some of the pressure difference is required to distend elastic structures and overcome inertia, in addition to overcoming frictional or viscous forces (Ingram & Pedley, 1986). Therefore:

$$P = P_E + P_R + P_I$$

where P = driving pressure; P_E = pressure required to overcome elastic forces; P_R = pressure required to overcome frictional forces; P_I = pressure required to accelerate and decelerate gas (Olson, 1981). The sum of the inertial and elastic component is known as reactance (Young & Hall, 1989). Due to the interaction of airway deformation and inertia at high respiratory rates, pressure and flow signals generated during exercise are not in phase (Derksen et al., 1986; Lavoie et al., 1995). Therefore, reactance and resistance are combined in one term called the "impedance," which is best thought of as the total opposition to change (Young & Hall, 1989). The measurement of impedance to inspiratory and expiratory flow provides a sensitive indicator of the functional consequences of upper airway obstruction and permits evaluation of the efficacy of corrective surgical techniques (Williams et al., 1990a).

Inertance values are sufficiently small at normal resting breathing frequencies to be ignored (Ingram & Pedley, 1986; Lavoie et al., 1995). However, high gas density, high cycling frequency, or large body weight gives inertance values great enough that

they should be taken into account (Ingram & Pedley, 1986). One could presume that inertia would be higher in horses, mainly because of their greater mass and biphasic respiratory pattern at rest (Lavoie et al., 1995). By using proper instrumental and display techniques and by using pressure in phase with flow to derive resistance, the correction is automatically made (Ingram & Pedley, 1986).

In people, phasic differences in flow resistance occurs in 3 sites: nasal resistance is greater during inspiration; pharyngeal and laryngeal resistance is greater during expiration; and lower airway resistance is greater during expiration. The first and last probably reflect the influence of transmural pressures on the caliber of the passage. Phasic differences in the pharynx and/or larynx probably have a neuromuscular basis (Ferris et al., 1964).

The contribution of the upper respiratory tract to total pulmonary resistance in horses varies between studies, ranging from 30–80% (Finucane & Mead, 1975; Robinson et al., 1975; Art et al., 1988; Lavoie et al., 1995). The discrepancy observed in partitioning of resistance between studies may be caused by measurement difficulties (Lavoie et al., 1995). Another, more probable, explanation for these differences is that the upper respiratory tract is a large resistor which can vary its contribution to total pulmonary resistance during each phase of the respiratory cycle. In resting horses, lower airway resistance does not change much during the different phases of the respiratory cycle. However, in the upper airway, nasal resistance increases slightly on inspiration and laryngeal resistance increases slightly on exhalation. With exercise, the lower airway's contribution to resistance decreases during inhalation and increases during

exhalation. The portion of resistance contributed by the upper respiratory tract is evenly divided between nasal and laryngeal resistance.

Airway Function and Laryngeal Paralysis

Laryngeal paralysis is characterized as a variable extrathoracic obstruction (Kashima, 1984). During inspiration, the intraluminal glottic pressure is subatmospheric (Amis et al., 1986). The paralyzed arytenoid cartilages and vocal folds are drawn into a median position resulting in an increased resistance to inspiratory air flow. The glottic narrowing results in increased linear velocity of inspired gas at the site of the narrowing and decreased lateral pressure. Upon closure, flow ceases, resulting in increased lateral pressure and reopening of the glottis (Amis et al., 1986a).

In horses with experimentally induced laryngeal hemiplegia (LH), peak inspiratory flow is decreased, and peak inspiratory pressure and impedance is increased during exercise (Derksen et al., 1986; Shappell et al., 1988; Belknap et al., 1990; Lumsden et al., 1993). Alterations in inspiratory flow, pressure, and impedance likely results from collapse of the unsupported arytenoid cartilage (Derksen et al., 1986). Laryngeal pressure becomes more subatmospheric, secondary to arytenoid collapse, which ultimately results in complete laryngeal closure (Derksen et al., 1986).

In summary, upper airway pressure and flow measurements are important to the understanding of the dynamics of the upper respiratory tract and to help determine effective treatments for diseases of the respiratory system. Pressure catheters must meet specific design criteria in order to accurately measure static pressure. Various types of breathing apparatuses worn during exercise can affect measured variables. Therefore,

investigators must be careful in their interpretation of data generated from upper airway function testing.

Reactance and resistance are combined in one term called "impedance," which represents the total opposition to motion. The upper airway represents a significant portion of the total pulmonary resistance. The larynx acts as a variable resistor which can change dramatically over time.

In horses with ILH, dynamic collapse of the paralyzed arytenoid cartilage results in an impediment to airflow. In order to maintain airflow, driving pressure is increased. However, despite this increase in driving pressure, flow cannot be maintained, therefore, impedance is increased.

Tidal Breathing Flow-Volume Loops

Pulmonary function testing has been widely used in human medicine to evaluate the type and severity of obstructive airway disease (Amis & Kupershoek, 1986). Spirometry is used to measure the movement of air into and out of the lungs during various breathing maneuvers (Crapo, 1994). Other common lung function tests include the measurement of lung volumes, airway resistance, carbon monoxide diffusing capacity, and arterial blood gases (Crapo, 1994).

One of the more common tests used in humans is forced or maximum expiratory flow-volume curves (MEFVC) (Amis & Kurpershoek, 1986). This technique was first described by Hyatt and colleagues in 1958 (Hyatt et al., 1958) and used clinically in 1968 (Jordanoglou & Pride, 1968). Airflow is plotted against volume during a single maximal inspiratory and expiratory effort (Hyatt et al., 1958). Characteristic changes

in flow-volume loops (FVL) are useful in identifying the site, type, and severity of obstructive airway processes (Amis & Kupershoek, 1986). Flow-volume loops (FVL) are non-invasive, convenient, and sensitive (Hyatt et al., 1958).

In non-cooperative patients, such as human infants, dogs, cats, and horses, tidal breathing flow-volume loops (TBFVL) are used to detect airway obstruction (Abramson et al., 1982; Amis & Kupershoek, 1986; McKiernan et al., 1993; Petsche et al., 1994). At rest, tidal breathing airflow and pressure changes in the airway are small, making TBFVL less sensitive in detecting airway obstruction when compared to MEFVC (Connally & Derksen, 1994). The sensitivity of TBFVL may increase as airflow rates approach maximum (Fry & Hyatt, 1960). During tidal breathing, airflow rates are likely to be effort dependent, a large flow reserve is usually available, and large variations in flow rates are possible (Amis & Kupershoek, 1986). A change in effort may have an effect on calculated indices and loop shape. Animals are free to choose their own breathing strategy (Amis & Kupershoek, 1986). During exercise, however, variability in breathing strategy is decreased and airflow rates increase (Lumsden et al., 1993). Therefore, the use of high speed treadmills in horses may result in near-maximal airflow rates, thereby improving the sensitivity of TBFVL in detecting airway obstruction (Lumsden et al., 1993).

Although restricted to nasal breathing, horses can accommodate large changes in flow and respiratory rate for sustained periods (Robinson et al., 1975). Both inspiratory and expiratory flow are frequently biphasic at rest compared to the more usual uniphasic sinusoidal flow of other mammals (Robinson et al., 1975; Lumsden et al., 1993; Petsche et al., 1994). Peak flows occur early or late in inspiration and early in expiration

(Lumsden et al., 1993; Petsche et al., 1994). Other TBFVL shapes observed in resting horses are monophasic or, less frequently, triphasic inspiratory curves (Lumsden et al., 1993). Flow-volume loops become less polyphasic with increasing respiratory frequency (Art & Lekeux, 1988). Biphasic flow could result from fluctuations in airway resistance, asynchronous movement of the ribs and diaphragm, or a peculiar combination of active and passive components during inspiration and expiration (Robinson et al., 1975).

Three functional groups of airway obstructions have been described: fixed, variable extrathoracic, and variable intrathoracic (Amis & Kurpershoek, 1986; Lumsden et al., 1993). Variable intrathoracic obstruction results in expiratory flow limitations, variable extrathoracic obstruction results in inspiratory flow limitations, and fixed obstructions result in changes in both inspiratory and expiratory flow rates (Lumsden et al., 1993).

Upper airway obstruction in the horse, secondary to dynamic collapse of unsupported soft tissue structures, results in an unchanged expiratory limb of the respiratory cycle, but the inspiratory limb exhibits decreased flow rates. When TBFVL are generated from exercising horses with experimentally induced LH, there is marked inspiratory flow limitations with preservation of the expiratory air flow curves (Lumsden et al., 1993). Peak inspiratory flow (PIF), IF_{50} (inspiratory flow at 50% of tidal volume), and IF_{25} (inspiratory flow at 25% of tidal volume) are decreased while PEF/PIF and EF_{50}/IF_{50} are increased (Lumsden et al., 1993).

Laryngeal paralysis in humans results in a reduction of both maximal and mid-vital capacity inspiratory flow rates. Flow volume loop characteristics of variable extrathoracic obstruction include decreased inspiratory flow rates, normal expiratory flow

rates, and increased V_{E-50}/V_{I-50} (ratio of mid-vital capacity flow rates on expiration and inspiration) (Kashima, 1984).

In dogs with non-fixed upper airway obstruction, Type 2 TBFVL are generated. These loops are characterized by a normal expiratory phase and flattening or reversal of the normal inspiratory loop shape (Amis et al., 1986).

In horses and humans, indices of mid-tidal inspiratory flow rates (IF_{50} and EF/IF_{50}) are the most reliable and sensitive indicator of dynamic upper airway obstruction (Lumsden et al., 1993).

Like other species, resting horses exhibit a large coefficient of variation (standard deviation expressed as a percentage of the sample mean) for TBFVL indices, which is indicative of the variability in breathing strategy (Lumsden et al., 1993). In exercising horses, breathing pattern is imposed by a coupling of respiratory and stride frequency (Manohar, 1986; Lumsden et al., 1993). This coupling forces a breathing strategy, thereby decreasing the coefficient of variation (Lumsden et al., 1993). In exercising horses, the shape of the TBFVL may be influenced by many factors including gait, stride frequency, and mechanical events related to locomotion, such as acceleration, deceleration, and weight bearing (Lumsden et al., 1993).

In summary, TBFVL are non-invasive, convenient, and sensitive in detecting airway obstruction in exercising horses. When TBFVL are generated from horses with LH, the inspiratory phase of the respiratory cycle shows flow limitations while the expiratory phase is preserved. Similar changes are observed in humans and dogs with laryngeal paralysis.

Chapter 4

TREATMENT OF IDIOPATHIC LARYNGEAL HEMIPLEGIA

One of the most important aspects of equine laryngeal disease is the understanding of treatment options available and the anticipated prognosis for future athletic performance. The surgeon must have a working knowledge of all the potential options in order to advise his/her client which treatment will yield the most satisfactory results.

Arytenoidectomy

In 1843, Günther first described the technique of partial arytenoidectomy as a primary treatment of ILH in horses (Liautard, 1892). The partial arytenoidectomy involves removal of both the corniculate process and arytenoid body, leaving only the muscular process (Tulleners et al., 1988). However, air flow limitations persisted (Speirs, 1986; Lumsden et al., 1994).

In 1866, Möller modified the technique to include removal of the muscular process (total arytenoidectomy). Access to the larynx was first achieved by cutting the cricoid cartilage and a number of tracheal rings. A cuffed tampon was left in the defect to control hemorrhage (Liautard, 1892). Möller later closed the defect in the mucous membrane to decrease the amount of post-operative hemorrhage (White & Blackwell, 1980). The total arytenoidectomy was, again, an unsuccessful search for a surgical cure

because of post-operative dysphagia and secondary aspiration pneumonia and death (Speirs, 1986).

With the development of the ventriculectomy procedure in the early 1900s, the arytenoidectomy fell out of use (Williams, 1907). In 1970, the laryngoplasty was developed, and combined with the ventriculectomy, is currently the treatment of choice for ILH (Haynes et al., 1984). In the late 1970's, the arytenoidectomy procedure began regaining popularity and became the treatment of choice for arytenoid chondritis (Haynes et al., 1984).

The purpose of the arytenoidectomy is to increase the cross-sectional area of the rima glottidis, thereby decreasing the resistance to air flow. Enlargement of the rima glottidis also prevents dynamic collapse by reducing the Bernoulli effect. During the procedure, the surgeon aims to remove all unsupported structures to prevent dynamic collapse during exercise. Therefore, not only is airway diameter and geometry important, but stiffness of the soft tissues is also important (Tulleners et al., 1988).

Currently, the partial or total arytenoidectomy is the treatment of choice for laryngoplasties that have failed due to inadequate abduction or release of the arytenoid cartilage, abnormalities of the laryngeal cartilages which precludes performance of the laryngoplasty procedure (chondritis, chondroma, laryngeal ossification, and focal lesions of the arytenoid cartilages), and for laryngoplasties that have resulted in chronic coughing due to piriform recess obstruction with resultant contamination of the larynx with ingesta (Haynes et al., 1984).

With the increasing popularity of the arytenoidectomy procedure for treatment of specific diseases of the larynx, investigations have been performed to determine which of the 3 techniques (subtotal, partial, or total) yields the best results.

The subtotal arytenoidectomy leaves the muscular process and corniculate process to protect the laryngeal lumen from aspiration of ingesta. Therefore, dysphagia and aspiration are not common sequelae (Haynes, 1984). The subtotal arytenoidectomy relies on scar formation between the laryngeal mucous membrane and underlying musculature to stabilize the laryngeal wall (Williams et al., 1990b). Belknap and colleagues reported that air flow mechanics and blood gas measurements are not improved in horses with experimentally induced LH treated with a subtotal arytenoidectomy and unilateral ventriculectomy (Belknap et al., 1990). The corniculate process and vocal fold is drawn into the airway during exercise resulting in continued dynamic collapse and interference with air flow (Stick & Derksen, 1989; Belknap et al., 1990).

The partial arytenoidectomy involves removal of both the arytenoid body and corniculate process (Speirs, 1987). Dysphagia or coughing and aspiration pneumonia may result if inadvertent removal of excessive mucosa near the piriform recess occurs (Tulleners et al., 1988). In a retrospective study of partial arytenoidectomies, 36% developed a nasal discharge of food and/or water, but only 9% were performance-limited (Speirs, 1986).

In 1993, partial arytenoidectomy was quantitatively evaluated using upper airway function testing. The partial arytenoidectomy combined with bilateral ventriculectomy improved upper airway function in exercising horses with experimentally induced LH. However, some flow limitation remained at near maximal air flow rates. Therefore,

partial arytenoidectomy successfully restores upper airway function in submaximally exercising horses. At maximal exercise, however, airway function is significantly improved but does not return to pre-LRLN values (Lumsden et al., 1994).

Finally, the total arytenoidectomy involves removal of the arytenoid body, muscular process, and corniculate process (Speirs, 1987). Dysphagia with secondary aspiration pneumonia has been described as a common, and sometimes life-threatening, complication (Haynes et al., 1984). Dysphagia is presumably due to removal of excessive tissue from the dorsal aspect of the rima glottidis (Speirs, 1986). As this tissue contracts, there is excessive distortion of the dorsal region of the larynx predisposing to dysphagia. Some surgeons transect the transverse arytenoid ligament when performing this procedure. This may allow the mucosal flap to be retracted further into the larynx resulting in a large, dorsal defect with subsequent dysphagia (Speirs, 1986).

In summary, three different arytenoidectomy procedures have been described: subtotal, partial, and total. The subtotal arytenoidectomy fails to restore airway function in submaximally exercising horses with experimentally induced LH. The partial arytenoidectomy improves airway function, though, some flow limitations persist at near maximal exercise. To date, the total arytenoidectomy has not been quantitatively evaluated.

Laryngeal Reinnervation

In 1885, Exner was the first to describe a technique for laryngeal reinnervation in rabbits. The first successful repair of the recurrent laryngeal nerve in people was

reported in 1909 by Horsley. Steindler (1916) and Elsberg (1917) also demonstrated that denervated muscles can be reinnervated by nerve transfers (Crumley, 1985).

Upon nerve transection, biochemical reactions are triggered in the denervated muscle making it more receptive to reinnervation. Substances (neurocletin, nerve-growth-factorlike substance, axon-sprouting inhibitor factor, and others) arising from muscle fibers near the motor end plate, the motor end plate itself, or the distal nerve fiber are known to promote or inhibit axon sprouting (Crumley, 1985).

When considering muscle reinnervation, several concepts must be kept in mind. The most significant factor which regulates reinnervation is the status of the motor end plates in the paralyzed muscle. Motor nerve fibers are well known to ramify and undergo axon sprouting among denervated muscle fibers. Axon sprouting is the critical neurophysiologic step in actual reinnervation in that it allows the nerve fibers from the implanted nerve to reach and mate with the denervated muscle's motor end plates. Secondly, axon sprouting increases the number of muscle fibers innervated by a single nerve fiber. Thirdly, reinnervated muscle assumes the contraction and biochemical characteristics of the implanted nerve. Finally, denervation atrophy is thought to render muscle incapable of reinnervation following a period of denervation (Crumley, 1985).

The time from nerve injury to onset of atrophy is unclear, probably varying from species to species, among individuals within a species, and among different muscles of the same subject. Evidence indicates that the laryngeal muscles are among the least hardy with regard to length of survival without innervation (Crumley, 1985).

Paralysis of laryngeal muscles secondary to damage to the recurrent laryngeal nerve results in loss of arytenoid abduction and adduction. The earlier reinnervation

occurs, the greater the chance that muscle contraction will be regained. Furthermore, early reinnervation is important, because, over time, the cricoarytenoid joint may ankylose causing impairment of arytenoid and vocal fold abduction or adduction (Crumley, 1985).

Three techniques for laryngeal reinnervation have been described in man and horses: nerve-pedicle transfer, nerve implantation, and nerve anastomosis (Ducharme et al., 1989I; Ducharme et al., 1989II; Ducharme et al., 1989III; Fulton et al., 1991). Nerve implantation in the horse has been performed using the cut end of the second cervical nerve which is then implanted into the CAD (Ducharme et al., 1989II). At rest, less than 30% abduction was achieved in 4 out of 6 horses with no abduction in 2 out of 6 by 6 months after implantation. The limited degree of abduction observed, despite histopathologic evidence of partial reinnervation, may have been due to: insufficient time to allow for subterminal axonal sprouting; recurrent laryngeal nerve regrowth preventing muscle fibers from being receptive to reinnervation; abduction only being seen during exercise; and/or inconsistent nerve firing (Ducharme et al., 1989 II). The major weakness of this study was the method of evaluation. The second cervical nerve is an accessory nerve of respiration which only fires with increasing respiratory efforts. Therefore, evaluation of the efficacy of the nerve implantation technique should be performed during exercise.

Nerve anastomosis involves anastomosing the first cervical nerve to the abductor branch of the LRLNv. At 6 months, clonic movement of the left arytenoid during inspiration was observed in 5 out of 6 horses. Although reinnervation was achieved as ascertained by resting endoscopy, pulmonary function testing, and histopathology, the

partial restoration of function observed did not appear to be sufficient for racing soundness. Whether the clonic movement was caused by incomplete reinnervation or the firing behavior of the first cervical nerve is unknown (Ducharme et al., 1989III). Again, the major weakness of this study was that evaluations were not performed during exercise.

The final technique for laryngeal reinnervation is the nerve-muscle pedicle graft (Greenfield et al., 1988; Ducharme et al., 1989I; Fulton et al., 1991). In 1970, Tucker found restoration of laryngeal function in humans and dogs by 2–6 weeks after surgery (Tucker et al., 1970; Tucker, 1976). Approximately 80% of the nerve fibers did not degenerate. In contrast to Tucker's conclusions, Ducharme and colleagues found that, in horses, reinnervation appeared to take the form of axonal subterminal sprouting or axonal rerouting; not direct transmission of impulses through the transplanted nerve-muscle unit (Ducharme et al., 1989I).

Two donor pedicles have been used for the nerve-muscle pedicle graft: the omohyoid and the sternothyroid muscle, which are both innervated by a branch of the first and second cervical nerves (Ducharme et al., 1989I). Since the omohyoid and sternothyroid muscles are accessory muscles of respiration, they may not become active until the animal exercises (Greenfield et al., 1988). In dogs, the sternothyroid pedicle graft resulted in restoration of arytenoid cartilage movement by 36 weeks after transplantation (Greenfield et al., 1988). In resting horses, use of the omohyoid pedicle graft resulted in poor restoration of arytenoid cartilage function (Ducharme et al., 1989I). However, different results may have been obtained if the evaluations were performed during exercise. In another study, the omohyoid pedicle graft returned inspiratory

impedance back to pre-LRLN values in submaximally exercising horses between 24 and 52 weeks after transplantation (Fulton et al., 1991).

Improvement in airway function after neuromuscular pedicle grafting may be due to surgery around the CAD resulting in the surgical scar tethering the arytenoid cartilage laterally to the thyroid cartilage, some degree of arytenoid cartilage stabilization which provides the cricothyroid muscle with a more physiologic fulcrum allowing it to produce vocal cord lengthening, and/or fixation which allows the sternothyroid's pull on the thyroid cartilage to become transferred to the arytenoid cartilage, thereby enhancing the sternothyroid's effect on glottic enlargement (Crumley, 1985).

An interesting alternative pedicle graft technique is the muscle-to-muscle graft using the contralateral CAD muscle. In muscle-to-muscle neurotization, an innervated muscle acts as a source of axons for a denervated muscle. An important aspect for graft survival is to preserve full muscle fiber length in the muscle grafts. However, using the CAD for muscle-to-muscle neurotization was found not to be a clinically useful technique in horses with experimentally induced LH (Harrison et al., 1992). Also, in horses with clinical ILH, this technique is unlikely to work since investigators have found evidence of denervation of the adductors on the right side.

In summary, laryngeal muscle reinnervation is theoretically the best treatment option for horses with ILH. Three techniques for laryngeal reinnervation in the horse have been described: nerve-pedicle transfer, nerve implantation, and nerve anastomosis. Nerve implantation and nerve anastomosis are unsatisfactory for resolving the airway obstruction produced by LH. However, these 2 techniques have only been evaluated in the standing horse. The nerve-muscle pedicle graft is effective in restoring airway

function in submaximally exercising horses. However, reinnervation does not occur until 6–12 months after transplantation.

Prosthetic Laryngoplasty

In 1888, Möller first introduced the idea of achieving and maintaining abduction of the paralyzed arytenoid cartilage and vocal fold (Speirs, 1987). However, his idea was not successfully explored until the prosthetic laryngoplasty technique was first reported in 1968 and described extensively in the literature in 1970 by Marks and colleagues (MacKay-Smith & Marks, 1968; Marks et al., 1970b).

The laryngoplasty procedure results in abduction and stabilization of the paralyzed arytenoid cartilage and tensing of the vocal fold (Williams et al., 1990b). This prevents dynamic collapse of the soft tissue structures of the larynx, thereby alleviating exercise intolerance and inspiratory noise in horses with ILH (Haynes, 1984; Derksen et al., 1986; Ducharme et al., 1991).

The goal of the laryngoplasty procedure is to produce mechanical abduction of the arytenoid cartilage in a position midway between normal resting and full abduction (Speirs et al., 1983; Derksen et al., 1986). It is believed that 60–70% of maximum abduction should be targeted (Ducharme et al., 1991). Stabilization appears to be more important than the degree of abduction (Derksen et al., 1986; Russell & Slone, 1994). The laryngoplasty procedure is the preferred treatment for selected Grade III and all Grade IV cases of ILH (Ducharme et al., 1991).

Maximum opening of the rima glottidis is not obtained with a prosthetic laryngoplasty (Ducharme et al., 1991). However, the dramatic improvement of some

horses after a laryngoplasty procedure indicates that it can be used to achieve near normal airway conformation (White & Dabareiner, 1994). The fixation prevents collapse of the paralyzed arytenoid cartilage into the airway during high inspiratory flow rates and pressures (Haynes, 1984). It appears that the degree of abduction has little effect on outcome except when the arytenoid cartilage is abducted in such a manner that there is a depression into the pharyngeal wall (Russell & Slone, 1994). Excessive abduction results in an increased prevalence of complications (Russell & Slone, 1994).

The placement of 2 sutures for the laryngoplasty procedure combined with a ventriculectomy procedure is recommended in order to achieve the best clinical results (Speirs et al., 1983; Speirs, 1987). One of the most important aspects of prosthesis positioning is dorsal and axial placement of the suture in the cricoid cartilage (Haynes, 1984). The CAD muscle fibers extend from the dorsal, caudal, and axial region of the cricoid cartilage to the muscular process of the arytenoid cartilage in a rostralateral direction. Fibers of the CAD attach perpendicularly to the axis of the cricoarytenoid articular surfaces, and the prosthesis should be placed in a similar direction (Haynes, 1984). In cases of Grade III ILH, it may be beneficial to transect and ligate the recurrent laryngeal nerve to prevent any residual contraction of the CAL and CAD which could result in suture pull-through and failure (Ducharme et al., 1991).

Clinical failure of the laryngoplasty technique can be due to infection, improper prosthesis placement, pull-out from the muscular process, and possibly age of the animal (younger horses have softer cartilages which increases the risk of suture pull-through). Biomechanical properties affecting cartilage retention of the prosthesis include cartilage strength, prosthesis tension, and prosthetic material variables. An in vitro study

evaluating retention strength of the laryngeal prosthesis indicated that age, side of prosthesis placement, and material used does not affect retention strength. Failure primarily occurred from pull-through through the muscular process. Reasons for this pull-through include acute mechanical cartilage failure, cyclic cartilage failure, pressure necrosis, improper suture placement, and cartilage disease. Cyclic movement of the cartilage may be caused by muscular contractions and changes in luminal pressure. Cyclic loading may result in failure over time (Dean et al., 1990). Therefore, transection of the adductor branch of the recurrent laryngeal nerve may decrease cyclic loading and cartilage pull-through (Goulden & Anderson, 1982). Also, the placement of 2 prostheses may slow or eliminate cutting through the cartilage of the cricoid or muscular process of the arytenoid (Speirs et al., 1983).

Several post-operative complications have been associated with the laryngoplasty procedure. They include failure to maintain abduction, ossification of the laryngeal cartilages, choke, reaction to the prosthesis, wound infection and dehiscence, seroma formation, tracheitis, suture sinus formation associated with contamination of the prosthesis, pneumonia, intralaryngeal granulomatous polyps, right-sided laryngospasm during exercise, death due to asphyxia, laryngeal edema, chondritis, regurgitation, and coughing (Speirs, 1987; Ducharme et al., 1991). The frequency of post-operative complications is reported to be 9–47% (Russell & Slone, 1994).

Coughing and regurgitation are considered the primary complications that develop after prosthesis insertion (Russell & Slone, 1994). Up to 40% of horses may cough immediately after surgery while 5–10% will become chronic coughers (Speirs, 1987; Ducharme et al., 1991). The exact pathogenesis of coughing is unknown. However,

contamination of the larynx and trachea with food particles and subsequent stimulation of the cough reflex is presumably the main mechanism involved (Speirs, 1987). The creation of permanent abduction interferes with laryngeal lumen protection (Haynes, 1984; Speirs, 1987). Excessive abduction can distort the lateral food channels resulting in contamination of the upper airway (Speirs, 1987). Cutting or removing the prosthesis has alleviated chronic coughing in some cases (Greet et al., 1979).

Using fluoroscopic techniques and videotape recordings, investigators demonstrated that after a laryngoplasty procedure, liquid food passes into the larynx and even lower respiratory tract (Greet et al., 1979). While most authors attribute aspiration to excessive abduction, food particles in the airway may also be caused by pharyngeal dysfunction secondary to surgical trauma to muscles or nerves (Greet et al., 1979; Speirs, 1987).

Histologic examination of muscles and cartilages near the anchorage of the prosthesis revealed a moderately severe inflammatory reaction. Fibrous tissue was deposited in the muscles around the prosthesis. A severe inflammatory reaction was also present in the laryngeal cartilages, with death of many chondrocytes (Greet et al., 1979). This perilaryngeal inflammation could be responsible for post-operative coughing. Other causes of coughing include intralaryngeal granulomas, protrusion of the prosthesis into the larynx, and pre-existing chondritis (Haynes, 1984; Speirs, 1987).

The second most common post-operative complication is nasal discharge of food and water. This likely occurs due to excessive abduction leading to interference with the palatopharyngeal arch and entrance of food and water into the esophagus (Speirs, 1987).

The success of the prosthetic laryngoplasty has been reported to range from 5–95% (Goulden & Anderson, 1982; Speirs, 1987; Russell & Slone, 1994; White & Dabareiner, 1994) with a greater success in non-racehorses (Russell & Slone, 1994). It has been reported that the success rate is lower when a ventriculectomy procedure is not performed in conjunction with the prosthetic laryngoplasty (Speirs, 1987). The improvement in inspiratory noise production of horses with ILH treated with a laryngoplasty and ventriculectomy has ranged from 25–85% (Goulden & Anderson, 1982; Speirs, 1987; Ducharme et al., 1991). The success rate of the prosthetic laryngoplasty is lower if a previous ventriculectomy was performed (Marks et al., 1970b).

In draft horses, there appears to be no difference in success rate between unilateral ventriculectomy, bilateral ventriculectomy, or prosthetic laryngoplasty plus bilateral ventriculectomy (Bohanon et al., 1990).

The laryngoplasty procedure alone reverses the decrease in inspiratory flow rate and increases inspiratory resistance in horses with experimentally induced left LH exercising submaximally on a treadmill (Derksen et al., 1986). The laryngoplasty plus ventriculectomy returns inspiratory pressure back to pre-LRLN values in horses ridden over a 1005 meter race course at maximal exercise (Williams et al., 1990b). Laryngoplasty plus ventriculectomy normalizes upper airway function in horses exercising at speeds greater than 15 meters/second (Ducharme et al., 1991). The improvement in inspiratory pressure after a laryngoplasty plus unilateral ventriculectomy is greater than after a subtotal arytenoidectomy plus unilateral ventriculectomy (Williams et al., 1990b). Also, laryngoplasty plus unilateral ventriculectomy, but not the subtotal

arytenoidectomy plus unilateral ventriculectomy, returns respiratory frequency to pre-LRLN values (Williams et al., 1990b). To date, there is no information that correlates airway cross-sectional area with airway impedance (Pascoe, 1994).

In summary, the prosthetic laryngoplasty is currently the treatment of choice for ILH in horses. The goal of the technique is to produce mechanical abduction of the paralyzed arytenoid cartilage and tense the vocal fold, thereby preventing dynamic collapse of soft tissue structures into the larynx during exercise. Several post-operative complications have been associated with the laryngoplasty procedure including prosthesis failure, coughing, regurgitation, and nasal discharge of food and water. The success rate of the procedure in alleviating exercise intolerance and respiratory noise is variable.

Ventriculectomy

Investigations using the ventriculectomy technique as a treatment for ILH were begun in 1834 by Professors F. and K. Günther (father and son, respectively) (Williams, 1911). The technique was first published by K. Günther in 1866 (Williams, 1911; Speirs, 1987). In 1907, a simplified version was developed by Williams and later popularized by Hobday (Speirs, 1987).

The objective of the ventriculectomy procedure is to produce abduction of the arytenoid cartilage by formation of adhesions between the arytenoid and thyroid cartilages and to reduce filling of the ventricle with air during inspiration. The latter objective was thought to be the primary reason for improvement in some horses, since abduction and fixation of the arytenoid cartilage are not effectively accomplished (Haynes, 1984).

Partial resection of the vocal fold, in conjunction with the ventriculectomy, has been proposed to result in closer adhesion of the arytenoid cartilage to the wing of the thyroid cartilage (Reynolds, 1934). Suturing of the vocal fold to the ventricle may result in stronger scar tissue formation due to organization of the hematoma within the saccule (Schebitz, 1964; Pouret, 1966). Transverse laryngeal webbing has been reported to occur in dogs with laryngeal paralysis treated with a bilateral ventriculocordectomy through an oral approach and horses treated with a ventriculocordectomy procedure without primary closure (Dixon et al., 1994; LaHue, 1995). Therefore, suturing may prevent laryngeal webbing and ventral glottic stenosis (Dixon et al., 1994; LaHue, 1995).

With the earlier techniques, potential sequelae of the ventricle stripping operation included laryngospasm, dyspnea, septic infection of the wound, ossification of the laryngeal cartilages, tetanus, swelling and granuloma formation, and fragmented tissue edges (Hobday, 1935; Haynes, 1978). With the advancement of surgical techniques and instrumentation, few complications remain. Healing of the ventricle wounds has been reported to take 14–21 days (Reynolds, 1934; Hobday, 1935) or 42 days when the procedure is performed with an nd:YAG laser (Shires et al., 1990).

The indications for ventriculectomy have included: partial LH which results in decreased abductor ability and/or asynchronous motion of the arytenoid cartilages; mild cases of total paralysis when the arytenoid cartilage is in a paramedian position; and animals which do not merit the cost of a laryngoplasty procedure (Haynes, 1978).

The success rate for improvement in exercise tolerance after a ventriculectomy procedure has been reported to range from 5–100%, with greater success in pleasure horses (Speirs, 1987). Some investigators believe that the improvement in performance

lasts only 1–2 years before regression occurs (Marks et al., 1970b). However, other authors believe the improvement is permanent (Hobday, 1912). A study by Reynolds in 1934 and by Barber and colleagues in 1984 indicated that 70–80% of horses improved following a ventriculectomy procedure (Reynolds, 1934; Barber et al., 1984). However, their findings were based on subjective evaluation. Other investigators report a much lower improvement rate (28%) (Baker, 1983b). In draft horses, 87% improvement has been reported, thereby supporting the continued use of the procedure to treat laryngeal hemiplegia and associated exercise intolerance in these horses (Ducharme et al., 1991).

The ventriculectomy procedure has also been used to decrease noise production in horses with ILH, but variable success rates have been reported (10–80%) (Reynolds, 1934; Schebitz, 1964; Ducharme et al., 1991).

In a quantitative analysis of the effects of ventriculectomy as a treatment for experimentally induced left LH, it was found that ventriculectomy alone failed to improve upper airway function in submaximally exercising horses (Shappell et al., 1988). The technique fails to adequately stabilize the arytenoid cartilage in the abducted position which results in airflow turbulence and inspiratory noise (Haynes, 1984). However, if the ventricle fills with air, the area of the ventral aspect of the glottis would decrease causing an increase in the degree of respiratory obstruction (Speirs, 1987). When the ventriculectomy is combined with the prosthetic laryngoplasty, further stabilization of the vocal fold may be achieved (Williams et al., 1990b). Although ventriculectomy alone does not improve airflow function after LRLN, it is not known if prosthetic laryngoplasty without ventriculectomy improves airway function to the degree reported for the combined procedure (Shappell et al., 1988).

The ventriculectomy/vocal cordectomy procedure may benefit horses with primary vocal fold collapse. Relaxation of the vocal folds may be due to paralysis of the cranial laryngeal branch of the vagus nerve without a disturbance in function of the intrinsic laryngeal muscles supplied by the recurrent laryngeal nerve. The cranial laryngeal branch of the vagus nerve supplies motor fibers to the cricothyroid muscle, which tenses the vocal fold (Quinlan & Morton, 1957).

In summary, the ventriculectomy alone fails to restore upper airway function in submaximally exercising horses with experimentally induced LH. However, it is not known whether combining ventriculectomy with the prosthetic laryngoplasty further stabilizes the vocal fold. If improved stabilization does occur, then the combined procedure may be more efficacious than the laryngoplasty alone.

Chapter 5

THE EFFICACY OF PROSTHETIC LARYNGOPLASTY WITH AND WITHOUT BILATERAL VENTRICULOCORDECTOMY AS TREATMENTS FOR LARYNGEAL HEMIPLEGIA IN HORSES

Introduction

Idiopathic laryngeal neuropathy in horses has been recognized for centuries as a cause of exercise intolerance and respiratory noise (Marks et al., 1970; Hillidge, 1986; Williams et al., 1990b). Horses with this condition have evidence of neurogenic atrophy of the intrinsic laryngeal muscles that are innervated by the recurrent laryngeal nerve (Cole, 1946; Duncan et al., 1974; Anderson et al., 1980; Cahill et al., 1986IV; Duncan et al., 1991; Lopez-Plana et al., 1993a). Paresis of the intrinsic laryngeal muscles results in dynamic collapse of the affected arytenoid cartilage into the airway during exercise (Derksen et al., 1986).

Surgical techniques developed as treatments for laryngeal hemiplegia include arytenoidectomy, laryngeal reinnervation, prosthetic laryngoplasty, and ventriculectomy (Derksen et al., 1986; Speirs, 1987; Shappell et al., 1988; Belknap, 1990; Fulton et al., 1991; Lumsden et al., 1994). Studies evaluating the efficacy of these procedures suggest that prosthetic laryngoplasty is the treatment of choice (Derksen et al., 1986; Shappell et al., 1988). While it has been shown that prosthetic laryngoplasty improves upper airway function in submaximally exercising horses with laryngeal hemiplegia, the

efficacy of this procedure has not been evaluated in horses exercising at maximum heart rates.

Although ventriculectomy by itself does not correct airway obstruction in horses with experimentally induced left laryngeal hemiplegia (Shappell et al., 1988), many equine surgeons perform a ventriculectomy/vocal cordectomy concurrently with the prosthetic laryngoplasty in an attempt to optimize airway function. However, it is not known if ventriculectomy combined with laryngoplasty is more efficacious than laryngoplasty alone.

For this reason, the present study was performed to determine the effect of prosthetic laryngoplasty with and without bilateral ventriculocordectomy on upper airway function in horses with experimentally induced left laryngeal hemiplegia, exercising at maximal heart rates.

Materials and Methods

Horses

Fifteen adult Standardbred horses (9 males and 6 females) with a mean age of 4.7 years (range = 3–8 years) and a mean weight of 404.7 kgs (range = 359–481 kgs) were used in this study. All horses were administered an anthelmintic and vaccinated against eastern and western equine encephalitis, tetanus, equine influenza, and rhinopneumonitis before the start of the study. Endoscopic evaluation of the upper airway, including trachea, was performed when horses were at rest, and the upper airway was evaluated during exercise (10 meters/second [m/s]). To be included in the study, all horses had to have endoscopically normal upper airways. Horses were maintained on pasture

between measurement protocols and surgical procedures. The studies described were approved by the All-University Committee on Animal Use and Care at Michigan State University.

Measurement Techniques

Measurements of upper airway function have been described previously (Derksen et al., 1986). Briefly, a fiberglass face mask, which covered the mouth and nostrils, was fitted to the horse and sealed with a rubber shroud and adhesive tape. A 15.2 cm diameter pneumotachograph (Laminar flow straightener element, Merriam Instruments, Grand Rapids, Mich.) was mounted on the face mask with a protective wire mesh (Mesh SS screen, McMaster Carr, Chicago, Ill.) located between the horse's muzzle and pneumotachograph screen. The resistance of the pneumotachograph was 0.04 cm of H₂O/liters/second (L/s) up to an air flow rate of 90 L/s. The combined resistance of the mask-pneumotachograph assembly was 0.05 cm H₂O/L/s at peak air flow rates. Pressure changes across the pneumotachograph were measured by use of a differential pressure transducer (Model DP 45-22, Validyne Sales, Northridge, Cal.). The signal produced was proportional to inspiratory and expiratory air flow. Before each measurement protocol, the pneumotachograph was calibrated using a rotameter flow meter (Model FF-2-37-P-10/77, Fisher & Porter Co., Warminster, Penn.) capable of measuring flow rates up to 90 L/s.

Inspiratory and expiratory transupper airway pressure (P_{ui} and P_{ue}) was defined as the pressure difference between tracheal and mask pressure. Tracheal pressure was measured by placement of a nasotracheal catheter positioned approximately 20 cm caudal

to the larynx. One horse in Group 2 resented placement of the nasotracheal catheter during the 180-day measurement period. In this animal therefore, pressure measurements were obtained via a lateral tracheal catheter placed percutaneously at the midcervical level (Derksen et al., 1986). In all horses, mask pressure was measured by means of a second catheter, positioned just cranial to the nostrils. A differential pressure transducer was used to measure P_u , and was calibrated before each protocol by use of a water manometer. To avoid phase differences between measuring devices, flow and pressure signals were phase-matched up to 10 Hz as previously described (Derksen et al., 1986).

Air flow and pressure signals were passed through low-pass filters, and the data were then fed into a respiratory function computer (Buxco LS-14, Buxco Electronics Inc., Sharon, Conn.). Tidal volume (V_T) was obtained by digitally integrating the flow signal with respect to time. Inspiratory and expiratory impedance (Z_I and Z_E) were calculated as the ratio of peak transupper airway pressure and peak air flow. Minute ventilation ($\dot{V}_{min}$) was calculated as the product of V_T and respiratory frequency (f). Heart rate (HR) was recorded using a telemetry system (Digital UHF Telemetry System, M1403A, Hewlett Packard, Palo Alto, Cal.). All measurements were obtained from 10 consecutive breaths.

From each exercise period, 10 tidal breathing flow-volume loops (TBFVL) were selected and analyzed using computer software (Buxco LS-14, Buxco Electronics Inc., Sharon, Conn.). Criteria for inclusion of a TBFVL included adequate loop closure ($<5\%$ difference between inspiratory and expiratory volumes) and lack of artifacts. Each TBFVL was quantitatively analyzed by calculating f , inspiratory and expiratory times (T_i and T_e), ratio of breathing times (T_e/T_i), total breathing time (T_{tot}), tidal volume

(V_T), V_T/T_i , T_i/T_{tot} , peak inspiratory and expiratory flow rates (PIF and PEF), flow rates at 50 and 25% V_T (IF_{50} , EF_{50} , IF_{25} , and EF_{25}), and the ratios of the flow rates (PEF/PIF, EF/IF_{50} , and EF/IF_{25}).

Experimental Design

Over a 7-day period, all horses were trained to work on a treadmill while wearing the face mask. Before upper airway function testing, maximal HR (HR_{max}) during exercise was determined. Each horse underwent a rapid incremental exercise test (RIET) to determine the relationship between treadmill speed and HR. During the RIET, horses wore the face mask-pneumotachograph assembly and were exercised on a 3° incline. Horses were warmed up for 3 minutes at 4 m/s and then speed was increased to 6 m/s for 90 seconds. Thereafter, the treadmill speed was increased every 60 seconds to 10, 11, 12, and 13 m/s, respectively. The RIET was terminated when the horse could no longer hold its position on the treadmill. Heart rate was measured during the last 15 seconds of each exercise period. Maximal heart rate was determined from the treadmill speed at which no further increase in HR was observed. The treadmill speed at which 75% of maximal HR ($HR_{0.75max}$) was obtained was also determined. In 4 horses this treadmill speed would have been below 6 m/s. Therefore, 6 m/s was chosen as the minimum treadmill speed for $HR_{0.75max}$.

Experimental Protocol

Horses were randomly assigned to 1 of 3 treatment groups by use of a random numbers table (Koopmans, 1981). Horses in group 1 served as controls, horses in group

2 received a left prosthetic laryngoplasty, and horses in group 3 received a left prosthetic laryngoplasty and bilateral ventriculocordecotomy. There were 5 horses per treatment group.

In each group, measurements were made at 4 time periods, before left recurrent laryngeal neurectomy (LRLN), 14 days after LRLN, and 60 and 180 days after surgical treatment. During each protocol, data were collected at rest, at $HR_{0.75max}$ and at HR_{max} . After the rest period, horses were warmed up for 2 minutes at 4 m/s with the treadmill at a 3° incline. Following this, horses were exercised at treadmill speeds corresponding to $HR_{0.75max}$ for 2 minutes. After a further 1-minute rest period, horses were then exercised at treadmill speeds corresponding to HR_{max} for 2 minutes or until the horse could no longer maintain its position on the treadmill. Data were collected during the last 1-minute of each 2-minute period.

Upper airway endoscopy was performed at rest before and immediately after LRLN to document the induction of Grade IV left laryngeal hemiplegia. Endoscopy was repeated 3–5 hours and 30 days after surgical treatment in Groups 2 and 3 to document adequate left arytenoid abduction. After data collection at the 60 and 180 day post-operative measurement period, upper airway endoscopy was performed at rest and during exercise (10 m/s at a 3° incline) in all horses. Horses in Group 3 were also endoscopically examined at rest at approximately 7, 14, 21, 28, and 120 days after surgery to monitor healing of the ventriculocordecotomy sites.

Surgical Procedures

After induction, maintenance of anesthesia was achieved with halothane in oxygen via an endotracheal tube and a semiclosed anesthetic system. Left recurrent laryngeal neurectomy was performed in the midcervical region. An incision was made just dorsal to the left jugular vein and the left recurrent laryngeal nerve was identified. Nerve identification was confirmed by endoscopic visualization of left corniculate process adduction during nerve stimulation. Subsequently the nerve was transected, the distal portion was cauterized, folded on itself, and ligated with 2-0 polydioxinone (PDS, Ethicon Inc., Somerville, N.J.) suture. Subcutaneous tissues and skin were closed in a routine fashion.

In all horses a left prosthetic laryngoplasty was performed by a modified Marks procedure (Marks et al., 1970). A single suture of 5 Mersilene (Ticron, Davis & Geck, Wayne, N.J.) was used for the laryngeal prosthesis. In Group 1, the suture was placed, tied, and then removed. A laryngotomy incision was performed on horses in Group 1, but no tissue was removed. One of the 10 horses (Group 2) with a laryngeal prosthesis had surgical failure by 32 days after surgery. The prosthetic laryngoplasty was repeated. During surgery, failure was determined to be a result of fracture of the muscular process of the arytenoid cartilage. Because endoscopic examination both during and after surgery revealed that adequate left arytenoid abduction had been achieved, this horse remained in the study.

A bilateral ventriculocordecotomy was performed on horses in Group 3. After making a laryngotomy incision through the cricothyroid membrane, a bilateral ventriculectomy was performed. All mucosal tissue was removed from the saccules.

The center of the vocal fold was then grasped with an Allis tissue forcep (Allis Tissue Forceps, Miltex Instrument Co. Inc., Lake Success, N.Y.), a mixer hemostat (Mixer Forcep, Miltex Instrument Co. Inc., Lake Success, N.Y.) applied, and the clamped tissue within the serrations of the hemostat was removed. The free edge of the vocal fold was apposed to the free edge of the saccule using 2-0 polydioxinone (PDS, Ethicon Inc., Somerville, N.J.) suture in a simple continuous suture pattern. The laryngotomy incision was left open to heal by second intention.

Perioperatively, all horses were administered procaine penicillin G (22,000 IU/kg, IM, q12h), gentamicin (6.6 mg/kg, IM, q24h), and phenylbutazone (2.2 mg/kg, PO, q12h). Following LRLN, horses were treated for 36 hours. After all other surgical procedures, horses were treated for 72 hours. The laryngotomy incisions were cleaned daily with dilute betadine solution until healed.

Statistical Analysis

A repeated measures analysis of variance was used to evaluate the effects of surgical treatments on indices of upper airway function. When F values were significant for a treatment or time effect at $P < 0.05$, treatment means were compared using a Tukey's test for post-hoc comparisons.

Results

The HR_{max} determined from the RIET was 224.4 ± 4.8 (mean $\pm$ SD), 222.4 ± 7.0 , and 225.6 ± 6.1 bpm and $HR_{0.75max}$ was 168.3 ± 3.6 , 166.8 ± 5.2 , and 169.2 ± 4.6 bpm in Groups 1, 2 and 3 respectively. When the horses were at rest, there were

no significant differences identified either during inhalation or exhalation. At all exercise intensities, there were no significant effects on airway function during exhalation (Figure 1).

Exercise at $HR_{0.75max}$

In all three groups of horses, sectioning the left recurrent laryngeal nerve increased Z_t which resulted in a decrease in inspiratory flow (PIF, IF_{50} and IF_{25}) despite an increase in driving pressure (P_{UJ}). Horses maintained V_T by prolonging T_i which led to a decrease in respiratory frequency (f) and therefore a decrease in $\dot{V}_{min}$. The increase in T_i also caused a decrease in mean inspiratory flow rate (V_T/T_i) and Te/T_i and an increase in T_i/T_{tot} .

Sixty days after surgical treatment, none of the indices of inspiratory function had improved in Group 1. In Groups 2 and 3, all of the variables that had indicated airway obstruction post-LRLN had returned to pre-LRLN values.

One hundred and eighty days after surgery, all airway function measurements except PIF showed that obstruction persisted in Group 1. In Groups 2 and 3, all indices had returned to pre-LRLN values except for f and T_i in Group 3 (Table 1).

Exercise at HR_{max}

Results obtained after LRLN were essentially the same as those at $HR_{0.75max}$ except that in Groups 2 and 3, the prolongation of T_i , and the decrease in f were not statistically significant. Sham surgery (Group 1) did not relieve the airway obstruction induced by LRLN at either 60 or 180 days after surgical treatment.

Sixty days after surgical treatment all of the variables for Groups 2 and 3 returned to pre-LRLN values except for IF₂₅ (Group 3 only). At 180 days, all indices of airway function had returned to pre-LRLN values (Table 2, Figures 2–6).

Does Ventriculocordectomy Add Significant Benefit?

There was no indication that ventriculocordectomy provided any additional benefit over that provided by laryngoplasty alone. There were no significant differences between any of the indices of airway function following surgery in Groups 2 and 3.

Endoscopic Examination

Endoscopic examination was performed immediately after surgical treatment. In 7 out of 10 horses with a laryngeal prosthesis, the degree of abduction was sufficient to cause obliteration of the pyriform recess. In the remaining 3 horses, the pyriform recess was still visible. In all cases, relaxation of the prosthesis occurred over time, resulting in the left arytenoid cartilage resting in the paramedian position at the time of second endoscopic examination i.e. before the day 60 measurement period.

During exercise, dynamic collapse of the paralyzed arytenoid cartilage and both vocal folds occurred in all horses in Group 1 at the 60- and 180-day measurement period. Also, both ventricles filled with air. The aryepiglottic fold was drawn axially in 3 horses. One horse achieved some degree of arytenoid cartilage stabilization by 180 days.

Four horses in Group 2 had filling of both ventricles during exercise at the 60- and 180-day measurement period. Left arytenoid cartilage abduction was maintained in all horses in this group. One horse drew its aryepiglottic fold axially.

All horses in Group 3 had moderate to marked swelling of the ventriculocordecotomy sites immediately after surgery. Minimal to no swelling was present at the 7-day examination period. In all horses, the ventriculocordecotomy sites looked the best at 14 and 180 days. In some horses, suture tags were visible at 30 and 60 days after surgery. One horse developed a pseudomembrane over the ventriculocordecotomy sites at 7 days, but this resolved by 14 days. Complete healing occurred in 2 horses by 120 days, and by 180 days all ventriculocordecotomy sites were healed. In 4 horses, the aryepiglottic fold was drawn axially during exercise.

Post-Operative Complications

The most common post-operative complications associated with the prosthetic laryngoplasty are coughing, regurgitation, and nasal discharge of food and water (Speirs, 1987; Dean et al., 1990). None of these complications were observed in our horses. Other complications were observed in 2 horses. In 1 horse (Group 2), a suture sinus developed secondary to suture penetration of the laryngeal mucosa, while in the second horse (Group 3) we observed a subcutaneous infection with secondary incisional dehiscence. This latter animal was treated with procaine penicillin G (22,000 IU/kg, IM, q12h), gentamicin (6.6 mg/kg, IM, q24h), and daily lavaging with dilute betadine solution until resolution of the infection. Surgical failure did not occur in these horses, and they remained in the study.

Discussion

The goal of the prosthetic laryngoplasty, the most commonly used treatment for idiopathic laryngeal hemiplegia, is to produce mechanical abduction and stabilization of the paralyzed arytenoid cartilage and tense the vocal fold (Williams et al., 1990b). This prevents dynamic collapse of soft tissue structures of the larynx during exercise, thereby alleviating upper airway obstruction in horses with recurrent laryngeal neuropathy (Derksen et al., 1986). In spite of its common use, prior to the present study, the technique had only been objectively evaluated in submaximally exercising horses (Derksen et al., 1986). Also, in the treatment of laryngeal hemiplegia by prosthetic laryngoplasty, prevention of dynamic collapse has been reported to be more important than obtaining maximum arytenoid abduction (Derksen et al., 1986). The efficacy of this surgical procedure in the treatment of laryngeal hemiplegia is supported by our study. Even though the left arytenoid cartilage was in a paramedian position in all horses treated with a laryngeal prosthesis, their airway function during exercise returned to pre-LRLN values. In both horses and people, it has been concluded that midtidal inspiratory flow (IF_{50}) is the most sensitive and reliable indicator of dynamic upper airway obstruction (Lumsden et al., 1993). In the present study, IF_{50} and other inspiratory variables all returned to pre-LRLN values in Group 2 and 3 with no significant difference between the groups. Our study unequivocally demonstrates therefore, that, in horses exercising at HR_{max} , prosthetic laryngoplasty reverses the inspiratory obstruction that occurs after left recurrent laryngeal neurectomy.

Ventriculectomy alone fails to improve upper airway function in horses with experimentally induced laryngeal hemiplegia (Shappell et al., 1988). However, it has

been hypothesized that further stabilization of the paralyzed arytenoid cartilage and vocal fold may be achieved when the ventriculectomy is combined with the prosthetic laryngoplasty (Williams et al., 1990b). Before the present investigation, no studies had been performed to compare the efficacy of the prosthetic laryngoplasty alone with that of the combined procedure. In our study, there were no significant differences between the groups of horses treated with prosthetic laryngoplasty alone and those treated with the combined procedure even though, during exercise, filling of the ventricles with air was documented in 4 out of 5 horses treated with laryngoplasty alone (Group 2). Therefore, these results clearly demonstrate that combining bilateral ventriculocordectomy with the prosthetic laryngoplasty does not enhance the results achieved with the prosthetic laryngoplasty alone.

Many surgeons routinely perform a unilateral rather than a bilateral ventriculectomy with the prosthetic laryngoplasty (Speirs, 1987). In our study, we performed a bilateral ventriculocordectomy because, had a unilateral technique been performed and no difference between treatment groups been observed, the question would remain as to whether a bilateral technique would have produced a significant difference between the groups. Also, both vocal folds and laryngeal saccules were removed to maximize the increase in cross-sectional area of the ventral aspect of the glottis.

The vocal fold was sutured to the ventricle in our study. It has been proposed that suturing may result in stronger scar tissue formation due to organization of the hematoma within the saccule (Schebitz, 1964; Pouret, 1966). Also, transverse laryngeal webbing has been reported in horses treated with a ventriculocordectomy procedure without primary closure (Dixon et al., 1994).

Our measurements of airway function demonstrate that combining bilateral ventriculocordectomy with prosthetic laryngoplasty has no additional benefit over laryngoplasty alone and from a surgical viewpoint the combined procedure may have distinct disadvantages. Surgery time is prolonged, horses need to be repositioned during surgery, and a contaminated wound, left open to heal by second intention, is immediately adjacent to the primary incision and prosthesis. The incidence of infection associated with the prosthetic laryngoplasty procedure may be reduced if prosthetic laryngoplasty is performed alone.

Even though the upper airway obstruction induced by LRLN persisted throughout the study in all horses in Group 1, there was a trend toward improvement in airway function over the 180-day measurement period. The reason for this is unknown but dynamic collapse of the paralyzed arytenoid cartilage during exercise was still visible in 4 out of 5 horses at the 180-day measurement period. In the remaining horse, arytenoid cartilage stabilization was evident.

It has been proposed that long-term cyclic loading with subsequent cartilage failure can occur over time after the placement of a laryngeal prosthesis (Dean et al., 1990). In the present study, this was not observed. The prosthetic laryngoplasty restored and maintained upper airway function in horses with induced laryngeal hemiplegia over the 180-day period.

In conclusion, 60 and 180 days after prosthetic laryngoplasty, upper airway function returns to pre-LRLN values in horses with experimentally induced left laryngeal hemiplegia exercising at HR_{max} . Combining ventriculocordectomy with prosthetic laryngoplasty does not further improve upper airway function in these horses.

TABLE 1: Effect of surgery on measured and calculated inspiratory variables at $HR_{0.75\max}$

Variable	Group	Measurement Period†			
		Before LRLN	14 days after LRLN	60 days after treatment	180 days after treatment
PIF (L/s)	1	47.44 ± 5.38	34.33 ± 5.78*	37.97 ± 5.52*	39.38 ± 5.80
	2	49.27 ± 4.80	35.96 ± 4.73*	45.79 ± 7.05	45.26 ± 4.62
	3	49.24 ± 3.18	34.75 ± 3.46*	43.28 ± 5.11	42.72 ± 3.24
P_{UI} (cm/H ₂ O)	1	19.19 ± 2.86	60.19 ± 8.55*	41.76 ± 12.06*	44.64 ± 15.16*
	2	20.49 ± 6.42	39.06 ± 16.17*	27.45 ± 5.01	29.04 ± 8.68
	3	23.63 ± 3.01	57.63 ± 3.55*	27.14 ± 2.78	29.95 ± 5.63
Z_I (cm H ₂ O/L/s)	1	0.41 ± 0.09	1.92 ± 0.34*	1.18 ± 0.50*	1.19 ± 0.46*
	2	0.43 ± 0.12	1.18 ± 0.65*	0.62 ± 0.09	0.64 ± 0.16
	3	0.48 ± 0.07	1.72 ± 0.11*	0.63 ± 0.06	0.71 ± 0.11
f (breaths/ min)	1	84.32 ± 20.01	60.78 ± 11.63*	68.80 ± 24.20*	66.76 ± 14.87*
	2	80.88 ± 20.25	63.72 ± 8.04*	66.50 ± 14.42	61.04 ± 9.66
	3	71.68 ± 9.12	55.22 ± 6.92*	64.92 ± 7.48	65.66 ± 7.35
Ti (ms)	1	385.20 ± 87.05	617.80 ± 127.23*	528.60 ± 145.21*	518.80 ± 123.52*
	2	408.20 ± 96.72	536.80 ± 71.82*	508.40 ± 107.42	545.80 ± 89.80*
	3	448.60 ± 67.02	646.60 ± 76.19*	505.40 ± 49.51	498.00 ± 72.75
Te/Ti	1	0.96 ± 0.09	0.66 ± 0.06*	0.79 ± 0.09*	0.82 ± 0.09*
	2	0.92 ± 0.09	0.79 ± 0.05*	0.87 ± 0.10	0.86 ± 0.05
	3	0.91 ± 0.08	0.71 ± 0.04*	0.85 ± 0.03	0.87 ± 0.10
Ti/T _{tot}	1	0.51 ± 0.03	0.61 ± 0.02*	0.56 ± 0.03*	0.55 ± 0.03*
	2	0.52 ± 0.02	0.56 ± 0.01	0.54 ± 0.03	0.54 ± 0.01
	3	0.53 ± 0.02	0.58 ± 0.02*	0.54 ± 0.01	0.54 ± 0.03
V_T/Ti	1	36.49 ± 4.67	23.85 ± 2.69*	29.78 ± 5.15*	31.11 ± 5.02*
	2	36.18 ± 4.42	27.69 ± 2.34*	32.45 ± 3.54	31.14 ± 2.14
	3	34.16 ± 2.06	25.67 ± 1.83*	30.67 ± 4.04	31.57 ± 3.50
IF ₅₀ (L/s)	1	41.79 ± 4.88	25.03 ± 2.06*	31.63 ± 5.32*	33.87 ± 5.53*
	2	38.94 ± 5.11	29.46 ± 3.41*	37.34 ± 4.22	34.94 ± 3.15
	3	40.18 ± 2.09	27.54 ± 3.28*	34.22 ± 4.21	35.42 ± 2.35
IF ₂₅ (L/s)	1	44.01 ± 5.98	24.93 ± 3.35*	31.86 ± 6.79*	33.03 ± 5.77*
	2	44.76 ± 5.65	31.80 ± 3.65*	40.15 ± 7.37	40.78 ± 4.67
	3	45.13 ± 2.25	27.08 ± 2.85*	39.50 ± 4.36	38.50 ± 5.06
PEF/PIF	1	1.16 ± 0.10	1.55 ± 0.03*	1.39 ± 0.08*	1.37 ± 0.12*
	2	1.15 ± 0.09	1.37 ± 0.13*	1.16 ± 0.10	1.18 ± 0.10
	3	1.14 ± 0.09	1.58 ± 0.11*	1.19 ± 0.06	1.25 ± 0.14
EF/IF ₅₀	1	1.21 ± 0.19	1.70 ± 0.16*	1.39 ± 0.21	1.34 ± 0.18
	2	1.16 ± 0.15	1.40 ± 0.21	1.15 ± 0.21	1.26 ± 0.19
	3	1.19 ± 0.17	1.57 ± 0.26*	1.28 ± 0.17	1.21 ± 0.21

TABLE 1 (cont'd).

Variable	Group	Measurement Period†			
		Before LRLN	14 days after LRLN	60 days after treatment	180 days after treatment
EF/IF ₂₅	1	0.96 ± 0.10	1.61 ± 0.32*	1.38 ± 0.13*	1.25 ± 0.23
	2	0.98 ± 0.12	1.15 ± 0.11	1.04 ± 0.22	0.98 ± 0.10
	3	0.84 ± 0.16	1.42 ± 0.15*	1.05 ± 0.13	1.00 ± 0.17
$\dot{V}_{\min}$	1	1129.25 ± 150.31	868.12 ± 114.74*	997.41 ± 145.13	1027.79 ± 126.97
	2	1132.82 ± 99.16	933.72 ± 86.72*	1049.90 ± 92.80	1008.74 ± 74.52
	3	1078.11 ± 56.97	904.85 ± 62.36	993.42 ± 122.31	1014.40 ± 78.16

† Mean ± SD

* Data significantly different from pre-LRLN values; $P < 0.05$

PIF = peak inspiratory flow, P_{ui} = peak inspiratory pressure, Z_i = inspiratory impedance, f = respiratory frequency, T_i = inspiratory time, T_e = expiratory time, T_{tot} = total breathing time, V_T = tidal volume, IF₅₀ = inspiratory flow at 50% V_T , IF₂₅ = inspiratory flow at 25% V_T , PEF = peak expiratory flow, EF₅₀ = expiratory flow at 50% V_T , EF₂₅ = expiratory flow at 25% V_T , $\dot{V}_{\min}$ = minute ventilation

TABLE 2: Effect of surgery on measured and calculated inspiratory variables at $HR_{\max}$

Variable	Group	Measurement Period†			
		Before LRLN	14 days after LRLN	60 days after treatment	180 days after treatment
PIF (L/s)	1	69.71 ± 10.35	37.65 ± 4.77*	40.08 ± 8.19*	42.56 ± 9.01*
	2	63.29 ± 6.04	40.51 ± 7.19*	52.68 ± 2.47	52.91 ± 5.25
	3	66.45 ± 8.42	36.90 ± 4.00*	55.37 ± 6.58	55.48 ± 5.05
P_{UI} (cm/H ₂ O)	1	36.32 ± 8.09	74.40 ± 8.63*	62.78 ± 6.53*	59.39 ± 8.29*
	2	31.13 ± 9.68	52.62 ± 9.12*	41.96 ± 7.11	44.31 ± 6.97
	3	34.33 ± 6.22	66.18 ± 13.05*	44.66 ± 5.78	45.11 ± 8.40
Z_1 (cm H ₂ O/l/s)	1	0.53 ± 0.13	2.11 ± 0.27*	1.65 ± 0.27*	1.52 ± 0.47*
	2	0.50 ± 0.17	1.39 ± 0.41*	0.81 ± 0.10	0.84 ± 0.17
	3	0.52 ± 0.09	1.87 ± 0.27*	0.82 ± 0.11	0.82 ± 0.14
f (breaths/min)	1	87.48 ± 30.84	63.90 ± 4.55*	67.18 ± 13.84	69.72 ± 9.09
	2	82.24 ± 26.58	71.82 ± 12.91	73.72 ± 20.92	73.34 ± 16.06
	3	77.48 ± 18.90	64.40 ± 10.90	75.42 ± 21.73	77.12 ± 19.96
Ti (ms)	1	390.80 ± 127.79	585.60 ± 39.18*	562.60 ± 148.12*	511.20 ± 79.78
	2	418.20 ± 104.68	501.80 ± 71.41	474.80 ± 100.43	450.80 ± 87.05
	3	445.00 ± 102.26	565.40 ± 100.69	455.00 ± 97.94	461.00 ± 92.73
Te/Ti	1	0.98 ± 0.16	0.63 ± 0.11*	0.71 ± 0.13*	0.74 ± 0.13*
	2	0.88 ± 0.07	0.76 ± 0.06	0.85 ± 0.09	0.94 ± 0.13
	3	0.88 ± 0.22	0.69 ± 0.06	0.90 ± 0.18	0.84 ± 0.17
Ti/T _{tot}	1	0.51 ± 0.05	0.62 ± 0.04*	0.59 ± 0.05*	0.58 ± 0.04*
	2	0.53 ± 0.02	0.57 ± 0.02	0.54 ± 0.03	0.52 ± 0.03
	3	0.54 ± 0.06	0.59 ± 0.02*	0.53 ± 0.05	0.55 ± 0.04
V_T/Ti	1	47.47 ± 9.09	25.41 ± 1.83*	29.54 ± 6.82*	31.92 ± 7.49*
	2	43.06 ± 6.76	30.96 ± 3.58*	37.27 ± 1.92	38.45 ± 4.02
	3	41.22 ± 6.54	26.98 ± 2.40*	37.25 ± 5.17	36.18 ± 4.12
IF ₅₀ (L/s)	1	52.59 ± 13.13	27.56 ± 1.04*	31.36 ± 7.61*	34.78 ± 8.71*
	2	48.85 ± 6.21	33.89 ± 4.07*	41.46 ± 1.97	41.99 ± 4.75
	3	48.11 ± 10.64	28.46 ± 2.90*	40.58 ± 6.46	37.55 ± 7.81
IF ₂₅ (L/s)	1	64.09 ± 13.18	24.96 ± 1.91*	30.44 ± 6.96*	34.07 ± 11.26*
	2	55.20 ± 7.73	32.67 ± 3.40*	47.59 ± 1.57	47.77 ± 6.31
	3	61.60 ± 9.49	28.18 ± 1.04*	46.27 ± 8.09*	50.30 ± 6.92
PEF/PIF	1	1.07 ± 0.05	1.65 ± 0.12*	1.58 ± 0.26*	1.51 ± 0.18*
	2	1.16 ± 0.10	1.54 ± 0.22*	1.26 ± 0.11	1.24 ± 0.16
	3	1.19 ± 0.22	1.70 ± 0.25*	1.12 ± 0.19	1.20 ± 0.22
EF/IF ₅₀	1	1.28 ± 0.45	1.74 ± 0.31*	1.82 ± 0.65*	1.62 ± 0.38
	2	1.23 ± 0.16	1.43 ± 0.24	1.30 ± 0.29	1.27 ± 0.17
	3	1.27 ± 0.29	1.73 ± 0.07	1.38 ± 0.39	1.57 ± 0.34

TABLE 2 (con't).

Variable	Group	Measurement Period†			
		Before LRLN	14 days after LRLN	60 days after treatment	180 days after treatment
EF/IF ₂₅	1	0.90 ± 0.25	2.01 ± 0.37*	1.72 ± 0.44*	1.61 ± 0.53*
	2	1.08 ± 0.43	1.40 ± 0.14*	0.98 ± 0.13	0.87 ± 0.16
	3	0.92 ± 0.18	1.62 ± 0.43*	1.06 ± 0.21	0.99 ± 0.18
$\dot{V}_{min}$	1	1455.08 ± 230.10	947.48 ± 101.12*	1062.09 ± 220.28*	1106.46 ± 191.48*
	2	1372.82 ± 179.85	1088.09 ± 85.48*	1231.50 ± 43.51	1215.49 ± 107.26
	3	1324.63 ± 120.89	957.62 ± 76.31*	1195.47 ± 101.92	1211.54 ± 95.38

† Mean ± SD

* Data significantly different from pre-LRLN values; P < 0.05

PIF = peak inspiratory flow, P_{al} = peak inspiratory pressure, Z_i = inspiratory impedance, f = respiratory frequency, Ti = inspiratory time, Te = expiratory time, T_{tot} = total breathing time, V_T = tidal volume, IF₅₀ = inspiratory flow at 50% V_T, IF₂₅ = inspiratory flow at 25% V_T, PEF = peak expiratory flow, EF₅₀ = expiratory flow at 50% V_T, EF₂₅ = expiratory flow at 25% V_T, $\dot{V}_{min}$ = minute ventilation

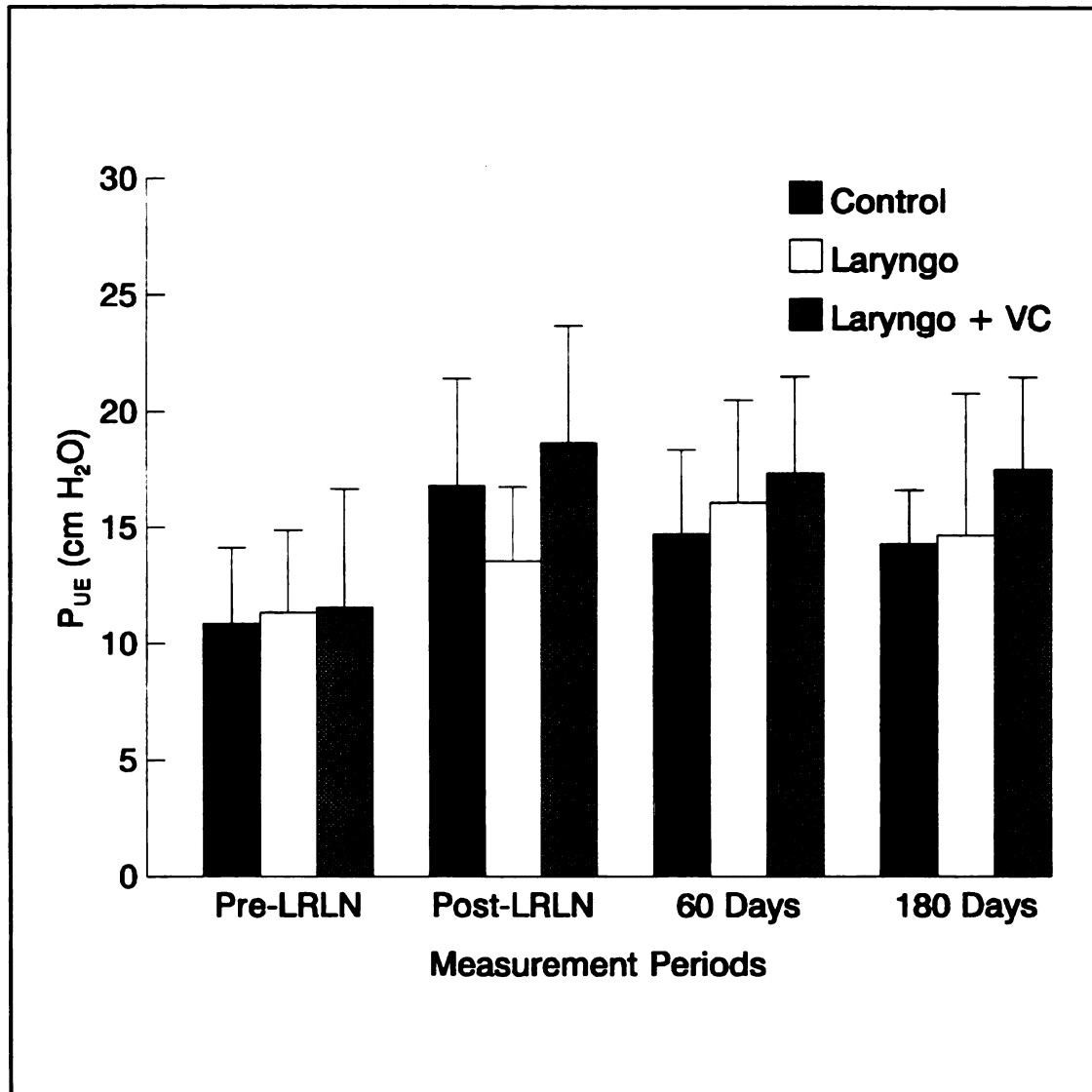


Figure 1a. Peak expiratory pressure at HR_{max} .

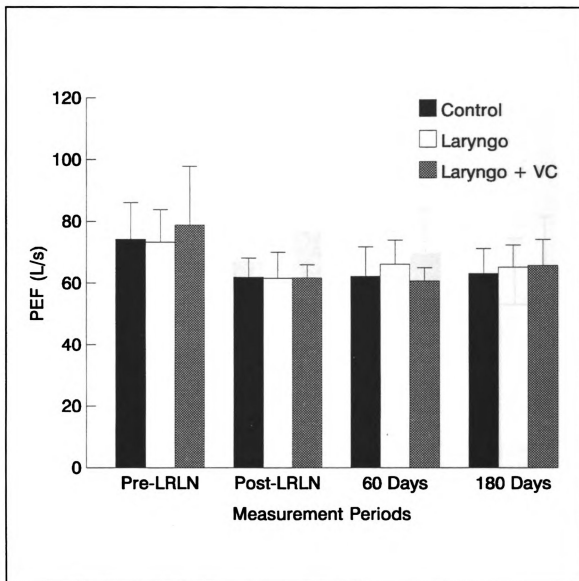


Figure 1b. Peak expiratory flow at HR_{max}.

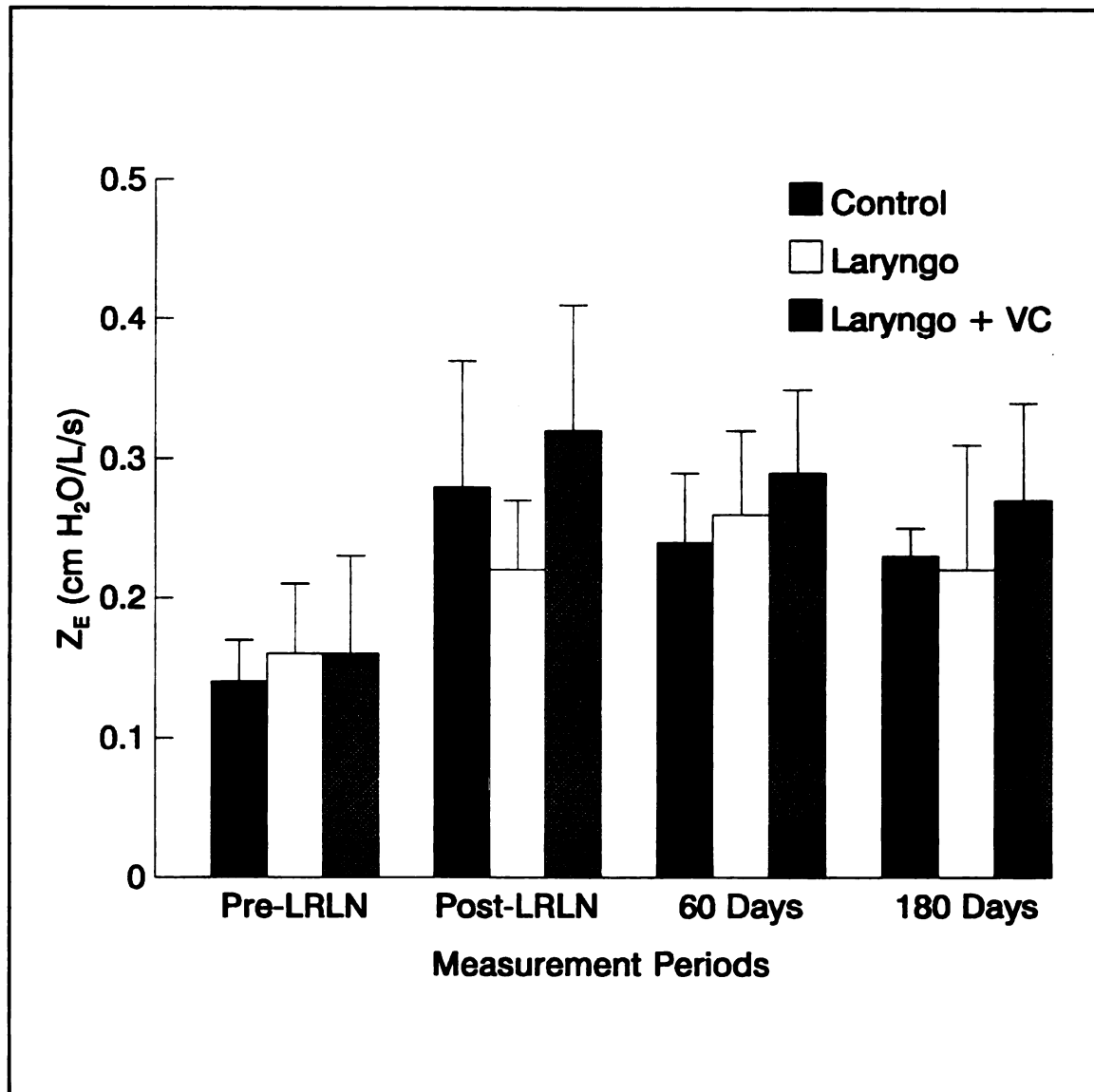


Figure 1c. Expiratory impedance at HR_{max} .

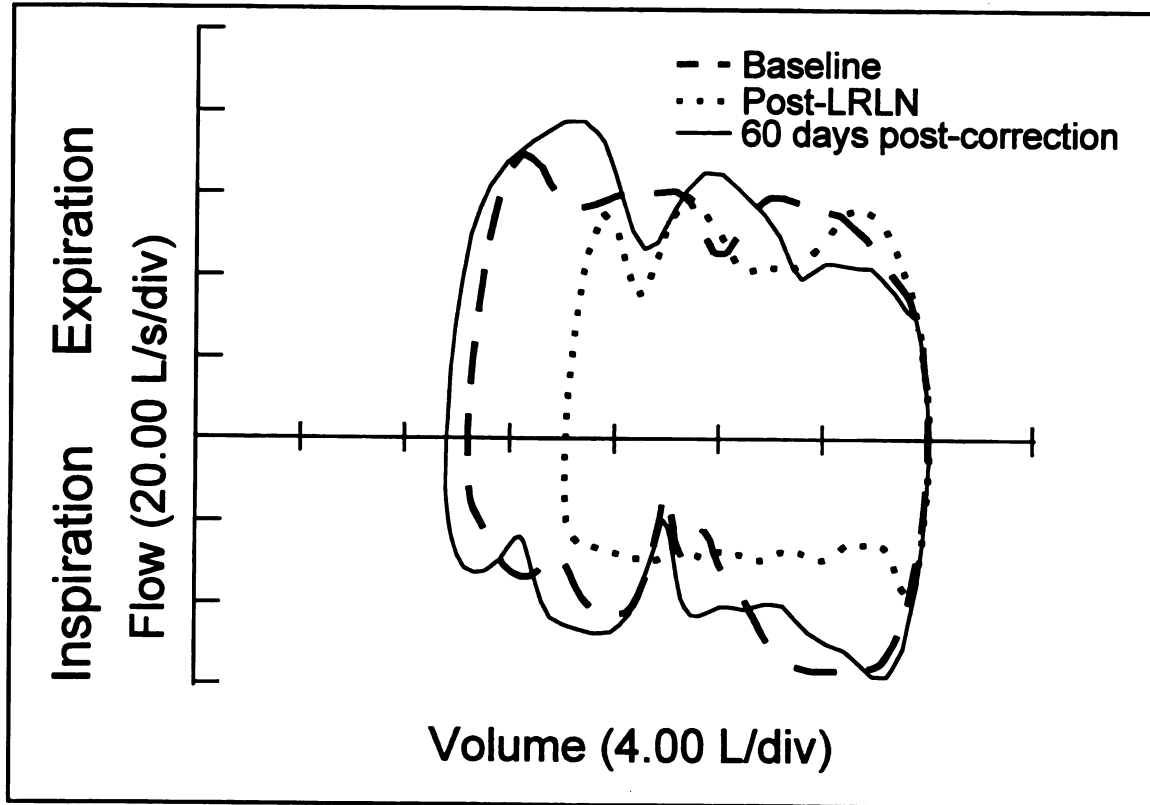


Figure 2. Tidal breathing flow-volume loops generated from one horse treated with a left prosthetic laryngoplasty and bilateral ventriculocordecotomy. Note reversal of inspiratory flow limitation 60 days after surgical treatment.

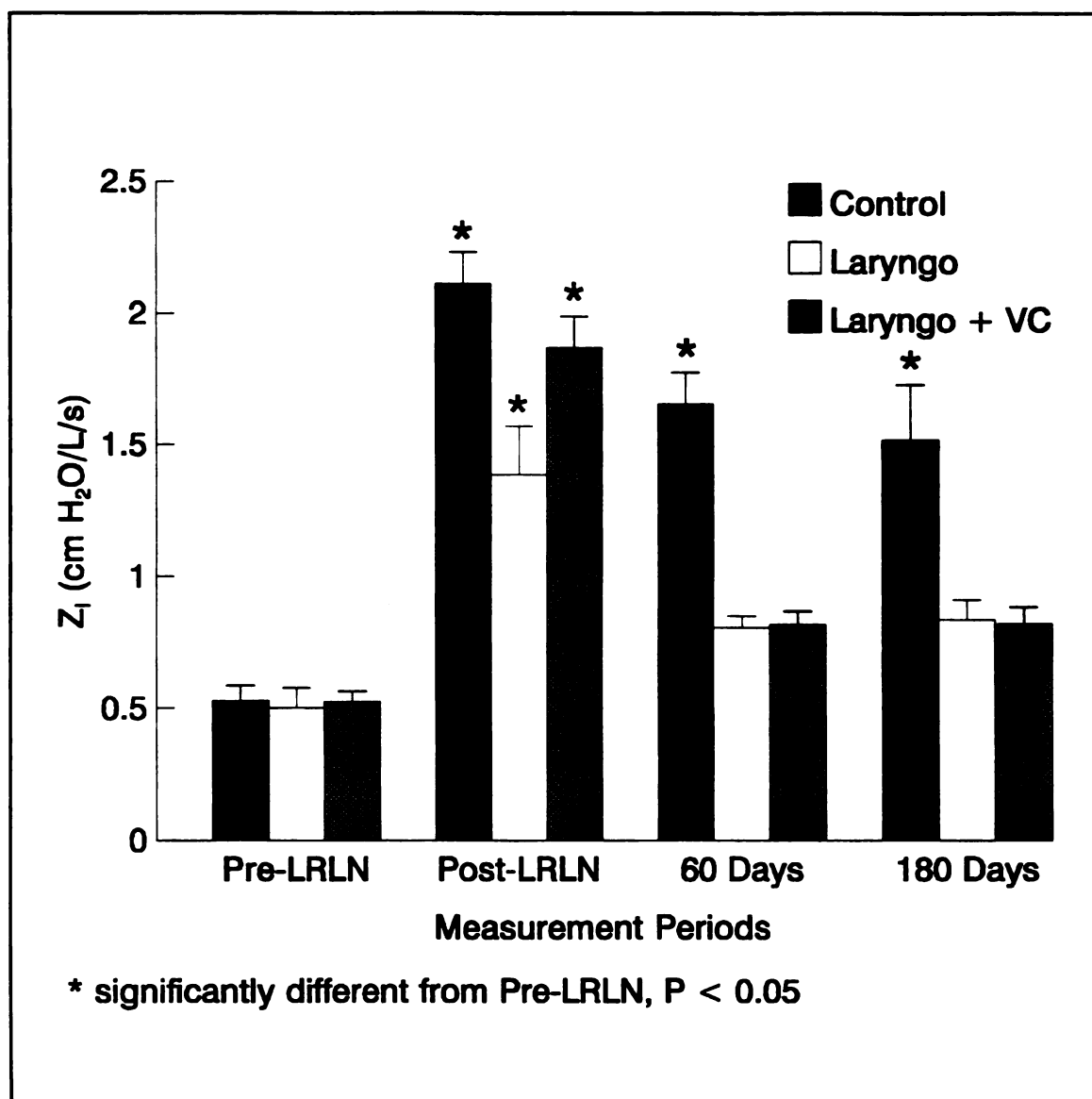


Figure 3. Inspiratory impedance at HR_{max} .

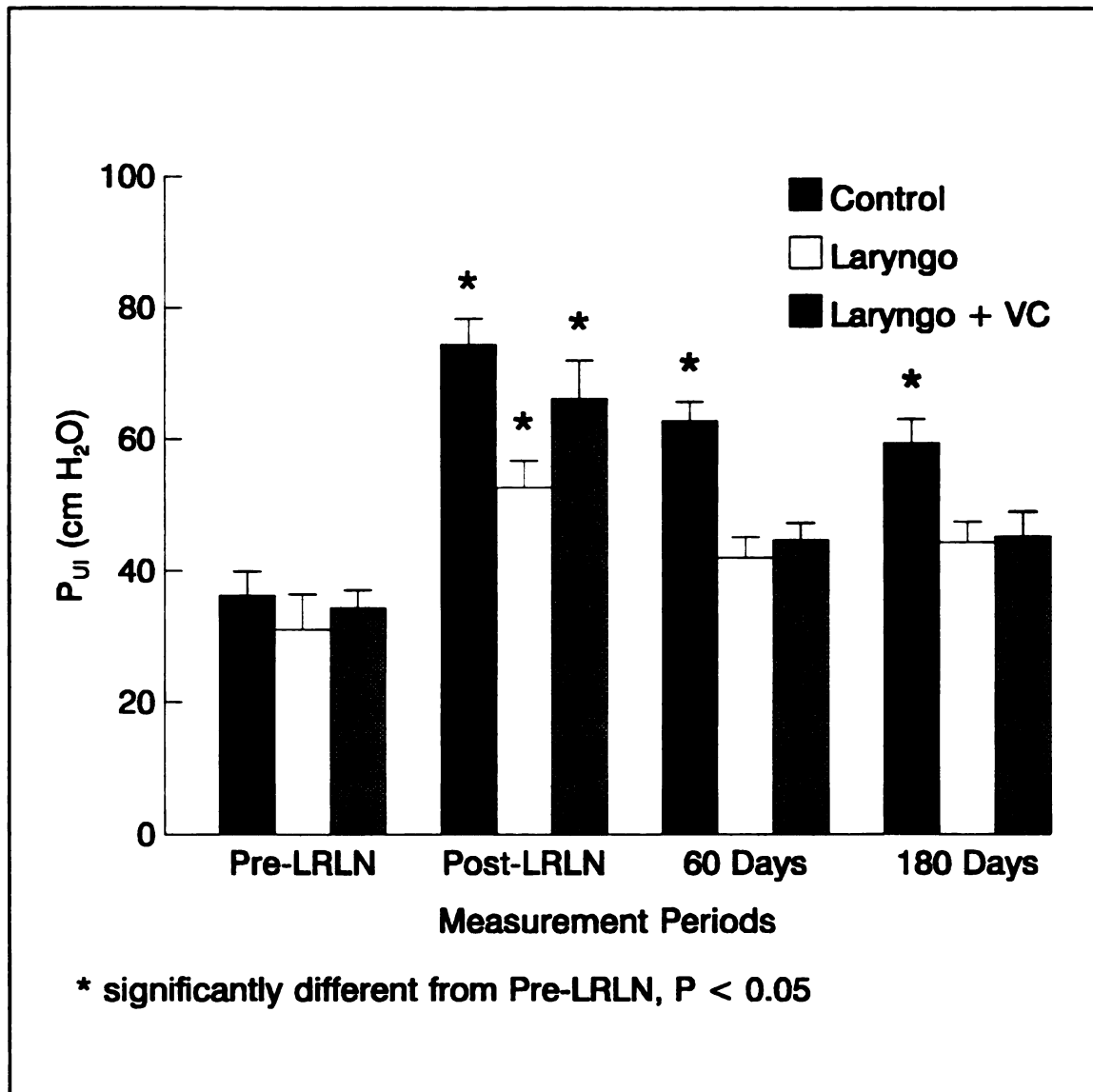


Figure 4. Peak inspiratory pressure at HR_{max} .

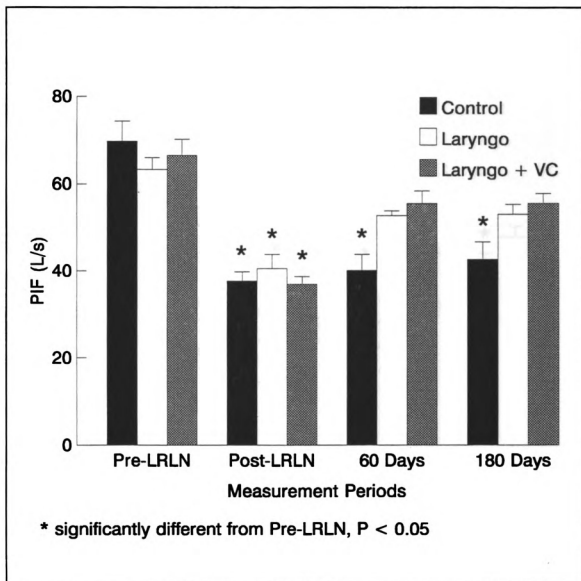


Figure 5. Peak inspiratory flow at HR_{max} .

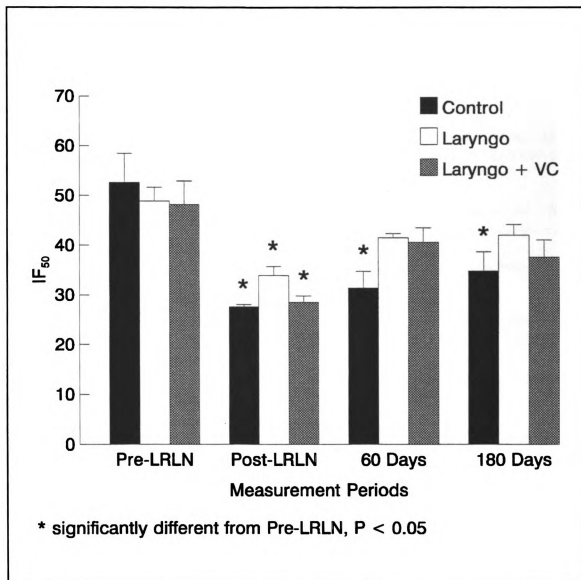


Figure 6. Inspiratory flow at 50% V_T at HR_{max} .

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