# Experimental evidence in the in vivo canine for the collapsible tube model of phonation

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# Experimental evidence in the *in vivo* canine for the collapsible tube model of phonation[a)]

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The *in vivo* canine model of the larynx was used to measure transglottic pressures and airflow during phonation. Conditions of supraglottal resistance were also simulated. Pressure drop-flow curves were compared with data on collapsible tubes. The *in vivo* in canine model of the larynx demonstrates a number of features similar to oscillation in collapsible tubes.

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## INTRODUCTION

Fluid flows in physiologic systems frequently occurs in vessels that collapse during normal function (for example, veins above the level of the heart; Shapiro, 1977). Collapse occurs when the external tissue pressure on such vessels becomes greater than the internal fluid pressure and the vessel becomes noncircular. In contrast to rigid laminar pipe flow, the relationship between the pressure gradient and flow rate in collapsed vessels becomes nonlinear (Kamm and Pedley, 1989). Under these circumstances, several interesting phenomena have been observed, including flow limitation (Dawson and Elliott, 1977) and oscillations (Brower and Scholten, 1975). Flow through collapsed vessels has been investigated both *in vitro* and *in vivo*, and also by mathematic modeling (Griffiths, 1971a,b; Griffiths, 1975a–c; Oates, 1975; Bertram and Pedley, 1982; Begis *et al.*, 1988). Research into artificial systems (i.e., collapsible rubber tubes) has also been extensively pursued in recent years (Kececioglu *et al.*, 1981; McClurken *et al.*, 1981). These studies have provided insight into the natural biomechanics of physiologic vessels.

The majority of experiments on collapsible tubes have been conducted on so-called Starling resistors. This experimental apparatus was devised by Knowlton and Starling in 1912. The device was initially developed to simulate resistances encountered by isolated mammmalian hearts; however, it has subsequently been used to simulate other biologic systems. A Starling resistor (Fig. 1) consists of a compliant tube (usually thin-walled) which is attached at each end to a rigid tube and enclosed in a chamber which adjusts the external pressure of the tube ($P_e$). In the following discussion, $P_1$ and $P_2$ denote the upstream and downstream pressures from a collapsible tube, respectively. Numerous hydraulic tests have been carried out on this device using an apparatus similar to that depicted in Fig. 1. Flow ($Q_1$) through the system can be adjusted. There are also variable upstream ($R_1$) and downstream ($R_2$) constrictions and variable external pressure ($P_e$). If $P_e$ and $R_2$ are held constant and $Q_1$ is varied by adjustment of either the upstream reservoir or $R_1$ then a pressure drop ($P_1 - P_2$) across the tube versus flow rate relationship, or $P - Q$ characteristic, similar to that shown in Fig. 2 can be obtained. An important property of this $P - Q$ characteristic is the region of negative slope. It is in this region that Starling resistors exhibit dynamic decreasing resistance with increasing flow (negative differential). When the external pressure $P_e$ exceeds the outlet pressure $P_2 (P_2 - P_e < 0)$ and the tube is partially collapsed, the outlet area has been observed to oscillate at characteristic frequencies. This corresponds to the region of negative slope of the $P - Q$ characteristic. This negative slope makes the system statically unstable. Dynamically, negative damping is present, which means that oscillations can grow and eventually build up to a limit cycle.

A variety of physiological and medical applications of flow in collapsible tubes have been studied. These include flow in venous (Brecher, 1952) and arterial systems (Conrad *et al.*, 1980), pulmonary circulation, pulmonary airways (Fry, 1958; Dawson and Elliott, 1977), the urethra (Griffiths, 1969), snoring (Shapiro, 1977) and also the vocal cords (Conrad, 1980). It has been hypothesized that oscillation of the vocal cords is similar to that of the Starling resistor in the negative differential resistance region. In this analogy, the external pressure acting on the collapsible tube is comparable to the active muscle tone of the vocal cords tending to produce closure. A prosthetic vocal source has been developed using a collapsible tube as a fluid mechanical oscillator (Schoendorfer and Shapiro, 1977). Conrad has proposed a model of the vocal cords based upon such a collapsible tube analogy (Conrad, 1983).

In 1969, Conrad reported a comprehensive set of data obtained from a model study on a Starling resistor. Conrad's results have subsequently been confirmed in a study by Pedley and Jensen (1989). In Conrad's study, $R_2$ and $P_e$ were independent variables. The flow rate through the system was varied independently. The results of such an experiment were presented as a plot of the pressure drop across the tube ($P_1 - P_2$) versus flow rate ($Q$).

The *P-Q* characteristic could be further divided into three distinct regions reflecting the flow regimes and state of

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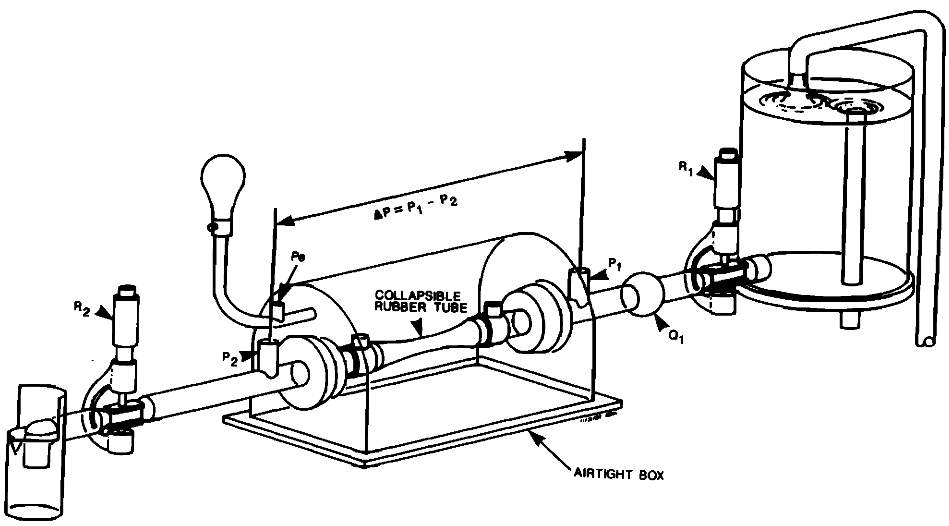


FIG. 1. Classical Starling resistor preparation: $R_1$ = upstream resistance; $R_2$ = downstream resistance; $P_1$ = upstream pressure; $P_2$ = downstream pressure; $P_e$ = external pressure on tube; $Q_1$ = flow through resistor.

collapse of the tube (Fig. 2). In region 1, as shown in Figure 2 the downstream pressure increases as $Q$ increases. For a constant downstream resistance $R_2$, the pressure increases linearly ($P_2 = R_2 Q$). For such a downstream resistance, $P_2$ exceeds $P_e$ for some $Q$, and hence the internal pressure throughout the collapsible tube can exceed the external pressure. The cross section of the tube is then almost circular throughout and, for the case of a thin-walled latex tube (Penrose surgical drain), the tube stiffness is very large. The tube stiffness can be specified for various tube materials or thicknesses by experimentally deriving the "tube law" which defines the cross-sectional area of the tube to the transmural pressure difference by a parameter $K_p$ (Shapiro, 1977, pp. 127–128). $K_p$ is proportional to the bending stiffness of the tube wall. For example, $K_p$ is proportional to the elastic modulus and to the cube of the thickness-radius ratio for a linear elastic material. In region 1, when the tube is circular, the differential pressure ($P_1 - P_2$) is then proportional to $Q$ with an almost constant resistance. In region 2, reduction of $Q$ below a certain critical value results in a reduction of $P_2$ to a value close to or below $P_e$, at which time the downstream end of the tube begins to collapse. Further reduction of $Q$

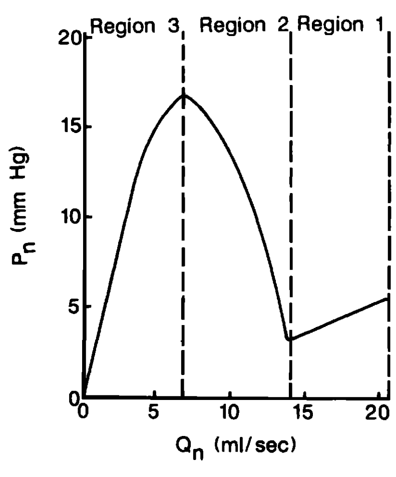


FIG. 2. Phase plane diagram of pressure drop $P_1 - P_2$ across Starling resistor versus flow rate relationship. Region 1 = tube fully open; region 2 = tube partially collapsed; region 3 = tube fully collapsed; $P_n$ = upstream–downstream pressure; $Q_n$ = flow rate (copyright 1969 IEEE). The subscript $n$ is used to denote the N shape of the characteristic.

results in rapid reduction of cross-sectional area in a thin latex tube due to the high distensibility of the partially collapsed tube as determined by the tube law. The smaller area then presents a greater resistance to the incoming flow. Thus, as the flow rate is decreased, a greater pressure drop is required to overcome the increase in resistance. Self-excited oscillations have been frequently observed in this region (Kamm and Pedley, 1989). At lower flow rates (region 3 in Fig. 2), the whole segment collapses and $P_1$ is less than $P_e (P_1 < P_e)$. In this region, the tube usually has a rather rigid dumbbell shape as determined by the tube law. The resistance flow in this region is many times higher than in the partially collapsed state. Conrad further reported that downstream conditions can be changed by an adjustment of the downstream resistance. This parameter modifies $P_2$ independently of $P_1$. When $P_2$ exceeds $P_e$ by a sufficient amount, the flow rate is proportional to the pressure drop across the tube. However, when $P_2$ falls below $P_e$, collapse begins at the downstream end and is localized, since $P_1$ remains high. Further reduction in $P_2$ has no affect on flow rate due to choked flow from tube collapse. In this mode, the collapsible tube can be used as a constant flow device. If $P_e < P_2$, the tube is open along its entire length and the flow rate is nearly independent of $P_e$. However, as $P_e$ is increased above $P_2$, the flow rate through the tube is governed by the pressure difference $P_1 - P_e$ and the flow rate is virtually independent of the downstream pressure. Finally, when $P_e$ and $R_2$ are held constant, a $P - Q$ characteristic shaped like the letter $N$ can be obtained with a region of negative $P_1 - P_2$ vs $Q$ slope. It is in this region of negative differential resistance that oscillations occur. Conrad used the concept of negative differential resistance to explain the oscillations observed in collapsible tubes (Conrad and McQueen, 1988). He proposed an electrical analog of his experiment on Starling resistors, in which the collapsible tube was represented by a flow-controlled nonlinear resistance. The equivalent circuit was described by van der Pol's equation (van der Pol, 1926). The analysis suggested that increasing tube compliance should result in oscillations of a relaxation type.

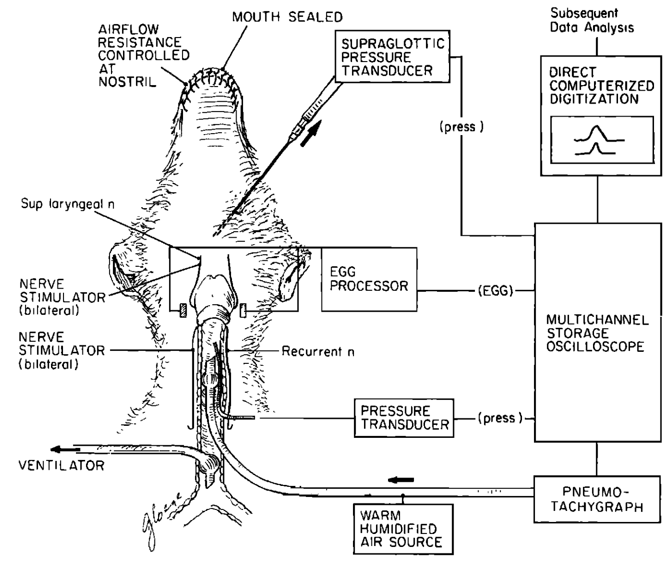


FIG. 3. *In vivo* canine preparation.

A previously developed *in vivo* canine model of phonation was utilized to simulate the conditions present in a Starling resistor experiment. Our goal was to determine how closely the larynx in an *in vivo* canine preparation would approximate the $P-Q$ characteristic present in Starling resistor studies, and whether oscillations would occur in the negative differential resistance zone.

## I. METHOD

Figure 3 demonstrates the *in vivo* canine model. Three mongrel dogs (25 kg) were premedicated with Innovar intramuscularly. Intravenous pentothal was administered to a level of corneal anesthesia, and additional pentothal was used to maintain this level of anesthesia throughout the experiment.

The animal was placed supine on the operating table, and a midline incision was made to expose the trachea from the hyoid to the sternal notch. Both recurrent laryngeal nerves were identified and preserved. Both superior laryngeal nerves were identified along their course to the cricothyroid muscles. A low tracheotomy was performed at the level of the suprasternal notch, through which an endotracheal tube was passed to allow ventilator assisted respirations. A second tracheotomy was performed in a more superior location, through which a cuffed endotracheal tube was passed in a rostral direction and positioned with the tip 10 cm below the vocal folds. The cuff was inflated to just seal the trachea. Humidified heated air was passed through this rostral endotracheal tube from a compressed air tank. Flow was controlled with a valve on the compressed air tank and measured with a Gilmont flowmeter (Great Neck, NY: model 4) and a pneumotachograph (OEM Fleisch 7, Richmond, VA). The pneumotachograph was then utilized with a differential pressure transducer (Fluid Precision Inc., Billerica, MA: model #183) to record input airflow. The airflow was humidified and heated by bubbling it through 5 cm of heated water so that the temperature of the air was 37 °C when measured at the glottic outlet.

One-centimeter segments of recurrent and superior laryngeal nerves were isolated, and Harvard bipolar miniature electrodes (model 50-1650, South Natick, MA) were applied around each nerve. A constant current nerve stimulator (WR Medical Electronics Co., St. Paul, MN: model S2LH) was used to stimulate the recurrent laryngeal nerves (RLN) and a constant voltage source (Grass, Quincy, MA, model 54H; WPI, New Haven, CT, 301-T) was used to stimulate the superior laryngeal nerves (SLN). These nerves were stimulated at 70–80 Hz, with 0.3- to 0.5-mA (RLN) or 1-1.4-V (SLN) intensity for 1.5-ms pulse duration. There was no observed contraction of the cricothyroid during maximal stimulation of the RLN at 2.0 mA. Similarly, there was no bulging or contraction of the thyroarytenoid muscle and no movement of the arytenoid during maximal stimulation of the SLN at 3.0 V. During each trial, airflow was gradually increased from 0–800 cc/s through the larynx by the rostrally directed endotracheal tube.

Upstream subglottic pressure was measured using a Millar (Houston, TX) Mikro-Tip catheter pressure transducer (model No. SPC-330, Size 3F). The subglottic pressure transducer was passed rostrally through the superior tracheotomy and placed 5 cm below the glottis. Downstream pressure was measured using a Statham pressure transducer (Hato Rey, Puerto Rico: model P23BB) connected to a 16 gauge needle inserted through the cheek mucosa to rest at the level of the base of the tongue. The pressure transducer was calibrated before and after the experiment against a mercury manometer at 37 °C.

Downstream resistance was controlled by tying off the esophagus at the level of the cricopharyngeus. The uvula was sewn to the area of the epiglottis to prevent palatal oscillation. A running locked 2-O silk suture, cyanoacrylic glue and silicone were used to seal the lips and oral cavity. The nasopharynx was then used as the sole output flow port. Downstream resistance was controlled by compressing the nasal ports in order to adjust the amount of resistance to flow which could exit solely through the nasal cavity.

Electroglottographic (EGG) signals were obtained with a Laryngograph (Synchrovoice, Harrison, NJ) with the two recording electrodes sutured into place on the right and left thyroid ala, just above the cricothyroid muscles. The reference electrode was secured to an adjacent strap muscle. The EGG signal was required to positively identify the onset and cessation due to acoustic muffling of phonation after sealing the oral cavity. The period between EGG waveforms was used for fundamental frequency analysis at the onset and before the end of phonation. The EGG, input airflow, supraglottic and subglottic pressure signals were low-pass filtered at 1 kHz, digitized at 2.5 kHz for 20 s, and stored on the hard disk of a personal computer. The pressure channels were processed in a signal analysis program to calculate the root-mean-square (rms) average pressures, using a 2000

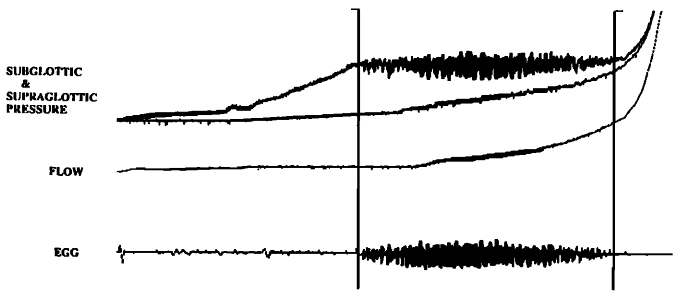


FIG. 4. Representative trial from *in vivo* canine preparation with downstream resistance. EGG = electroglottograph; flow = airflow rate, supraglottic pressure (third trace from the bottom), subglottic pressure (upper trace). Left and right cursors depict onset and cessation of phonation, respectively.

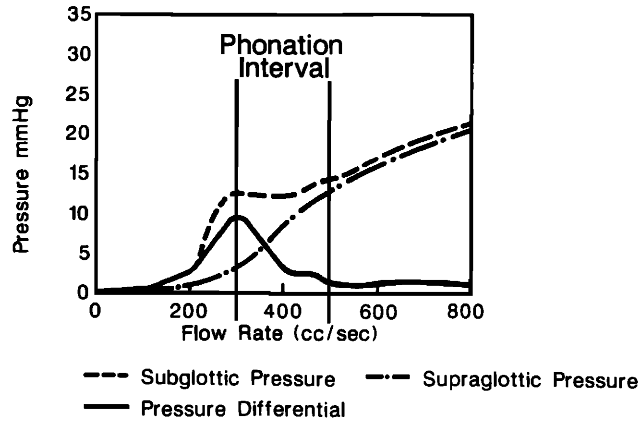


FIG. 5. Phase-plane diagram derived from Fig. 4 of root-mean-square of subglottic and supraglottic pressure differential versus input airflow.

point window moved in one-point increments.

Subglottal videoendoscopy was performed using a Storz Xenon light source (Culver City, CA: model 487) to illuminate the subglottis through a zero degree documentation sheath, connected to a Jed Med CCS Camera (St. Louis, MO: model 70-5150), and recorded on a SONY video recorder (Park Ridge, NJ: model VO5850). The sheath was passed rostrally through the superior tracheotomy site and the endotracheal tube was inflated around it to seal the trachea.

A moderate level of cricothyroid stimulation (0.5 V) and a low level of recurrent laryngeal nerve stimulation (0.2 mA) were used to produce closure of the glottal aperture. Flow was then increased from 0 to 800 cc/s over a 20-s period while maintaining a constant compression of the nasal ports in order to obtain an output flow resistance of 0.023 mm Hg/cc/s at 400-cc/s airflow. During this time EGG, input airflow, supraglottic and subglotti pressure signals were digitized. Subsequent to digitization, subglottic videoendoscopy was performed.

## II. RESULTS

Figure 4 depicts recorded signals of subglottic and supraglottic pressure, input airflow, and EGG versus time during a representative trial. Left and right cursor placement depicts the onset and cessation of phonation, respectively. Subglottic pressure increased with the increase in input airflow until phonation ensued. During the phonation interval, peak subglottic pressures fluctuated less than 0.5 cm/$H_2O$ in spite of increasing input airflow. This indicated a decreasing glottic resistance with increasing airflow during phonation. A delay in the rise of the supraglottic pressure was noted due to the filling of the cheek walls of the oral cavity. Once the cheeks became distended, supraglottic pressure rose steadily in parallel with the increase in input airflow. Vocal fold vibration dampened out as supraglottic pressure approached the subglottic pressure. Subsequent to the cessation of phonation, the two pressures rose in parallel for the remainder of the trial as a function of $Q$. EGG measurement of the period of each cycle indicated that increasing airflow was associated with a shortening of the period and an increase in oscillation frequency from 32 Hz at onset to 83 Hz prior to cessation of phonation.

Figure 5 shows a phase-plane diagram of the rms subglottic/supraglottic pressure differential versus input airflow derived from Fig. 4. Phonation occurred during the region of negative differential resistance.

Videosubglottoscopy demonstrated that stimulation of the RLN and SLN without flow produced complete closure. During low flow states ( $< 300$ cc/s), the larynx did not vibrate. This is analogous to region 3 of the $P - Q$ characteristic in Fig. 2 when the tube is completely collapsed. Increasing $Q$ to $> 300$ cc/s led to vocal fold vibration. This is analogous to region 2 (Fig. 2) when the tube is partially collapsed. At flow rates $> 467$ cc/s, the rise in supraglottic pressure produced a dampening of oscillation, and the glottis was noted to open as in region 1 of Fig. 2. Interestingly, at high flow rates opening first occurred in the posterior commissure of the glottis.

## III. DISCUSSION

Table I summarizes a number of the features of collapsible tube Starling resistor studies that can be observed in this *in vivo* canine preparation. In Conrad's collapsible tube study (1969), upstream pressure increased with flow rate until the onset of oscillation, but then plateaued at a value close to the external pressure on the tube (Fig. 6). In this *in*

TABLE I. Summary of analogies between collapsible tube models and the *in vivo* canine model of phonation.

| Collapsible tube models | *In vivo* canine laryngeal model |
|---|---|
| $P_e$ | vocalis muscular contraction |
| $P_1$ | subglottal pressure |
| $P_2$ | supraglottal pressure |
| $Q$ | glottal air flow |

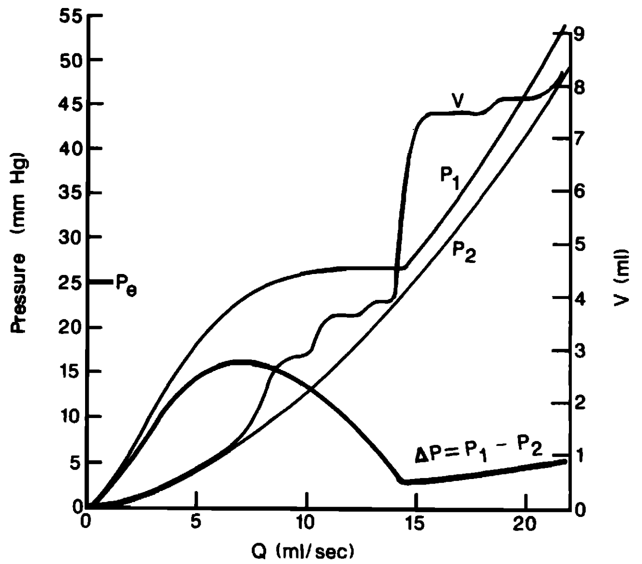


FIG. 6. Upstream and downstream gauge pressures $P_1$ and $P_2$ and their difference $P_n$ as well as the volume $V$ of the tube as functions of $Q_n$ for Starling Resistor experiment. $P_e = 25$ mm Hg; $k = 0.08$ mm Hg/(ml/s)$^2$ (copyright 1969 IEEE).

*vivo* canine preparation, subglottic pressure also rose until the onset of phonation and then plateaued (Fig. 4). The plateau has been observed by others in both excised canine larynges and *in vivo* canine studies (Muta and Fukuda, 1988; Koyama *et al.*, 1969; Berke *et al.*, 1989). In both this canine model and collapsible tubes, downstream pressures continued to rise in parallel with the increase in flow rate, due to the fixed outflow tract resistances.

In region 3 of the collapsible tube studies (Fig. 2), the tube remains collapsed and acts as a rigid resistance until the internal pressure rise becomes equal to the external pressure on the tube. In the case of the *in vivo* model, one might theorize that, until the subglottic pressure increases to the point of overcoming the closing pressure forces of the vocal folds, the glottis stays closed and acts as a fixed rigid resistance. In collapsible tube studies, when the upstream internal pressure finally reaches a level of the external pressure, the tube partially opens. During partial tube collapse in region 2, increasing flow rate does not produce proportional increases in upstream pressure. The upstream pressure is determined primarily by the external pressure and tube viscoselastic characteristics. Similarly, in this *in vivo* canine model, increasing airflow produced a rise in subglottic pressure prior to the onset of phonation. Following the onset of phonation, increasing flow rate had little influence on subglottic pressure during the phonation interval, implying that the soft yielding walls of the vocal folds controlled the subglottic pressure and that it did not act as a fixed rigid resistance during phonation. Studies calculating impedance using static models may not accurately simulate the pressure-flow relationships that exist during vocal fold vibration. Finally, in this model and the collapsible tube model, as the downstream or supraglottic pressures exceeded the pressure required for partial tube collapse and phonation, the tube or glottis opened and the pressure-flow relationship again approximated a rigid, fixed linearity (Figs. 5 and 6). After tube and glottal opening both downstream and upstream pressures rose in parallel with further increases in flow. It should be pointed out that Figs. 1, 2, and 6 refer to fluid flow in collapsible tubes. Thus comparisons between Figs. 5 and 6 relate to the shape of the characteristics not absolute pressure-flow values.

It is important to realize that the negative slope of the $P - Q$ characteristic in the *in vivo* canine model and collapsible tube studies occurred because of comparing the pressures produced by a fixed downstream resistance to an upstream nonlinear flow-controlled resistance. Negative differential resistance in this study was the result of comparing a relatively constant subglottic pressure to a rising supraglottic pressure during the phonation interval. We chose to set up this experiment with a downstream resistance in order to observe how the larynx compared to a collapsible tube when subjected to the classical experimental paradigm. Although this was a highly unnatural state, scientific investigations are replete with studies in which natural systems are subjected to unnatural conditions in order to gain insight into the phenomena that govern the system in its natural state. Examples can be found all the way from high-energy particle physics to placement of oral prostheses in the measurement of the articulators during speech. Fixed downstream resistances have been used in collapsible tube studies because they enabled the experimenter to adjust downstream pressure conditions in order to observe the effects downstream pressure had on upstream pressure and collapsible tube mechanics. Without a downstream resistance, the downstream pressure in this study would have remained fixed at zero atmospheric pressure. The magnitude of the downstream resistance utilized was determined by the requirement that the resulting value of the supraglottic pressure had to approach the subglottic pressure within the limits of the span of airflows delivered. If a small downstream resistance had been employed, the value of the supraglottic pressure would have never approached the subglottic pressure and the existence of negative differential resistance could not have been determined nor would vibratory damping have occurred.

Because a supraglottic resistance does not normally exist during most normal phonatory modes, one could question whether the presence of negative differential resistance is a prerequisite for sustained oscillation. Obviously, the larynx can oscillate without a downstream resistance, but collapsible tubes can also oscillate without a downstream resistance. When an air-filled balloon is released and flutters around a room, it is exhibiting collapsible tube oscillation without a downstream resistance. Thus it may be more appropriate to ask which essential elements of nonlinear flow controlled resistance leads to instability and oscillation. The essence of this matter has stimulated numerous theoretical and experimental studies on collapsible tube biomechanics. Its answer may elucidate problems ranging from the physiologic requirements for biologic fabrication of neolarynges to a simplified understanding of the components essential for vocal fold oscillation and how the dependent and independent variables interact. Based on the collapsible tube analogy some insights can be made into how laryngeal physiologic control parameters affect upstream resistance in the presence or absence of a downstream resistance. In a Starling resistor, progressively diminishing downstream resistance has the effect of decreasing the negative slope of the $P-Q$ characteristic thus shifting the oscillation threshold toward higher flow rates and expanding the range of flows during which vibration occurs. In a larynx without a downstream resistance, the $P-Q$ characteristic would be close to zero slope or slightly positive during the phonation interval. In a Starling resistor, increasing $P_e$ has the effect of proportionally increasing the upstream resistance initially at low flow rates. In contrast, $P_e$ has little effect on upstream resistance at high flow rates. From this, one can postulate that increasing stimulation to the recurrent or superior laryngeal nerves would produce an increase in the glottal resistance at low flow rates, but at high flow rates glottal resistances would converge toward the same value regardless of the extent of muscular contraction. Further, the resistance would be higher at low flow rates when the glottis is relatively "collapsed" than at high flow rates when it is relatively "distended." This implies that the larynx is a more efficient vibrator at low flow rates than at high flow rates. Thus supraglottic constrictions commonly observed in professional singers may permit stable vibration to occur at low flow rates where the larynx is most efficient and where changes in muscular contraction would have their greatest influence on vocal control.

An important difference between collapsible tube studies and this *in vivo* canine study is the dependence of frequency on increasing airflow. Collapsed latex tubes demonstrate a decrease in oscillation frequency as flow increase. This is because increasing airflow leads to tube expansion and, as determined by the tube law, less tube rigidity. This *in vivo* canine preparation demonstrated an increase in oscillation frequency for increasing airflow. Whether the increase in oscillation frequency represents amplitude dependent stiffness effects (as suggested by Titze, 1980), a purely flow-dependent function, or some other factor, remains an additional topic for further exploration.

## IV. SUMMARY

In the presence of a supraglottic outflow tract resistance, measurements of the subglottic and supraglottic pressures were made during stimulation of laryngeal phonation. During constant laryngeal nerve stimulation and increasing airflow, vocal fold oscillation occurred in the region of the negative slope of the pressure differential versus flow curve. This *in vivo* canine preparation exhibited some characteristics consistent with collapsible tube oscillation.

## ACKNOWLEDGMENTS

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