Ann Otol Rhinol Laryngol 98:1989

EFFECT OF VOCAL FOLD AUGMENTATION ON LARYNGEAL VIBRATION IN SIMULATED RECURRENT LARYNGEAL NERVE PARALYSIS: A STUDY OF TEFLON AND PHONOGEL

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Flaccid laryngeal nerve paralysis may be treated by vocal fold augmentation with Teflon injection, which is successful to various degrees depending on the subjective interpretation of the patient or clinician. A new material, Phonogel, consisting of cross-linked bovine collagen, is available but not approved for human use in this area. Ten dogs were submitted to videostroboscopy, photoglottography, electroglottography, and acoustic analysis in the normal state, with simulated recurrent laryngeal nerve paralysis, and with injection of either Teflon or Phonogel. A statistical comparison and the advantages and disadvantages of each material are discussed in relation to this study and its clinical use.

KEY WORDS — flaccid laryngeal nerve paralysis, Phonogel, recurrent laryngeal nerve, Teflon, vocal fold injection.

INTRODUCTION

Paralysis of the human vocal folds is a problem frequently encountered by otolaryngologists. Usually a unilateral paralysis is encountered and the majority of these are caused by injury to the vagus or recurrent laryngeal nerve by surgery or an adjacent tumor.[1]

For most patients with unilateral vocal fold paralysis, compensation takes place over a period of several months, allowing resumption of acceptable communication, absence of aspiration, and an effective cough. For those patients whose laryngeal dysfunction does not improve, a variety of methods have been developed to treat unilateral vocal fold paralysis. Reinnervation techniques focus on providing a neural or neuromuscular transplant to the affected lateral cricoarytenoid muscle—the primary adductor of the vocal fold.[2,3] Although these techniques have potential for reinnervating the larynx, they have not had widespread acceptance. In contrast, most currently used methods rely on passive techniques to medialize the paralyzed vocal fold. Methods of passive medialization rely on an intact separate innervation to the contralateral vocal fold that when tensed can abut the ipsilateral paralyzed, but now medialized, vocal fold. One method, thyroplasty type I, uses thyroid cartilage as an autograft placed in a pocket developed between the thyroid ala of the affected fold and the fold itself.[4] Other methods of medialization by augmentation rely on the use of inert substances such as Gelfoam,[5] glycerin,[6] and Teflon.[7-9] The last substance has been the mainstay of treatment, as it seems to be the most easily used and produces the most predictable results. Recently, several investigators have reported preliminary results in treating vocal fold paralysis with bovine cross-linked collagen (Phonogel, Collagen Corp, Palo Alto, Calif).[10-12]

Regardless of which form of surgical treatment is used, results vary according to subjective evaluation of phonation and glottic competency. In fact, among physicians trained in laryngology it is not uncommon to have differing opinions regarding the outcome of these treatments in individual patients. In addition, a single otolaryngologist may have difficulties in assessing the results of vocal fold augmentation over time.

Several investigators have used various objective measures in human subjects to evaluate the effect of Teflon augmentation on vocal fold paralysis. Rontal et al[13] used voice spectrography to monitor the performance of vocal fold Teflon injection procedures. Cormier et al[14] measured forced inspiratory and expiratory airflows in patients before and after Teflon injection. Rubin[15] demonstrated the vibratory characteristics of the vocal folds by high-speed photography both preinjection and postinjection. Von Leden et al[16] used several objective measures of laryngeal function in addition to acoustic analysis of the paralyzed and Teflon-injected states.

Currently, a number of objective tests may be used as aids in diagnosis and therapy of dysphonias. Photoglottography (PGG) is a method that measures the amount of light transmitted through the vocal folds during phonation. Typically, a light

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Presented at the meeting of the American Laryngological Association, Palm Beach, Florida, April 23-25, 1988.
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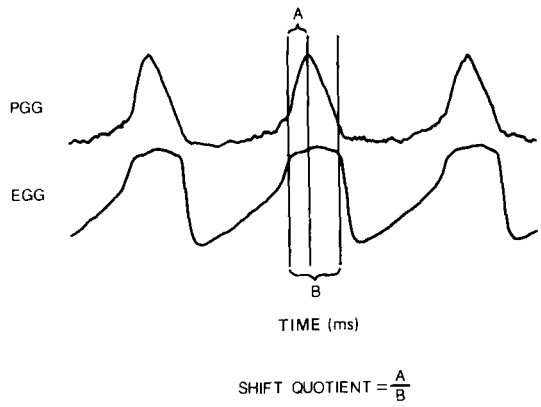

Fig 1. Calculation of shift quotient in dog with phonation produced in normal state. PGG — photoglottographic waveform, EGG — electroglottographic waveform.

source is placed in the mouth or pharynx while a photosensor is placed on the neck below the folds. As the vocal folds vibrate, changes in the glottal area produce proportional changes in the intensity of light transmitted. It has been shown by comparison with high-speed photography that the intensity of the transmitted light during PGG is a good approximation of cross-sectional area of the glottic aperture during phonation.[17-19]

Another technique, electroglottography (EGG), measures change in electric impedance across the larynx as the vocal folds vibrate. Comparison between EGG and stroboscopic investigation of the vibrating vocal folds substantiates the view that the EGG signal reflects variations of lateral vocal fold contact area.[20] Baer et al[19] stated that EGG and PGG are complementary measures, in that the former provides information about glottic closure, while the latter helps describe glottic opening.

Two measures of the glottic cycle with potential clinical application that can be calculated by use of PGG and EGG waveforms are the open quotient (OQ) and the speed quotient (SQ). Open quotient is defined as the fraction of time the folds are open during the glottic cycle. Speed quotient is the duration of time the folds are opening divided by the duration of time the folds are closing. Trapp and Berke[21] recently presented a new measure, the shift quotient (ShQ), that may be valuable in identifying flaccid laryngeal paralysis (Fig 1). Each of these measures, OQ, SQ, and ShQ, holds potential as an objective measure for judging the outcome of various treatments for vocal fold paralysis.

Another objective though less quantifiable measure of vocal fold vibration is videostroboscopic laryngoscopy. Recent miniaturization of videocameras combined with available fiberoptic systems has created a tremendous clinical interest in this form of documentation. Moore et al[22] recently studied videolaryngoscopy in an in vivo canine model of phonation with the addition of stroboscopy to detail the unique characteristics of normal vocal fold vibration in addition to the vibratory characteristics of recurrent laryngeal, superior laryngeal, and vagal nerve paralyses.

Although laryngologists have been using Teflon to augment vocal folds for the past 20 years, the optimal amount of Teflon to inject into the vocal fold has not been determined by any objective measurement. Most experienced laryngologists have estimated a quantity in the range of 0.2 to 0.5 mL. It became apparent to us that photoelectric techniques and videostroboscopy might be useful in determining the amount of synthetic material needed for return to optimal pre-paralysis vocal function.

Ten adult male mongrel dogs were studied by EGG and PGG to compare the effects of Phonogel and Teflon augmentation on simulated unilateral recurrent laryngeal nerve paralysis. This was performed according to a previously reported in vivo canine model of phonation.[23] Photoelectric data and videostroboscopic images of laryngeal vibration were obtained for normal phonation, simulated recurrent nerve paralysis phonation, and postinjected states—both Teflon and Phonogel. This study reports the results obtained.

MATERIALS AND METHODS

Operative/Photoelectric. Ten adult male mongrel dogs 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 animals were placed supine on the operating table, the neck was shaved, 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 just lateral to their entrance into the cricothyroid muscles. Figure 2 is a schematic representation of the experimental setup. A low tracheotomy was performed at the level of the suprasternal notch, through which an endotracheal tube was passed to allow spontaneous respirations. A second tracheotomy was performed in a more superior location, through which a cuffed endotracheal tube was passed in a rostral direction for several centimeters and positioned 10 cm below the vocal folds. The cuff was inflated to just seal the trachea. Humidified heated air was passed subglottically through this second endotracheal tube from a compressed air canister, and flow was controlled with a valve and flowmeter. The warmth and humidification of the air were provided by bubbling the air through 5 cm of heated water to provide a constant temperature of 37°C as measured at the laryngeal lumen. A 1-cm button was used to suspend the epiglottis from a fixed point to provide

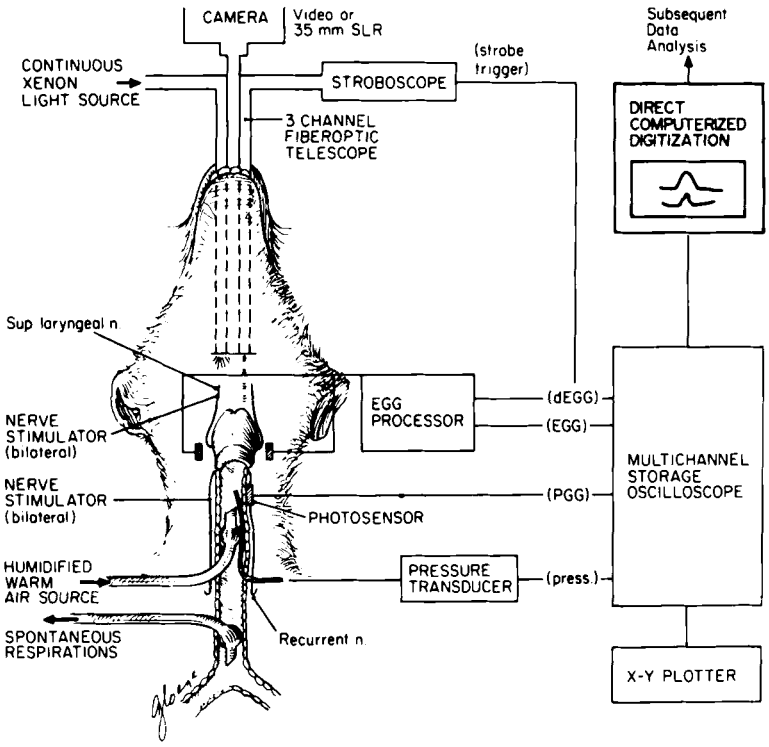

Fig 2. Schematic representation of experimental set-up for in vivo canine model of phonation. SLR — single lens reflex, EGG — electroglottography, dEGG — differentiated electroglottography, PGG — photoglottography.

direct visualization of the larynx through the oral cavity.

A 1-cm segment of the recurrent and superior laryngeal nerves was isolated and Harvard silver electrodes were applied around the nerve. The electrodes then were insulated from the surrounding tissue. Two nerve stimulators (Grass Instruments) with direct current isolation units were used to stimulate the recurrent and superior laryngeal nerves. These nerves were stimulated at 70 to 90 Hz stimulus frequency, with 2 to 7 mA intensity for 1.5 ms pulse duration. Phonation was produced with airflow of 375 mL/s supplied through the laryngeal aperture by the rostrally placed endotracheal tube while the laryngeal nerves were being stimulated.

Changes in glottic area were monitored by PGG. The larynx was illuminated from above with a fiberoptic xenon light source secured in the oral cavity and directed toward the glottis. Light transmission through the vocal folds was transduced with a photosensor (Centronics OSD 502) placed on the trachea just below the cricoid cartilage. Electroglottographic signals were obtained with a laryngograph (Synchrovoice) with the two recording electrodes placed in pockets just above the cricothyroid muscles adjacent to the thyroid cartilage. The ground electrode was secured to adjacent strap muscles. Photoglottographic and EGG tracings were observed on a storage oscilloscope (Tektronix 5116) and directly digitized and stored onto the hard disk of a personal computer (80286 microprocessor).

Acoustic data were acquired with a highly sensitive Bruel & Kjaer condensor microphone placed at a constant distance (30 cm) from the glottis and were stored on the hard disk of a personal computer.

Computerized Data Digitization, Storage, and Analysis. Analog data from EGG, PGG, and acoustic signals were low-pass filtered at 3,000 Hz and digitized real-time at 20,000 Hz by use of the personal computer equipped with a math coprocessor (80287) and a commercial software program (C-Speech, Paul Milenkovic, PhD, University of Wisconsin). The EGG and PGG waveforms obtained were examined briefly after each trial of phonation to evaluate the adequacy of the waveforms. Three seconds of waveform data was stored on the computer's hard disk and later recovered for analysis and calculation of the OQ and SQ. In addition, the ShQ was derived from the EGG and PGG waveforms (Fig 1). This was done by calculating the distance from the beginning of the plateau phase of the EGG to the apex of the PGG as it was superimposed directly on the EGG and dividing this by the duration of the plateau phase of the EGG (Fig 1). Points of glottic opening and closing were determined in the manner previously described by Childers et al.[24] Vocal fold opening was marked at the peak of the differentiated EGG waveform, and closing at the nadir of the differentiated EGG waveform.

Data were analyzed in the following format. Within each trial of simulated phonation a stable

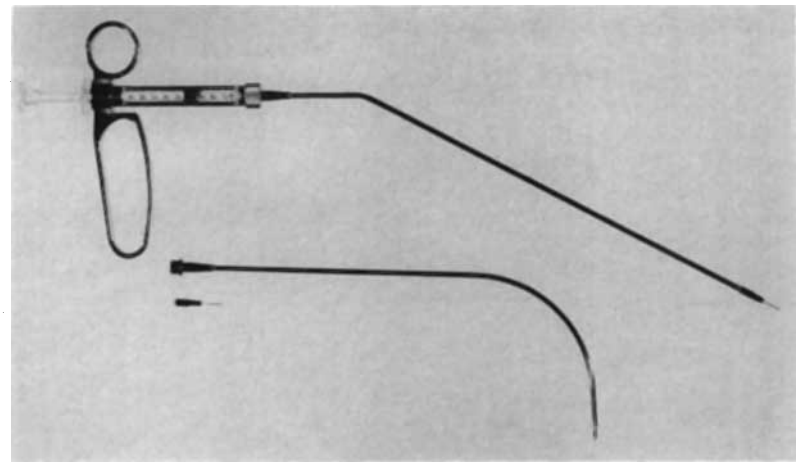

Fig 3. Phonogel injector apparatus with 26-gauge needle and single-use syringe of Phonogel in position.

0.25-second portion was chosen in four equally separated parts of the 3-second recording. Within these 0.25-second segments, five consecutive waveforms were analyzed interactively and averaged to calculate a single value for OQ, SQ, and ShQ. The values then were compared with those obtained in the three other 0.25-second segments and a mean value was calculated and recorded as the OQ, SQ, and ShQ for each simulated phonation. The values of each of three trials were compared and averaged so that each dog had one value for OQ, SQ, and ShQ.

Signals also were examined qualitatively to determine how their overall shape related to the vibratory patterns seen on videostroboscopy.

Available software was used to obtain the fast Fourier transformation from the acoustic signals (C-Speech).

Video Imaging. A Storz laryngostrobe unit (model 8000) was used for stroboscopic video imaging that was performed with each trial of phonation after the photoelectric data had been recorded. The stroboscope was connected to a Storz 0° telescope via a fluid-filled light cable. The image from the 0° scope was recorded on a Storz CCD (charge-coupled device) video camera (model 9000) and a Sony U-matic videocassette recorder (VO-5800). The video images subsequently were analyzed frame-by-frame by use of the same videorecording unit.

Injection of Teflon/Phonogel. Injections were carried out by use of fiberoptic laryngoscopy. Five dogs each were injected with Teflon and Phonogel, respectively. Teflon was injected in the standard method as reported by Arnold[7] with a Breuning's syringe. This injection was placed so that the Teflon was lateral to the vocalis muscle. Phonogel was injected with a specially designed injector (Collagen Corp, Palo Alto, Calif) (Fig 3). This injection was performed within the submucosa just deep to the mucosal plane as described by Ford et al.[10]

Increments of 0.1 mL of Teflon or Phonogel injection were analyzed stroboscopically and by photoelectric waveform analysis during each experiment. The end point of Teflon or Phonogel augmentation was considered to have been reached when vocal fold vibration most closely appeared as a travelling mucosal wave. Several animals then underwent overinjection of Teflon or Phonogel and stroboscopic images and photoelectric signals were obtained.

Experimental Design. Recordings were taken for a minimum of three trials of each state: normal (simultaneous bilateral recurrent and superior laryngeal nerve stimulation), unilateral recurrent laryngeal nerve paralysis, and postinjection/augmentation (Phonogel or Teflon).

A constant low level of bilateral cricothyroid tension (0.2 mA stimulation) was maintained in all ten dogs. The recurrent laryngeal nerves then were stimulated bilaterally until phonation ensued to provide data for normal phonation. These ten dogs

TABLE 1. QUOTIENT VALUES FOR TEFLON GROUP

Dog	*Normal*	*Paralysis*	*Teflon Injection*
Open quotient			
1	0.22	0.30	0.31
2	0.30	0.52	0.42
3	0.23	0.42	0.28
4	0.30	0.39	0.30
5	0.25	0.31	0.31
Mean	0.26	0.39	0.32
Speed quotient			
1	1.14	1.01	1.15
2	0.92	0.92	0.96
3	1.02	1.03	0.86
4	1.13	1.19	1.06
5	1.19	0.60	1.02
Mean	1.08	0.95	1.01
Shift quotient			
1	0.76	0.38	0.57
2	0.51	0.29	0.60
3	0.68	0.38	0.73
4	0.62	0.47	0.55
5	0.65	0.51	0.79
Mean	0.64	0.41	0.65

TABLE 2. QUOTIENT VALUES FOR PHONOGEL GROUP

Dog	*Normal*	*Paralysis*	*Phonogel Injection*
Open quotient			
6	0.19	0.48	0.31
7	0.22	0.42	0.40
8	0.36	0.65	0.53
9	0.27	0.29	0.17
10	0.13	0.51	0.34
Mean	0.23	0.47	0.35
Speed quotient			
6	1.07	0.63	0.61
7	1.10	1.21	0.95
8	1.00	1.32	1.50
9	0.69	1.03	1.16
10	1.74	1.09	1.08
Mean	1.12	1.06	1.06
Shift quotient			
6	0.47	0.36	0.45
7	0.56	0.33	0.49
8	0.53	0.29	0.31
9	0.56	0.31	0.63
10	0.73	0.33	0.67
Mean	0.57	0.32	0.51

then each underwent trials of phonation with one recurrent laryngeal nerve transected and stimulation to both superior laryngeal nerves and the remaining recurrent laryngeal nerve. The dogs then were divided into two groups. The first group of five dogs was treated with Teflon augmentation of the vocal fold on the side of the transected recurrent laryngeal nerve. The second group of five dogs had the paralyzed fold augmented with Phonogel.

Statistical Analysis. Data for each quotient group were subjected to a 2 x 3 mixed-factor analysis of variance (ANOVA), substance by phonation, respectively. In addition, post hoc Newman-Keuls testing was used to compare states of phonation for the OQ and ShQ values.

RESULTS

Photoelectric Data. A mean value for OQ, SQ, and ShQ was calculated for each of the ten dogs in each experimental cell—normal phonation, phonation with unilateral recurrent laryngeal nerve paralysis, and phonation after augmentation with Teflon or Phonogel. Tables 1 and 2 depict the mean quotient values for each treatment cell.

Figure 4A compares the mean values for OQ—Teflon versus Phonogel. As seen from the graph, the preinjection states were similar, ie, there was no main effect for treatment group on OQ. Further, there was no interaction between treatment group and state of phonation. There was however, a significant main effect for state of phonation attributable to the paralyzed condition: $F(2,16) = 17.75$, $p < .001$. A post hoc Newman-Keuls test was applied and showed that the paralyzed condition was significantly different from normal ($p < .05$) and

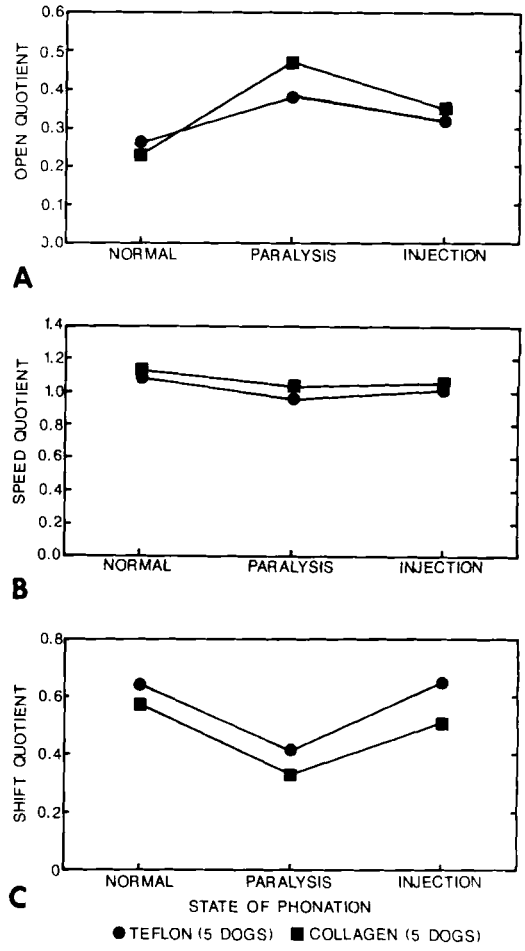

Fig 4. Mean values of A) open quotient, B) speed quotient, and C) shift quotient.

that paralyzed and injected states were similar. In addition, normal and injected states were significantly different ($p < .05$). In other words, neither group of dogs recovered to "normal" values and the injected dogs were not statistically different from those in the paralyzed state. In addition, there was no statistically significant difference in the performance of Teflon when compared to Phonogel for changes in OQ.

Figure 4B compares the mean values for SQ. No statistically significant difference was observed between the Teflon and Phonogel groups, and no difference between the normal, paralyzed, and postinjected states.

Figure 4C compares mean values for ShQ. There was no main effect for treatment group on ShQ and there was no interaction between treatment group and state of phonation. There was a significant main effect for state of phonation attributable to the paralyzed condition: $F(2,16) = 25.86$, $p < .001$. Post hoc testing was applied and showed that the paralyzed condition was significantly different from normal ($p < .05$) but that normal and injected states were not significantly different from one another.

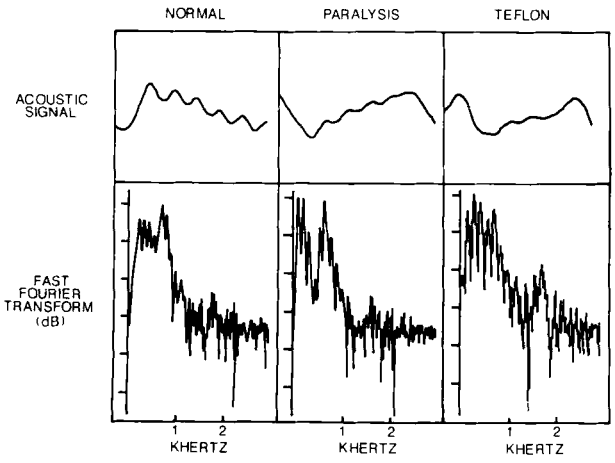

Fig 5. Sample of acoustic waveforms and fast Fourier transformation analysis of single dog in normal, recurrent laryngeal nerve paralysis, and post-Teflon injection states.

Videostroboscopy. Videotapes of each of the ten dogs in each of the two preinjected states of phonation (normal and recurrent nerve paralysis) were compared to the vibratory patterns of the postinjected states (Teflon and Phonogel). As previously reported by Moore et al,[22] a symmetric travelling mucosal wave normally occurs from the lower to the upper fold margin as the glottic air puff is released. The characteristic findings with unilateral recurrent laryngeal nerve paralysis were loss of the travelling mucosal wave bilaterally as the glottic air puff was released and a homogeneous lateral excursion to the paralyzed vocal fold (one mass). The nonaffected vocal fold remains tense near the midline with little excursion.

After minimal augmentation of the paralyzed fold with Teflon, a return toward the normal two-mass (upper and lower margin) model of oscillation with resumption of the travelling mucosal wave to the nonparalyzed fold was noted. With further augmentation this effect was enhanced.

With overinjection it was observed that the paralyzed flaccid fold became the tensed vocal fold and that the normal nonparalyzed fold vibrated in a manner similar to that of the previously paralyzed fold. The same was true for dogs overinjected with Phonogel. A videotape summarizing the results was presented recently.[25]

Acoustic Analysis. Of interest was the effect of laryngeal paralysis and vocal fold augmentation on the acoustics of phonation. Figure 5 depicts the acoustic signal and fast Fourier analysis of the acoustic signal for normal, paralyzed, and Teflon-injected states of phonation. All three phonation states are characterized by a strong formant visible at about 800 Hz. The paralyzed state shows a sharp drop-off in the amplitude of the third and fourth harmonics due to the breathy phonation. Teflon injection to the point at which the ShQ was corrected to normal shows a resumption in harmonic amplitudes. This also was associated with a perceptual increase in the acoustic intensity of phonation.

With simulated normal phonation a change in fundamental frequency (F0) was related to changes in recurrent laryngeal nerve stimulation. In the paralyzed state there was no change in F0 associated with changes in recurrent laryngeal nerve stimulation because of loss of subglottic pressure modulation. Vocal intensity was not measured in each case, but perceptual decrease in intensity was noted in the paralyzed state and was associated with the decrease in harmonics seen in Fig 5.

DISCUSSION

Open quotient, a relative measure of the time period the glottis is open as a function of the entire glottic cycle, has been found to increase with flaccid laryngeal paralysis of the recurrent nerve type.[26] The clinical correlate is observed when the patient has a weak and breathy voice. This value would be expected to decrease toward normal with augmentation by either Teflon or Phonogel, as it did, though not to a degree that was statistically significant.

Speed quotient was not found to alter significantly in this study and in similar studies.[21]

We have found the ShQ to be a useful measure in the identification of flaccid laryngeal paralysis. A shift of the peak of the PGG to the left in relation to the EGG occurred because the paralyzed flaccid vocal fold vibrates in a one-mass mode. This implies no phase lag between the opening of the lower margin and upper margin excursion. The homogeneous lateral excursion of the paralyzed fold caused the vocal fold aperture to be at its maximum (ie, peak of PGG) when the cord unzips completely in the horizontal plane (ie, plateau phase of EGG). It is possible to measure this shift in the apex of the PGG with respect to the beginning of the plateau phase of the EGG (length A, Fig 1). We quantitate its relative value by using the duration of the EGG plateau phase as the denominator (length B, Fig 1).

Figure 6A,B shows the contrast in ShQ typically seen for dogs with normal phonation and dogs with unilateral recurrent nerve paralysis, respectively. Figure 6C shows that with Teflon augmentation, the peak of the PGG is shifted back into a later portion of the EGG plateau phase, as seen in normal phonation. Figure 6D depicts similar findings in another dog when a paralyzed vocal fold was injected with Phonogel. This shifting of the PGG peak relative to the EGG plateau phase has been quantified, and when statistically compared, the normal and injected states were not found to be statistically different.

The morphology of the photoelectric waveforms also changed with augmentation. With recurrent

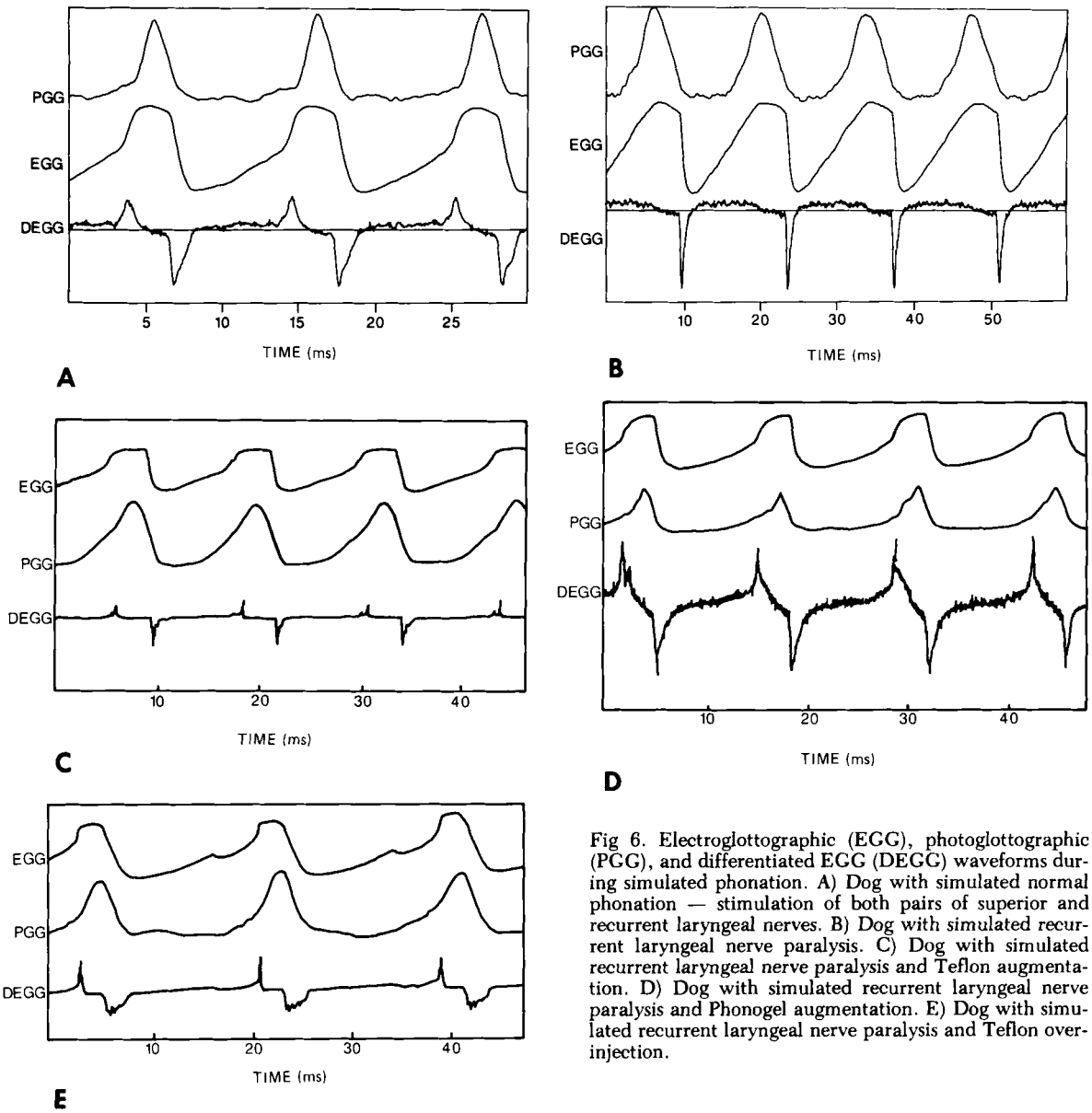

Fig 6. Electroglottographic (EGG), photoglottographic (PGG), and differentiated EGG (DEGG) waveforms during simulated phonation. A) Dog with simulated normal phonation — stimulation of both pairs of superior and recurrent laryngeal nerves. B) Dog with simulated recurrent laryngeal nerve paralysis. C) Dog with simulated recurrent laryngeal nerve paralysis and Teflon augmentation. D) Dog with simulated recurrent laryngeal nerve paralysis and Phonogel augmentation. E) Dog with simulated recurrent laryngeal nerve paralysis and Teflon overinjection.

nerve paralysis the slope of the opening phase of the EGG waveform usually failed to demonstrate the discontinuity that represents the normal transition from vertical to horizontal fold separation. This loss of change in EGG slope is due to the simultaneous opening of the upper and lower vocal fold margins that results when the two-mass movement is lost (compare Fig 6A and B). After injection of the paralyzed fold a hint of the two-mass morphology reappears, as there is discontinuity in the waveform during the opening phase of the glottic cycle (see PGG wave in Fig 6C).

Videostroboscopy confirmed the return to a more normal two-mass model of vocal fold vibration after treatment with either Teflon or Phonogel. There were no obvious performance differences between the two substances that supported the use of one of these synthetic agents over the other. We did note on careful review that a noticeable degree of augmentation achieved with Phonogel was lost over a period of time, sometimes as short as 30 minutes. This is apparently a function of the high water content of Phonogel in the cross-linked bovine form. Overinjection was needed in the initial treatment to attain a degree of vocal fold closure that could be maintained throughout the experimentation with Phonogel. This problem potentially seriously limits the usefulness of Phonogel as a vocal fold augmentation agent.

With overinjection of Teflon into the paralyzed fold, further shifting of the PGG peak to the right was observed. Several trials of phonation were recorded after an adequate amount of augmentation was exceeded; the ShQ value was not calculable because the peak of the PGG now was shifted beyond the plateau phase of the EGG. Figure 6E depicts the EGG and PGG waveforms from one trial of Teflon overinjection. It was observed that

with overinjection of Teflon there was a reversal of the relationship between the tension in the normal and that in the paralyzed folds. The overshifting of the ShQ probably represents the flaccid fold's now being the least compliant of the two folds.

It is important to note that the two-mass vibration occurred after injection, when the stiffness or mechanical compliance of the paralyzed fold most closely approximated the mechanical compliance of the normal fold. When this occurred the subglottic air pressure was distributed evenly over the paralyzed and nonparalyzed vocal folds, and the travelling mucosal wave was resumed. It is our contention that the reappearance of the travelling mucosal wave after augmentation allows the acoustic signal to improve the amplitude in the third and fourth harmonics because of the asymmetric nonsinusoidal nature of the glottic airflow.

Future work should attempt to define a method for obtaining equivalent mechanical compliance in the paralyzed and nonparalyzed vocal folds during intraoperative Teflon injection.

It should be noted that application of our results to clinical cases may be limited because laryngeal tension was controlled by "electric" stimulation of the laryngeal nerves. However, preliminary experience with a clinical case of laryngeal paralysis treated by percutaneous injection of Teflon supports our results.

CONCLUSIONS

Photoelectric measures were useful in the evaluation and treatment of laryngeal paralyses. Both Teflon and Phonogel changed vibration of the paralyzed fold toward a more normal two-mass upper and lower margin system of vocal fold vibration. The ShQ, a measure useful in differentiating the normal versus flaccid paralysis states, returned to normal values when the mechanical compliance of the respective vocal folds was approximately equal.

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