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# STUDIES ON LARYNGEAL CALIBRE DURING STIMULATION OF PERIPHERAL AND CENTRAL CHEMORECEPTORS, PNEUMOTHORAX AND INCREASED RESPIRATORY LOADS

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SUMMARY

1. The effects of asphyxia, hypoxia, hypercapnia, stimulation of peripheral chemoreceptors, pneumothorax and breathing through resistances have been investigated on laryngeal resistance to airflow in anaesthetized cats, with and without bilateral vagotomy below the origin of the recurrent laryngeal nerves.

2. Resistance to airflow of the innervated larynx was usually measured with the larynx isolated *in situ* with constant flow from the trachea to a pharyngeal opening, and expressed by the relationship between translaryngeal pressure and airflow.

3. Asphyxia, hypoxia and hypercapnia each stimulated breathing and decreased laryngeal resistance to airflow, in both the inspiratory and expiratory phases. After vagotomy the effect was reduced, abolished or (usually) reversed to a laryngeal constriction, especially in expiration.

4. Intra-arterial injections of potassium cyanide (to stimulate carotid body chemoreceptors) caused a short apnoea or an augmented breath followed by hyperpnoea, concurrently with expiratory constrictions of the larynx. The responses were usually stronger after bilateral vagotomy.

5. Pneumothorax caused tachypnoea, inspiratory dilatations and expiratory constrictions of the larynx. The responses were abolished by vagotomy.

6. Imposition of respiratory resistances dilated the larynx, in inspiration and expiration, while complete closure of trachea caused expiratory

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constrictions of the larynx. These changes did not depend on intact vagal pathways.

7. The results are discussed in terms of nervous control of the larynx in the different conditions.

## INTRODUCTION

The larynx is the main physiologically variable resistance in the upper respiratory tract. The control of its lumen depends on a complicated system of afferent information integrated in the central nervous system. Some lung reflexes (Szereda-Przestaszewska & Stransky, 1972; Stransky, Szereda-Przestaszewska & Widdicombe, 1973; Szereda-Przestaszewska & Widdicombe, 1973*a*), and chemical irritation of the upper airways (Szereda-Przestaszewska & Widdicombe, 1973*b*) increase expiratory laryngeal resistance to airflow. Initial experiments have shown similar effects on intravascular injections of potassium cyanide to stimulate peripheral chemoreceptors (Stransky *et al.* 1972). We have extended these observations by studying laryngeal resistance to airflow in cats with asphyxial blood gas changes, pneumothorax and breathing against respiratory loads. These conditions do not seem to have been studied previously by direct measurements of laryngeal resistance, although Bartlett, Remmers & Gautier (1973) have investigated the effect of hypercapnia. In addition there have been some investigations based on recording action potentials in laryngeal motor fibres or muscles. The interpretation of these latter indirect observations is not always clear, and there are inconsistencies in the literature. These will be considered in the Discussion.

All the studied conditions stimulate respiratory drive and alter respiratory rate. Since lung volume changes influence laryngeal calibre by the Hering–Breuer inflation reflex (see Discussion), any primary reflex change in laryngeal resistance might be modified secondarily by the changes in breathing. We have therefore repeated our observations in the cats after their vagus nerves had been cut in the chest below the origin of the recurrent laryngeal nerves.

## METHODS

Adult cats weighing 2·0–3·0 kg were anaesthetized with sodium pentobarbitone (30 mg/kg of body weight, I.P.), and were spontaneously breathing through a cannula in the lower cervical trachea. A second tracheal cannula was inserted just below the cricoid cartilage, directed rostrally. The pharynx was opened widely on the right and the epiglottis was usually pulled ventrally with a suture. The recurrent laryngeal nerves were spared.

Laryngeal resistance was measured in two ways.

(1) A constant stream of humidified warm air was passed through the upper cannula and the larynx at a constant rate (0·1–6·0 l./min, but usually 0·2–4·0 l./min)

continuously measured by a rotameter, and the inflow pressure was recorded and its ratio to laryngeal airflow was regarded as an index of laryngeal resistance.

(2) The upper tracheal cannula was connected in series with the lower cannula by glass tubes containing a Fleisch pneumotachograph head, so that the animal breathed through its larynx. The ratios of the pressure in the upper tracheal cannula (i.e. translaryngeal pressure) to airflow, taken at peaks of inspiratory and expiratory flow, were calculated and taken as indices of laryngeal resistance. Further details of these methods are given elsewhere (Stransky *et al.* 1973).

Upper tracheal pressure was measured with a capacitance manometer (Hilger). Transpulmonary pressure was measured from an air-filled polyethylene catheter tied into a lower right intercostal space and from a wide-bore needle inserted into the lower tracheal cannula, using a differential capacitance manometer (Hilger). Blood pressure was recorded from a catheter in a femoral artery by means of a strain gauge manometer (C.E.C.). Tidal volume and airflow were measured from a Fleisch pneumotachograph head attached to the lower tracheal cannula and to a differential inductance manometer with electrical integration (Godart, G.M. 0577). Blood pressure, tidal airflow and volume, upper tracheal pressure and transpulmonary pressure were continuously recorded on a seven-channel tape recorder (Ampex SP 300), displayed on an oscilloscope (Tektronix 551) and photographed when appropriate with a modified Cossor camera. Tidal carbon dioxide percentage was measured with an infra-red analyser (Beckman Spinco LBI) sampling from the lower tracheal cannula. Arterial blood oxygen and carbon dioxide tensions were determined in some experiments with Radiometer gas electrodes. All variables were recorded also on ultraviolet sensitive paper (Oscillograph UV 31, Honeywell).

In order to abolish lung vagal reflexes without interruption of the motor pathways to the larynx, bilateral intrathoracic vagotomy was performed in the chest just below the origins of the recurrent laryngeal nerves; it was usually necessary to open the chest on both sides. The chest was subsequently closed and spontaneous breathing restored. The absence of the Hering–Breuer inflation reflex was used to establish the effectiveness of lung denervation.

Asphyxia was induced by making the animal rebreathe through a wide-bore tube; the tube volume was in the range 45–83 ml., usually 83 ml. Hypoxia was produced by connecting a 5 l. bag containing 8% oxygen in nitrogen to the lower tracheal cannula, and hypercapnia by using a bag with 8% carbon dioxide in oxygen. Controls with a bag containing pure oxygen were done. Potassium cyanide was injected through a catheter tied into a lingual artery in a dose of 100 $\mu$g and washed in with saline. In some experiments intravenous injections of 250 $\mu$g were used. Right-sided pneumothorax was induced by injecting air from a syringe into the pleural space through a three-way tap and polyethylene catheter; 50 ml. and sometimes 100 ml. was injected. High and low resistances to breathing were applied by adding narrow tubes of known resistance to the lower tracheal cannula in experiments with constant flow through the larynx. Complete closure of the trachea was performed by clamping the tracheal tube.

Changes in laryngeal resistance are expressed as comparisons of control values over five to ten breaths with average or maximum changes depending on how long the peak response was maintained. All results are given as means and standard errors.

## RESULTS

Most of the experiments were with constant flow through the larynx, since the pressure/flow relationship of the larynx is alinear (see Stransky *et al.* 1973, and Discussion). Control values for 'resistance' therefore

TABLE 1. Changes in laryngeal resistance due to various interventions

| Condition | Vagi intact | | | Lung vagi cut | | |
|---|---|---|---|---|---|---|
| | *n* | Inspiration | Expiration | *n* | Inspiration | Expiration |
| Rebreathing | 27 | $-2{\cdot}13 \pm 0{\cdot}45$** | $-9{\cdot}39 \pm 2{\cdot}30$** | 14 | $-0{\cdot}11 \pm 0{\cdot}06$ | $+19{\cdot}42 \pm 11{\cdot}72$ |
| Hypoxia | 4 | $-1{\cdot}52 \pm 0{\cdot}66$ | $-3{\cdot}55 \pm 1{\cdot}17$ | 2 | 0, $+2{\cdot}60$ | $+8{\cdot}26$, $+21{\cdot}00$ |
| Hypercapnia | 4 | $-1{\cdot}42 \pm 0{\cdot}25$ | $-6{\cdot}99 \pm 3{\cdot}64$ | 3 | $+0{\cdot}73 \pm 1{\cdot}04$ | $+4{\cdot}29 \pm 2{\cdot}57$ |
| Cyanide | 17 | — | $+59{\cdot}2 \pm 25{\cdot}3$* | 19 | — | $+58{\cdot}4 \pm 20{\cdot}2$** |
| Pneumothorax | 16 | $-1{\cdot}33 \pm 0{\cdot}34$** | $+5{\cdot}10 \pm 2{\cdot}15$** | 4 | $-0{\cdot}38 \pm 0{\cdot}30$ | $-0{\cdot}35 \pm 0{\cdot}31$ |
| Resistance | 8 | $-2{\cdot}50 \pm 1{\cdot}22$** | $-2{\cdot}81 \pm 1{\cdot}39$** | 4 | $+1{\cdot}23 \pm 2{\cdot}36$ | $-0{\cdot}60 \pm 0{\cdot}31$ |
| Tracheal closure | 4 | — | $+10{\cdot}8 \pm 4{\cdot}82$ | 5 | — | $20{\cdot}8 \pm 9{\cdot}12$ |

Values are means and standard errors, in cm $H_2O$/l. sec. *n* gives number of experiments. $^{**}P < 0{\cdot}01$, $^{*}P < 0{\cdot}05$ for mean change compared with zero effect, by Wilcoxon's signed-rank test.

varied with airflow; the latter was set at a slow value if large increases in expiratory resistance were anticipated (e.g. for cyanide injections and tracheal closure) and, in these conditions, changes in inspiratory resistance were not recorded. With slow flows, mean control expiratory resistance was $4{\cdot}89 \pm 0{\cdot}95$ cm $H_2O$/l. sec before cutting the pulmonary vagi, and $6{\cdot}46 \pm 0{\cdot}95$ after nerve section. When laryngeal dilations were anticipated, larger flow rates were used with correspondingly larger control resistances.

Table 1 summarizes the changes in inspiratory and expiratory laryngeal resistance for the various conditions studied.

*Rebreathing, hypoxia and hypercapnia*

Preliminary experiments were with a small (45 ml.) rebreathing tube; rebreathing decreased expiratory laryngeal resistance by $-1{\cdot}82 \pm 0{\cdot}96$ cm $H_2O$/l. sec (six tests in four cats) when the vagus nerves were intact, and increased expiratory resistance by $+19{\cdot}50 \pm 16{\cdot}06$ cm $H_2O$/l. sec (four tests in three cats) when both vagi had been cut in the chest.

Results of more extensive experiments with a larger rebreathing tube (83 ml.) are shown in Table 1, and confirm the preliminary study. Rebreathing significantly lowered both inspiratory and expiratory laryngeal resistances, while tidal volume (mean increase +99 %), breathing frequency (+14 %) and end-tidal carbon dioxide (+11 torr) each increased (Fig. 1). Arterial blood gas tensions were measured in five cats. $P_{a,CO_2}$ increased by 5·4 torr, and $P_{a,O_2}$ decreased by 46·0 torr (mean changes). Rebreathing through the same added dead space was tested in the cats after bilateral intrathoracic vagotomy to see if reflexes from afferent end-organs in the lungs, stimulated during the hyperpnoea, contributed to the decrease in laryngeal resistance (Fig. 1). Rebreathing now caused a smaller, not significant, decrease in inspiratory laryngeal resistance, and a mean increase in expiratory resistance (Table 1). In both instances analysis of paired values for before and after vagotomy showed that vagotomy made the laryngeal dilation due to rebreathing less pronounced or reversed it to a constriction (Wilcoxon signed-rank test, $P < 0{\cdot}01$). After vagotomy the increases in breathing frequency, tidal volume and end-tidal carbon dioxide due to rebreathing were smaller (+5 %, +78 % and +8 torr respectively).

To test whether the effects of rebreathing were due to hypoxic hyperpnoea, hypercapnic hyperpnoea or both, we made a few cats rebreathe from 5 l. bags containing 8 % oxygen in nitrogen and 8 % carbon dioxide in oxygen. Controls rebreathing pure oxygen were also done. Both hypoxia and hypercapnia caused changes in laryngeal resistance similar to those produced by asphyxial rebreathing, and the effects of vagotomy on the responses were also similar (Table 1). The numbers of experiments

were too small to allow valid statistical analysis. The four hyperoxic controls showed insignificant changes in laryngeal inspiratory resistance ($+0{\cdot}07 \pm 0{\cdot}14$ cm $H_2O$/l. sec) and expiratory resistance ($-1{\cdot}91 \pm 1{\cdot}21$ cm $H_2O$/l. sec) before vagotomy. After vagotomy the corresponding values were $+0{\cdot}83 \pm 0{\cdot}14$ and $-0{\cdot}17 \pm 1{\cdot}00$ cm $H_2$/l. sec. Blood gas analysis showed that the hypoxic cats were not hypercapnic ($P_{a,CO_2}$ decrease, $-2{\cdot}9$ torr), and the hypercapnic ones were not hypoxic ($P_{a,O_2}$ increase, $+15{\cdot}3$ torr).

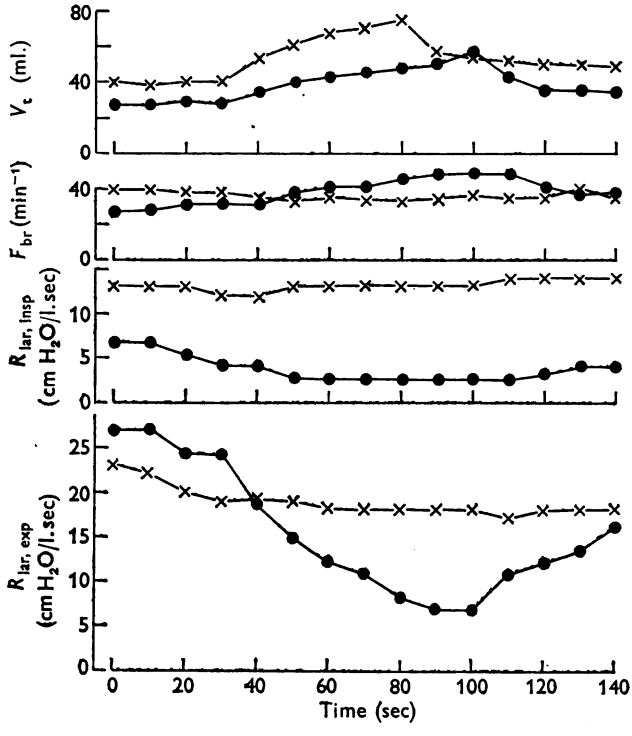


Fig. 1. Effect of rebreathing through an 83 ml. tube on tidal volume ($V_T$), frequency of breathing ($F_{BR}$), and laryngeal resistance in the inspiratory and expiratory phases ($R_{lar,\ insp}$, $R_{lar,\ exp}$). Rebreathing started at 10 sec and stopped at 100 sec. ●, before vagotomy in the chest; ×, after vagotomy in the chest. Vagotomy reduced or abolished the decreases in laryngeal resistance and the increase in frequency of breathing due to asphyxia.

### *Potassium cyanide*

The main reflex action of intra-carotid arterial injection of potassium cyanide is by stimulation of peripheral chemoreceptors (Heymans, 1955; Comroe, 1964). In our experiments intra-arterial injections of 100 $\mu$g potassium cyanide caused a short apnoea at the end-expiratory level or an

augmented breath (Glogowska, Richardson, Widdicombe & Winning, 1972), followed by deeper, faster breathing.

The results are summarized in Table 1. Cyanide increased laryngeal resistance at the beginning of the apnoea or augmented breath. During the subsequent hyperpnoea expiratory laryngeal resistance increased in eleven of seventeen tests (Fig. 2*A*).

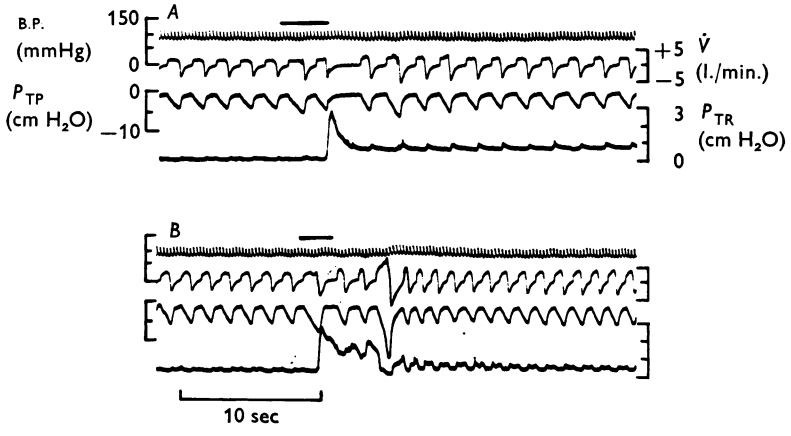


Fig. 2. Effects of 100 $\mu$g potassium cyanide injected into the right common carotid artery to stimulate the carotid body. From above down: signal, blood pressure (B.P.), lower tracheal airflow ($\dot{V}$), transpulmonary pressure ($P_{TP}$) and translaryngeal pressure ($P_{TR}$) at constant airflow through the larynx. *A*, cyanide was injected at the signal and caused an increase in laryngeal resistance, mainly in early expiration, without expiratory efforts. *B*, the same dose of cyanide was injected while the right superior thyroid artery was clamped, with a similar laryngeal response.

The increases in resistance induced by intra-arterial injections of potassium cyanide were usually larger and more consistent after bilateral intrathoracic vagotomy. This was true for twelve of nineteen tests (Fig. 3).

It was possible that the cyanide was influencing laryngeal calibre by reaching the larynx via the superior thyroid artery and having a direct action on the laryngeal muscles or causing a reflex constriction by stimulating afferent end-organs in the laryngeal mucosa (Szereda-Przestaszewska & Widdicombe, 1973*b*). We therefore repeated the injections in four tests in three cats with the superior thyroid artery occluded with a clip. In no instance was the increase in laryngeal resistance abolished, and the mean responses were as large as when the artery was patent (Fig. 2*B*).

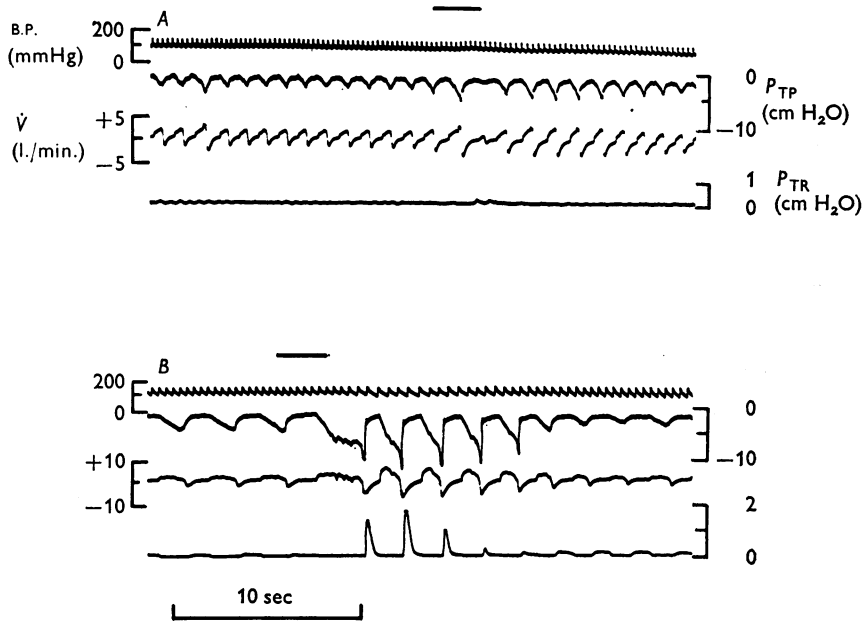


Fig. 3. Effects of 100 $\mu$g potassium cyanide injected into the right common carotid artery. Traces as in Fig. 2, but airflow and transpulmonary pressure displaced. *A*, cyanide caused a very small increase in resistance. *B*, after bilateral section of the vagus nerves in the chest the same dose of cyanide caused far larger constrictions of the larynx in early expiration.

### *Pneumothorax*

The main reflex action of pneumothorax on breathing is by stimulation of lung receptors (Sellick & Widdicombe, 1969; Mills, Sellick & Widdicombe, 1970). In our experiments induction of right-sided pneumothorax caused hyperpnoea without any prominent cardiovascular changes apart from occasional respiratory waves on the blood pressure record (Fig. 4).

In an initial series of twenty-one tests on eight cats with slow constant flow through the larynx, pneumothorax (50 ml.) increased laryngeal resistance in the expiratory phase (mean increase, $+24{\cdot}9 \pm 10{\cdot}60$ cm $H_2O$/l. sec, $P < 0{\cdot}05$). Results of a second series are given in Table 1. Here laryngeal flow was faster to allow measurement of possible decreases in resistance. The expiratory increase in resistance was confirmed, and an inspiratory dilation of the larynx established (Fig. 4*A*). The laryngeal responses depended on preserved vagal pathways. In the initial series of experiments, in seven tests on six cats after denervation of the lungs pneumothorax no longer increased expiratory resistance (mean change, $-1{\cdot}44 \pm 1{\cdot}21$ cm $H_2O$/l. sec), and in the second series there were

no significant changes in either inspiratory or expiratory resistance (Table 1, Fig. 4*B*). The increase in breathing frequency was abolished or smaller after vagotomy (Fig. 4*B*).

Larger pneumothoraces (100 ml.) not only increased expiratory laryngeal resistance when the vagi were intact but sometimes also did so after bilateral vagotomy (six of twelve experiments). These constrictions tended to be late in onset and slow in development, with pronounced cardiovascular changes, unlike those seen in cats with smaller pneumothoraces.

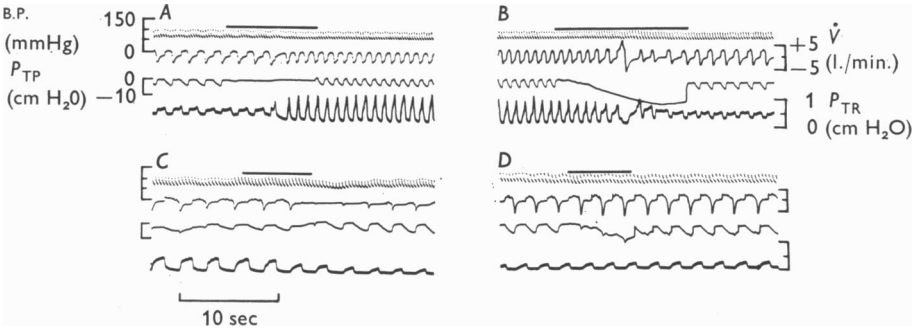


Fig. 4. Effects of 50 ml. pneumothorax. Traces as in Fig. 2. *A*, during signal 50 ml. air were injected through the pleural catheter (interruption of transpulmonary pressure signal). Expiratory constrictions and inspiratory dilations of the larynx are caused. *B*, removal of the air during signal. *C* and *D*, as *A* and *B*, but after bilateral intrathoracic vagotomy.

### *Respiratory loads*

The main reflex action on breathing of respiratory loads is via pulmonary stretch receptors, although those in respiratory muscles may also play a part (Widdicombe, 1961; Dziewanowska & Szereda-Przestaszewska, 1973). In our experiments respiratory resistances decreased respiratory frequency with an increase in transpulmonary pressure swings and a decrease in airflow. We did not see any cardiovascular changes apart from respiratory waves on the arterial blood pressure.

In preliminary experiments with a slow laryngeal flow rate, insertion of a resistance (either 5 or 2·6 cm $H_2O$/l. min) decreased expiratory laryngeal resistance in ten of fourteen tests on five cats, the mean response being slightly larger with the lower resistance. In a further eight experiments (Table 1, Fig. 5), both inspiratory and expiratory resistances decreased. Bilateral intrathoracic vagotomy did not appreciably change the dilator expiratory responses in the first series of experiments (mean decrease, $-1{\cdot}77 \pm 0{\cdot}77$ cm $H_2O$/l. sec, $P < 0{\cdot}05$); in the second series numbers were

too small to allow valid statistical analysis. After vagotomy addition of resistance no longer caused slowing of breathing.

Complete closure of the trachea increased laryngeal resistance in each of four tests on four cats (Table 1). Bilateral intrathoracic vagotomy did not alter the responses qualitatively (Table 1), but there was now no slowing of breathing.

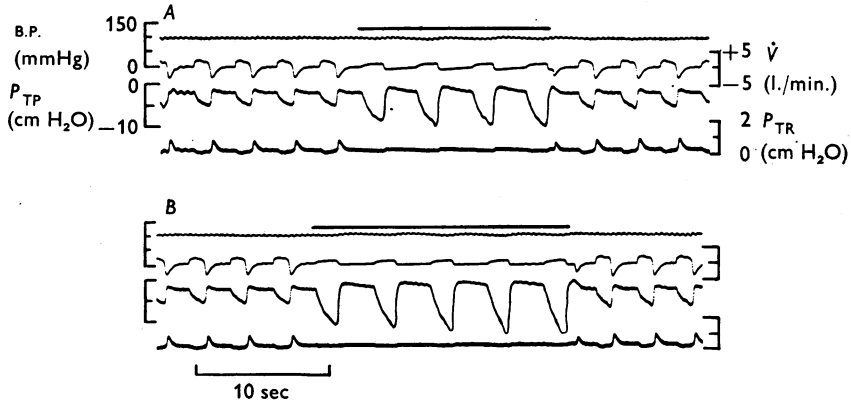


Fig. 5. Effects of adding 'viscous' resistances to the lower tracheal airway. Traces as in Fig. 2. *A*, resistance (2·6 cm $H_2O$/l. min) added to the airway causes stronger inspiratory efforts and decreases in expiratory laryngeal resistance. *B*, as *A*, but the resistance was 6 cm $H_2O$/l. min.

### *Experiments with larynx in circuit*

A few experiments were done with the cats breathing through the larynx while laryngeal resistance was measured.

Injections of cyanide (twelve tests in nine cats) increased both inspiratory ($+0{\cdot}53 \pm 0{\cdot}22$ cm $H_2O$/l. sec, $P < 0{\cdot}05$) and expiratory resistance ($+10{\cdot}42 \pm 7{\cdot}02$ cm $H_2O$/l. sec, n.s.). The mean responses were larger after cutting the intrathoracic vagi ($+0{\cdot}95 \pm 0{\cdot}42$, $P < 0{\cdot}05$, and $+60{\cdot}9 \pm 44{\cdot}25$ cm $H_2O$/l. sec, n.s., respectively).

Pneumothorax (eight tests in six cats) increased both inspiratory ($+2{\cdot}7 \pm 0{\cdot}64$ cm $H_2O$/l. sec) and expiratory resistances ($+5{\cdot}36 \pm 3{\cdot}38$ cm $H_2O$/l. sec) when the intrathoracic vagi were intact.

## DISCUSSION

### *Methods*

Measurements of laryngeal resistance when the animal is breathing through its larynx will represent the laryngeal resistive load applied to breathing at times of peak inspiratory and expiratory flow and will show

qualitative changes in 'laryngeal resistance'. However, the fact that the larynx has an alinear flow-pressure relationship means that measured resistance will depend on rate of flow (Stransky *et al.* 1973). This is both because of turbulence in the larynx and because large inspiratory flows may induce a valvular closure of the larynx if the abductor muscles do not hold it open (M. Dixon & J. G. Widdicombe, unpublished). Changes in laryngeal airflow might also reflexly change laryngeal calibre by actions on laryngeal mucosal receptors sensitive to flow rate. The various tests we have used changed the pattern of breathing. Thus measured resistance with the larynx 'in circuit' may give an imprecise indication of laryngeal calibre, and of the actions of laryngeal muscles.

With constant flow through the larynx isolated *in situ*, changes in measured resistance must be a more accurate indication of neuromuscular changes in laryngeal calibre than with breathing through the larynx. If there are clear qualitative differences between the changes in resistance measured with the larynx in circuit and with constant flow respectively, the probable explanation is that changes in translaryngeal airflow may distort the potential neuromuscular alteration in calibre.

The mean control values for laryngeal resistance show considerable variation in this study, and also compared with a previous one (Stransky *et al.* 1973). As indicated above the measured 'resistance' depended on rate of constant airflow through the larynx. They are variable from animal to animal and from time to time in an experiment, and some means are weighted by a few animals with unusually high resistances. Towards the end of an experiment resistance values were often high, but this did not change the qualitative pattern of the responses studied. Human laryngeal resistance also seems to be very variable, even in quiet breathing in a calm environment (Peslin, Hixon & Mead, 1971).

Other aspects of the methods have been discussed previously (Stranksy *et al.* 1973).

### *Asphyxia, hypercapnia and hypoxia*

Rebreathing through an added dead space decreased laryngeal resistance in both inspiratory and expiratory phases. Similar responses were produced by hypercapnia and by hypoxia. Bartlett *et al.* (1973) have also found that asphyxia (mainly hypercapnia) dilates the larynx of cats in both the inspiratory and expiratory phases. The results are in general consistent with recordings from laryngeal motor fibres and muscles.

For the inspiratory phase, asphyxia due to rebreathing increases the discharge of inspiratory laryngeal motor fibres in the cat (Glogowska, Stransky & Widdicombe, 1974). Breathing carbon dioxide rich gas mixtures increases the inspiratory-phasic discharge of recurrent laryngeal

fibres (Eyzaguirre & Taylor, 1963) and of those with inspiratory rhythm entering the posterior cricoarytenoid muscle (Suzuki & Kirchner, 1969). Electromyographic activity (inspiratory) in the cricothyroid muscle is increased (Suzuki, Kirchner & Murakami, 1970). Hypoxia increases the discharge of inspiratory units in the recurrent laryngeal nerves of cats (Eyzaguirre & Taylor, 1963).

For the expiratory phase, asphyxia abolishes the discharge of expiratory motor fibres in the cat (Glogowska *et al.* 1974). Expiratory phased fibres going to the posterior cricoarytenoid muscle have their discharge decreased or abolished by carbon dioxide (Suzuki & Kirchner, 1969), and the same is true for expiratory-phased fibres in the recurrent laryngeal nerve (Eyzaguirre & Taylor, 1963).

If inspiratory-phased fibres and muscles are abductor, and expiratory ones are adductor, these indirect results are in general consistent with our direct measurement of laryngeal resistance. In man, inhalation of carbon dioxide decreases upper airway resistance, an effect presumably involving mainly the larynx (Spann & Hyatt, 1971).

The laryngeal dilator responses with rebreathing hypercapnia and hypoxia were abolished or even reversed when the same stimuli were tested after denervating the lungs (leaving the motor innervation of the larynx intact). This suggests that the dilator responses are not a primary response to stimulation of peripheral or central chemoreceptors, but could be secondary to enhancement of activity in pulmonary stretch receptors mediating the Hering–Breuer inflation reflex. The time relationships of the laryngeal and breathing responses are consistent with this view (Fig. 1). On the other hand Dziewanowska & Szereda-Przestaszewska (1973) have shown that inspiratory vagal motor fibres (presumably going to the larynx) increase their discharge during hypoxia in vagotomized rabbits, and Glogowska *et al.* (1974) have found the same with cats. Species or experimental differences could explain this discrepancy.

The action of the Hering–Breuer inflation reflex on laryngeal calibre is equivocal. Some studies of laryngeal motor fibre discharge indicate that lung inflation inhibits inspiratory (abductor) discharge (Green & Neil, 1955; Fukuda, Sazaki & Kirchner, 1973; Eyzaguirre & Taylor, 1963); other work suggests that the Hering–Breuer inflation reflex dilates the larynx in experimental animals (Bianconi, Cangiano & Raschi, 1967; Bartlett *et al.* 1973) and in man (Stanescu, Pattijn, Clement & van der Woestijne, 1972; Hyatt & Wilcox, 1963; Blide, Kerr & Spicer, 1964; Spann & Hyatt, 1971). Our results are best explained by a reflex laryngeal dilator influence from inflation of the lungs in our experimental conditions. The fact that laryngeal resistance was generally greater after denervation of the lungs is consistent with this hypothesis. In the absence of this

secondary dilator influence asphyxia, hypercapnia and hypoxia each caused no change or an increase in laryngeal resistance.

### *Potassium cyanide*

In view of the results with asphyxia we were surprised to observe that intra-carotid arterial injections of cyanide caused consistent increases in laryngeal resistance, since these results seemed to be opposed to those with hypoxia. There are three possible explanations. (1) The vigorous transient stimulation of inspiration by cyanide may be associated with different expiratory laryngeal responses compared with those due to the more gradual stimulation of breathing by hypoxia. In this respect we have consistently seen an expiratory increase in laryngeal resistance after spontaneous deep augmented breaths, which may be analogous to the cyanide-induced deep breaths (Glogowska *et al.* 1972). (2) Cyanide may stimulate afferent endings in the carotid sinus – body region other than peripheral chemoreceptors, such as vascular nociceptive endings. (3) The cyanide may have acted on central nervous structures (Brodie & Borison, 1956), although the respiratory and cardiovascular responses are characteristic of peripheral chemoreceptor stimulation and the doses injected into the common carotid artery were smaller than those used by other authors (Neil & O'Regan, 1971; Comroe & Mortimer, 1964; Eterradossi, Benchetrit, Idelman, Poupot & Lemarchands, 1967). We cannot say which of these possibilities applies, but it is worth mentioning that Daly (1972) found rather similar qualitative differences in the reflex cardiac responses to cyanide injected locally into the circulation in the carotid body of the dog compared with the responses to local hypoxia.

The effects of pulmonary denervation on the laryngeal responses to cyanide are in general consistent with the results with asphyxia, namely that intact pulmonary innervation tends to have a dilator influence on the larynx during chemical stimulation of breathing.

In the cat with intact vagi, intravenous injections of cyanide increase the discharge of both inspiratory and expiratory laryngeal motor fibres (Glogowska *et al.* 1974).

### *Pneumothorax*

Pneumothorax (50 ml.) consistently caused expiratory laryngeal constriction when the pulmonary vagi were intact. This intervention stimulates lung irritant receptors (Sellick & Widdicombe, 1969) which reflexly constrict the larynx in expiration (Stransky *et al.* 1973) and inhibits pulmonary stretch receptors the excitation of which may dilate the larynx (see above). The fact that the laryngeal response to pneumothorax was abolished by pulmonary denervation suggests that one or both of

these reflexes were involved. Changes in blood gas tensions due to hyperventilation could also be a factor when the vagi were intact (Binet, Strumza & Leobardy, 1948; Simmons & Hemingway, 1957; Hemingway & Simmons, 1958), since the hyperventilation also depends mainly on a reflex from the lungs.

Inspiratory laryngeal resistance was decreased by pneumothorax in cats with intact vagi, when there was constant flow through the larynx, but this was not confirmed by studies with the cat breathing through the larynx. There could be an increase in inspiratory dilator neuromuscular tone, but the measured inspiratory resistance with the larynx in circuit may also increase, presumably because of extra turbulence due to the larger airflow. The results are consistent with the observation that in the cat with intact vagi a 50 ml. pneumothorax increases the discharge of both inspiratory and expiratory motor fibres; the former response is greatly reduced by vagotomy (Glogowska *et al.* 1974). With very large pneumothoraces (100 ml.) reflexes from the chest wall or haemodynamic changes could play a part in the laryngeal constrictions that occurred with the pulmonary vagi intact or cut (see below).

*Respiratory loads*

Imposition of a 'viscous' resistive load to the airway dilated the larynx in the inspiratory and expiratory phases. Similar loads have been shown to increase the discharge of inspiratory units in the cricothyroid and posterior cricoarytenoid muscles (Suzuki *et al.* 1970; Fukuda & Kirchner, 1972; Fukuda *et al.* 1973), and to dilate the larynx of man (Rattenborg, 1961), although negative results have also been described for man (Spann & Hyatt, 1971). Recordings from inspiratory motor fibres (in the vagotomized rabbit) show an increase in discharge on resistance breathing (Dziewanowska & Szereda-Przestaszewska, 1974) and in the cat with intact or cut vagi (Glogowska *et al.* 1974), and expiratory laryngeal fibres cease their discharge under similar conditions (Glogowska *et al.* 1974).

Since in our experiments the dilations were present after denervating the lungs they cannot be mainly due to a changed pattern of discharge from lung mechanoreceptors, a conclusion which supports the view of Dziewanowska & Szereda-Przestaszewska (1973).

With a complete tracheal closure there were increases in resistance. These were similar to those seen with large pneumothoraces, and both were present after vagotomy in the chest. Their cause is not known, but they could be related to reflexes set up by the very vigorous forces applied to the thoracic wall in both conditions.

Our results show that laryngeal calibre is determined by the interaction of a number of nervous influences. With the lung nerves intact hyperpnoea

exerts a reflex dilator effect which may outweigh primary constrictor mechanisms, and pneumothorax causes expiratory constrictions and inspiratory dilatations by a vagal reflex. With the lungs denervated, the larynx is constricted in expiration by tracheal closure, large pneumothorax and injections of cyanide acting on the carotid body region; it is dilated in inspiration and expiration by addition of a resistance in breathing whether the vagi are intact or cut.

In general these results are consistent with recordings from expiratory laryngeal motor fibres, but less consistent with studies on inspiratory laryngeal fibres. This problem is considered further elsewhere (Glogowska *et al.* 1974).

We have previously discussed possible physiological advantages of changes in laryngeal calibre. In hypercapnia due to asphyxia, hypoxia, or hypercapnia, the lowered laryngeal resistance should decrease the total load on breathing and shorten the duration of expiration (Gautier, Remmers & Bartlett, 1973), and the same is true of the responses to an added external resistance. With pneumothorax the expiratory increase in resistance could tend to maintain or augment functional residual capacity and possibly promote gas exchange (Nye, 1970). The results with cyanide and tracheal closure are more difficult to explain by teleological arguments.

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