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REFLEX EFFECTS OF LARYNGEAL IRRITATION ON THE PATTERN OF BREATHING AND TOTAL LUNG RESISTANCE

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SUMMARY

1. The reflex responses to chemical and mechanical irritation of the laryngeal mucosa have been studied by applying stimuli to the open larynx of tracheostomized cats while monitoring ventilatory and circulatory variables. The responses were studied before and after vagotomy and before and after denervation of the larynx by transection of the superior and recurrent laryngeal nerves.

2. The immediate response to laryngeal irritation was not consistent. The most frequent responses were coughing, and slowing and deepening of breathing without coughing. Less common were expiratory apnoea and sustained, simultaneous inspiratory and expiratory activity.

3. A consistent late change in the pattern of breathing occurred. Slower, deeper breathing with increased total lung resistance (bronchoconstriction) was seen after the immediate response abated.

4. The slowing of breathing was due to prolongation of both the time for inspiration and the time for expiration. The rate of increase in phrenic nerve activity was also slowed.

5. Vagotomy did not alter qualitatively the reflex changes in the pattern of breathing, although bronchoconstriction no longer occurred.

6. The responses were abolished by denervation of the larynx.

INTRODUCTION

Since Paul Bert (1867, 1869) observed that chloroform introduced into the lungs through a subglottal cannula in the rabbit had different effects from those seen when it was introduced through the nose and mouth, stimulation of the upper respiratory tract has been known to have impor-

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tant reflex actions on the pattern of breathing. Kratschmer (1870) showed that chemical, mechanical or thermal irritation of the upper respiratory tract caused slowing of breathing or an expiratory arrest. He concluded that this reflex depended upon the trigeminal nerve. This was confirmed by Beyer (1901) and again by Magne, Mayer & Plantefol (1925) who showed that the inhibitory reflex caused by insufflation of irritant gas into upper tract disappeared after section of the trigeminal nerve. François Franck (1876), however, noted the usual inhibitory reflex after application of weak ammonia solution to the laryngeal mucosa, even when precautions were taken to prevent diffusion of ammonia vapour to other sites. He concluded that the superior laryngeal nerve may have an important role in the defensive reflexes of the respiratory tract. Investigators have since recognized that the laryngeal mucosa is richly innervated and is an exquisitely sensitive site for eliciting the cough reflex by mechanical stimulation (Ivanço & Korpaš, 1954; Widdicombe, 1954; Tomori, 1962, 1965; Tomori, Javorka & Stransky, 1972). Nadel & Widdicombe (1962) and Tomori & Widdicombe (1969) detailed the effects of mechanical irritation of the larynx as cough, bronchoconstriction and a rise in blood pressure. They did not report reflex changes in the pattern of breathing apart from coughing. In most other reports of laryngeal reflexes the reflexes have been elicited by electrical stimulation of the superior laryngeal nerve (Aldaya, 1936; Hammouda & Wilson, 1938; Gesell & Hamilton, 1941; Larrabee & Hodes, 1948). The reported actions are variable and include expiratory apnoea, slowing of breathing with either increase or decrease in inspiratory duration, and either increase or decrease of tidal volume. There is no mention of coughing. This variety of response is perhaps not surprising with electrical stimulation of a mixed afferent nerve.

Thus in the early literature the stimulus in the upper respiratory tract was usually not very precisely located, and in this and later literature the resultant changes in respiratory pattern vary greatly, possibly because more than one respiratory reflex can be elicited from the laryngeal mucosa. Therefore we have tried to investigate more precisely the reflex changes in the pattern of breathing and in total lung resistance elicited by mechanical and chemical irritation of the larynx. This has been attempted both by more accurate localization and control of intensity of chemical stimuli and by more sophisticated methods of assessing changes in the pattern of breathing than those available to most earlier workers.

METHODS

Eleven adult cats weighing from 1·9 to 4·0 kg were used. We induced anaesthesia with I.P. sodium pentobarbitone (32 mg/kg), and maintained it with injections through a femoral venous catheter, checking the anaesthetic level frequently.

Tracheal cannulae were inserted just below the cricoid cartilage, taking care to identify and spare the recurrent laryngeal nerves. The larynx was opened in the ventral mid line and packed with a saline-soaked cotton wool pledget until haemostasis was achieved. Blood pressure was recorded from the left femoral artery through a polyethylene catheter by a capacitance manometer (Consolidated Electrodynamics Corp.). Transpulmonary pressure was measured from an air-filled polyethylene cannula tied into a lower intercostal space in the right anterior axillary line and from a wide-bore needle inserted through a rubber tube connexion to the tracheal cannula, using a differential capacitance manometer (Hilger), range ± 25 cm H_2O. Tidal volume was measured from a Fleisch pneumotachograph head connected to an inductance differential pressure recorder and integrator (Godart). Tidal CO_2 % was measured with a Beckman Spinco LBI infra-red analyser, sampling from the tracheal cannula at 300–400 ml./min. We measured rectal temperature with a mercury thermometer, and we checked the arterial blood gas tensions of heparinized blood from the arterial catheter with Radiometer B.M.S. 3 blood gas electrodes.

The right phrenic nerve was transected low in the neck, stripped of adventitia, and placed in a paraffin-filled trough. Platinum electrodes and conventional amplifiers (Tektronix 122) were used to obtain multifibre activity. The resulting signal was electrically rectified and integrated. The integrator circuit allowed the rectified voltage to charge a condenser which leaked to earth through a resistance so that the integrated record returned to zero in between phrenic bursts. The time constant of the circuit was 50 msec. In five cats an expiratory electromyogram (e.m.g.) was obtained via a platinum concentric needle electrode inserted into the rectus abdominis muscle. The signal was amplified (Tektronix 122) and recorded.

Total lung resistance and compliance were measured by the subtractor method of Mead & Whittenberger (1953) as modified by Nadel & Widdicombe (1962). This involves displaying the transpulmonary pressure required to overcome resistance and tracheal airflow on the two axes of a storage oscilloscope. The slope of the resulting 'loop' or curve is proportional to total lung resistance.

Blood pressure, airflow, tidal volume, transpulmonary pressure and phrenic and abdominal e.m.g.s were recorded on a 7-channel FM tape recorder (Ampex SP 300). The seventh channel was used for a voice signal. This allowed re-evaluation of total lung resistance and compliance and other variables after the experiment had been completed. During each experiment tracheal CO_2 %, blood pressure, tidal volume, phrenic activity and phrenic integral were recorded on ultra-violet sensitive paper by a Honeywell UV-31 recorder.

The mechanical stimuli studied included repetitive touching of the laryngeal mucosa with a nylon filament both above and below the vocal cords and introduction of a saline-soaked cotton wool pledget into the larynx. Chemical stimuli were injected from a syringe through a polyethylene catheter the tip of which was positioned in the laryngeal lumen. They included 10–50 ml. of ammonia vapour in air (molecular concentration 1 part in 200 to 1 part in 10^6) and 25 ml. of cigarette smoke drawn 'undiluted' into a syringe from a filter-tipped cigarette. Other vapours included 100 P.P.M. SO_2 and air cooled by passage through an ice and salt mixture in a conical flask. Injection of warm air was used as a control to test the effects of mechanical distortion of the mucosa by the stream of the gas.

The positions of the laryngeal catheter and of the tracheal cannula were such that inhalation of irritant gases and aerosols into the lungs would be absent or minimal; the fact that respiratory responses to laryngeal irritants were abolished by denervation of the larynx (see Results), although any lung inhalation would be unchanged, confirms that the irritants were effectively excluded from the lungs. Other chemical stimuli included solutions (in 0·9 % sodium chloride) of phenyl diguanide (1 mg/ml.),

veratrine (1 mg/ml.) and veratridine (100 mg/ml.). Two or three drops of these solutions were applied to the laryngeal mucosa after a control application of the same amount of saline. These stimuli were studied in spontaneously breathing cats, before and after vagotomy (four cats) and before and after denervation of the larynx by transection of the recurrent and superior laryngeal nerves. In five cats the stimuli were also studied after paralysis induced with 40 mg gallamine triethiodide intravenously.

Analysis of data

For five breaths before each intervention tidal volume, total lung resistance, blood pressure, pulse rate, time for inspiration (T_{insp}), time for expiration (T_{exp}), phrenic amplitude, and 'initial phrenic slope' were measured and averaged. The phrenic functions were obtained from the record of the integral of phrenic activity. T_{insp} is defined as the time from the first positive deflexion to the mid-point of exponential decay. T_{exp} is defined as the time from the end of T_{insp} to the next positive deflexion. Phrenic amplitude is the maximum height of the integrated phrenic. 'Initial phrenic slope' (hereafter called phrenic slope) is the ratio of half the peak phrenic amplitude to the time required to reach that point. The same measurements were made over the first five breaths after a near-stable pattern of breathing was noted after each laryngeal stimulus. As the absolute values of the phrenic functions (peak phrenic amplitude and phrenic slope) are arbitrary, depending on the setting of the electrical integrator, changes are expressed in percentages of the control values.

The significance of the differences between responses to irritant stimulation and responses to appropriate controls (air or saline) were computed by a paired comparison analysis, using Student's t test.

RESULTS

Immediate respiratory response

The immediate response was not consistent. Different responses to the same agent were seen, not only in different cats, but also in the same cat at different times. As expected, coughing (defined here as a swing in transpulmonary pressure to a positive value or an increase in expiratory muscle e.m.g., or both) was frequently seen, as in Fig. 1 where the stimulus is 1:200 ammonia vapour. Coughing more often occurred after mechanical (nylon filament and saline pledget) than chemical (ammonia, phenyl diguanide, cigarette smoke, veratrine) stimulation. Another common pattern of response was prompt slowing of breathing, without coughing as in Fig. 2, where the stimulus is again 1:200 ammonia vapour. This pattern was more often seen after chemical stimulation, and was almost the invariable response after insufflation of weak ammonia vapour ($< 1:1000$), which only once caused coughing. Mechanical stimulation caused coughing in fifteen and slowing without coughing in five of twenty trials. Chemical stimulation caused coughing in seven and slowing without coughing in twenty-two of twenty-nine trials.

Other patterns, seen less often, included sustained expiratory apnoea (Fig. 3) and sustained simultaneous discharge of both the phrenic nerve and the expiratory muscle (Fig. 4). Intense bursts of phrenic activity sometimes

occurred at a rate of about 10 Hz with little or no discharge between the bursts (see Fig. 4). Bursts of such activity were generally followed by expiratory efforts.

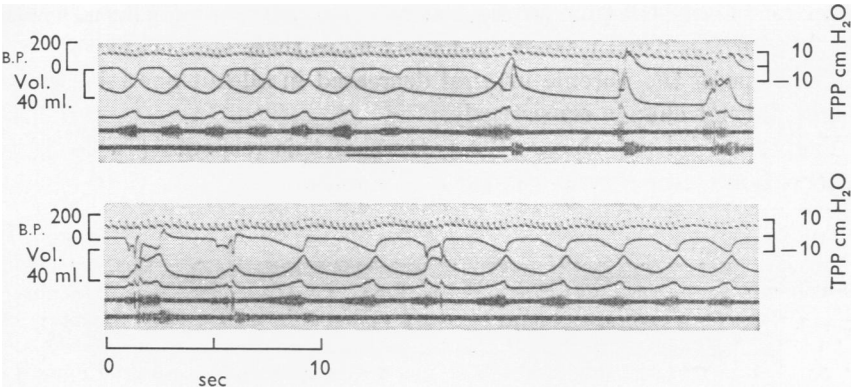

Fig. 1. Coughing caused by insufflation of 20 ml. 1:200 ammonia vapour in air into the larynx. Note positive deflexion of transpulmonary pressure (TPP) coinciding with activity in abdominal electromyogram. From above downwards: blood pressure, transpulmonary pressure, tidal volume, phrenic integral, phrenic activity, abdominal electromyogram, and signal. Continuous record.

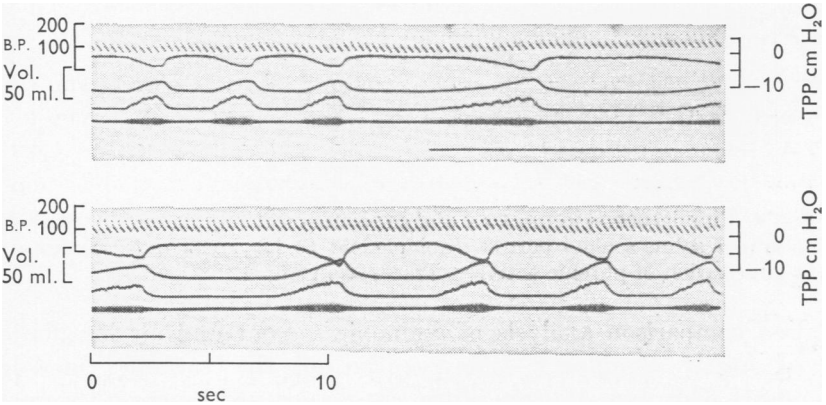

Fig. 2. Slowing of breathing without coughing caused by insufflation of 20 ml. 1:200 ammonia vapour in air. Upper and lower records continuous. From above downward: blood pressure, transpulmonary pressure, tidal volume, phrenic integral, phrenic activity and signal.

Late respiratory response

After the initial reaction, lasting from 10 to 35 sec, the pattern of breathing changed to one of slower deeper breaths. The magnitude of this change appeared to depend on the intensity of the stimulus, but qualita-

tively the response was remarkably consistent. Slowing of the respiratory rate of up to 65% was seen after chemical or mechanical irritation in all but two of eighty-three trials. The slowing of breathing was due to prolongation of both the time for inspiration (T_{insp}) and the time for expiration (T_{exp}), with T_{exp} usually being prolonged more than T_{insp} (Table 1).

The slope of the phrenic integral decreased in all but one trial but the height did not change consistently.

Vagotomy did not change the pattern of this response (Table 2), but denervation of the larynx ablated it (Table 3).

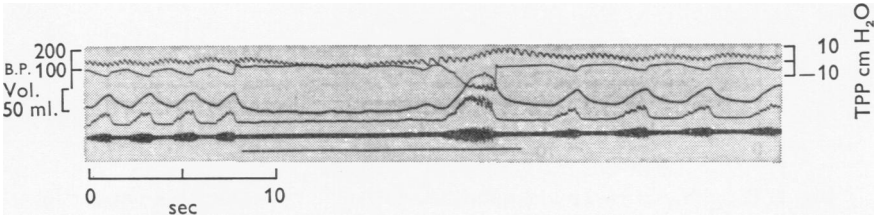

Fig. 3. Expiratory apnoea caused by application of saline-soaked cotton-wool pledget to laryngeal mucosa. Note sustained positive deflexion of transpulmonary pressure trace, shift in F.R.C. in tidal volume trace, and absence of phrenic activity. Traces as in Fig. 2.

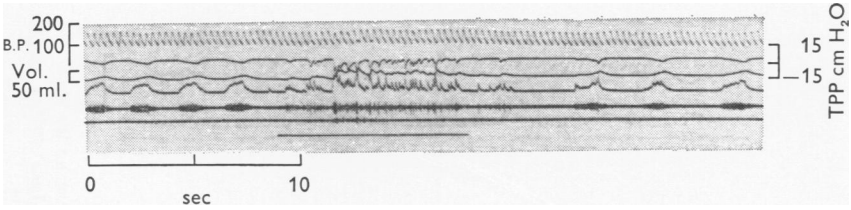

Fig. 4. Simultaneous inspiratory and expiratory activity caused by application of saline-soaked cotton wool pledget to laryngeal mucosa. Note fragmentation of phrenic activity. Traces as in Fig. 1.

Paired comparison analysis of ammonia vapour and air insufflations showed highly significant differences in all the variables measured ($P < 0{\cdot}01$). This was also true of the changes caused by cigarette smoke. Although all the changes due to phenyl diguanide application were greater than those seen after saline, only the change in respiratory rate was significant ($P < 0{\cdot}05$). Veratrine and veratridine administration caused obvious profound reflex effects (Fig. 5) although the drugs were not given often enough to justify statistical analysis. Neither sulphur dioxide (five cats) nor cold air (four cats) affected any of the variables measured, and we have excluded these results from those described above.

TABLE 1. Changes with laryngeal irritation, all nerves intact

Stimulus	No. of cats	No. of trials	Frequency	T_{insp}	T_{exp}	Phrenic slope	Tidal volume
Nylon filament	9	15	$-27{\cdot}5^{*} \pm 3{\cdot}9$	$+19{\cdot}7^{*} \pm 4{\cdot}9$	$+60{\cdot}1^{*} \pm 12{\cdot}6$	$-31{\cdot}2^{*} \pm 4{\cdot}6$	$+39{\cdot}1^{*} \pm 12{\cdot}6$
Saline pledget	9	16	$-34{\cdot}3^{*} \pm 2{\cdot}3$	$+33{\cdot}1^{*} \pm 5{\cdot}6$	$+61{\cdot}3^{*} \pm 8{\cdot}7$	$-44{\cdot}6^{*} \pm 2{\cdot}9$	$+41{\cdot}2^{*} \pm 6{\cdot}3$
Ammonia (all concentrations)	10	23	$-33{\cdot}3^{*} \pm 4{\cdot}5$	$+52{\cdot}4^{*} \pm 12{\cdot}1$	$+80{\cdot}9^{*} \pm 14{\cdot}3$	$-37{\cdot}6^{*} \pm 4{\cdot}7$	$+39{\cdot}4^{*} \pm 7{\cdot}3$
Cigarette smoke	3	6	$-48{\cdot}6^{*} \pm 7{\cdot}3$	$+65{\cdot}0^{**} \pm 24{\cdot}2$	$+190{\cdot}8 \pm 92{\cdot}6$	$-61{\cdot}5^{*} \pm 4{\cdot}4$	$+29{\cdot}4^{*} \pm 6{\cdot}5$
Air	10	20	$-3{\cdot}8 \pm 2{\cdot}1$	$+2{\cdot}9 \pm 1{\cdot}5$	$+6{\cdot}7 \pm 3{\cdot}3$	$-2{\cdot}1 \pm 2{\cdot}8$	$+0{\cdot}1 \pm 1{\cdot}5$
P.D.G. drops	7	9	$-18{\cdot}2^{*} \pm 5{\cdot}1$	$+24{\cdot}4^{**} \pm 10{\cdot}5$	$+33{\cdot}3^{**} \pm 13{\cdot}8$	$-18{\cdot}3^{**} \pm 6{\cdot}5$	$+21{\cdot}3 \pm 12{\cdot}7$
Saline drops	7	9	$-8{\cdot}9^{*} \pm 2{\cdot}3$	$+7{\cdot}6^{**} \pm 2{\cdot}5$	$+10{\cdot}9^{*} \pm 2{\cdot}9$	$-12{\cdot}3 \pm 5{\cdot}5$	$+3{\cdot}8 \pm 3{\cdot}2$

Values are mean percentage changes and S.E.
* $P < 0{\cdot}01$, ** $P < 0{\cdot}05$ for comparison of mean change with value of control before intervention.

TABLE 2. Mean changes with laryngeal irritation following vagotomy

Stimulus	No. of cats	No. of trials	Frequency	T_{insp}	T_{exp}	Phrenic slope
Nylon filament	4	4	$-23{\cdot}5 \pm 8{\cdot}9$	$+2{\cdot}8 \pm 6{\cdot}8$	$+31{\cdot}3^{**} \pm 6{\cdot}2$	$-21{\cdot}5 \pm 8{\cdot}0$
Saline pledget	4	4	$-40{\cdot}3^{*} \pm 3{\cdot}5$	$+18{\cdot}2 \pm 14{\cdot}0$	$+89{\cdot}0^{*} \pm 10{\cdot}40$	$-31{\cdot}3^{*} \pm 3{\cdot}3$
Ammonia (all concentrations)	4	4	$-41{\cdot}0^{**} \pm 8{\cdot}1$	$+38{\cdot}8 \pm 20{\cdot}8$	$+113{\cdot}0 \pm 47{\cdot}6$	$-25{\cdot}8^{*} \pm 3{\cdot}6$

Values are mean percentage changes and S.E.
* $P < 0{\cdot}01$, ** $P < 0{\cdot}05$ for comparison of mean change with value of control before intervention.

TABLE 3. Mean changes with laryngeal irritation, laryngeal nerves cut

Stimulus	No. of cats	No. of trials	Frequency	T_{insp}	T_{exp}	Phrenic slope	Tidal volume
Nylon filament	4	4	$+1{\cdot}0 \pm 1{\cdot}5$	$-2{\cdot}3 \pm 1{\cdot}4$	$-0{\cdot}3 \pm 1{\cdot}4$	$+5{\cdot}3 \pm 2{\cdot}9$	$+1{\cdot}0 \pm 1{\cdot}0$
Ammonia (all concentrations)	5	5	$-1{\cdot}8 \pm 2{\cdot}1$	$-0{\cdot}4 \pm 2{\cdot}3$	$+9{\cdot}6 \pm 7{\cdot}8$	$0{\cdot}0 \pm 4{\cdot}9$	$+4{\cdot}0 \pm 3{\cdot}0$
Saline pledget	6	6	$-0{\cdot}7 \pm 2{\cdot}2$	$+2{\cdot}2 \pm 1{\cdot}0$	$+2{\cdot}3 \pm 1{\cdot}2$	$-4{\cdot}0 \pm 1{\cdot}8$	$-2{\cdot}7 \pm 2{\cdot}9$
Cigarette smoke	2	2	$+8{\cdot}0 \pm 7{\cdot}5$	$-7{\cdot}5 \pm 6{\cdot}5$	$-1{\cdot}5 \pm 0{\cdot}5$	$+2{\cdot}5 \pm 0{\cdot}5$	$+0{\cdot}5 \pm 0{\cdot}5$
P.D.G.	4	4	$+2{\cdot}0 \pm 0{\cdot}6$	$-1{\cdot}7 \pm 1{\cdot}3$	$-2{\cdot}7 \pm 2{\cdot}4$	$+4{\cdot}3 \pm 6{\cdot}5$	$+2{\cdot}0 \pm 0{\cdot}6$

Values are mean percentage changes and S.E.
None of the changes is significant ($P < 0{\cdot}05$).

Effects on total lung resistance

In non-paralysed animals a striking increase in total lung resistance was seen after mechanical irritation of the larynx, as has been reported (Sandmann, 1890; Nadel & Widdicombe, 1962; Tomori & Widdicombe, 1969). The mean increase after nylon filament stimulation was 45 % ± 12 (S.E.) and after saline pledget 174 % ± 71. Increases of the same magnitude were seen after chemical stimulation. The mean increase after ammonia

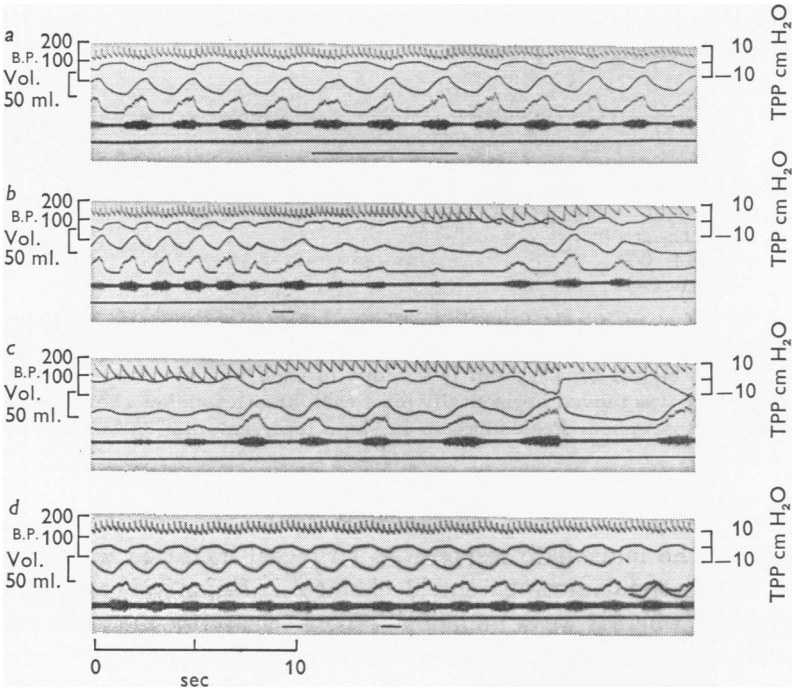

Fig. 5. Veratrine applied to larynx: *a* Saline applied to laryngeal mucosa; *b* and *c* (continuous), two drops of veratrine, 1 mg/ml., are applied at the signal. Note bradycardia preceding change in blood pressure; *d*, veratrine applied after denervation of larynx.

was 122 % ± 43, after cigarette smoke 191 %, and after phenyl diguanide 178 %. Because coughing and deep breathing alter lung mechanics, we confirmed these findings in five paralysed, artificially ventilated cats. The percentage increases noted correlate closely with those seen in the spontaneously breathing cats (Fig. 6).

Cardiovascular effects

In spontaneously breathing cats, changes in the pattern of breathing could have caused the observed changes in blood pressure. No consistent effect was noted in paralysed cats. Pulse rate was usually unchanged, but slowing of the pulse was sometimes seen after intense laryngeal irritation (Fig. 5*b* and *c*). This occurred twice after saline pledget stimulations, twice after 1:200 ammonia insufflation and after each of the single applications of veratrine and veratridine. The change in pulse rate did not appear to be due to a reflex response to a rise in blood pressure, as slowing of the pulse preceded any changes in pressure.

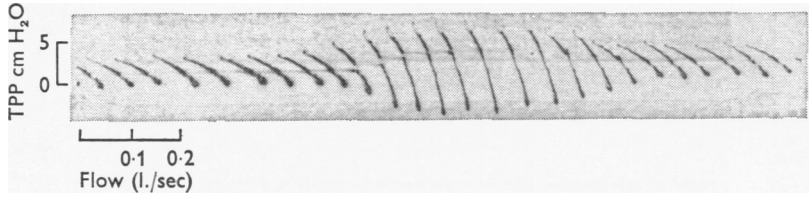

Fig. 6. Effect of intralaryngeal insufflation of ammonia vapour (1:1000) on total lung resistance of paralysed, artificially ventilated cat. Ammonia applied at eighth breath from left. Slope of each line represents T.L.R. Closed loop was moved horizontally after each breath to allow the tracings to be photographed. Peak increase in slope represents 430% increase in T.L.R.

DISCUSSION

Although the immediate response to laryngeal irritation was not consistent, certain trends are apparent. Mechanical irritation was often followed by coughing, whereas weak ammonia vapour, cigarette smoke, or phenyl diguanide more often produced prompt slowing and deepening of breathing without coughing. Coughing may result from the stimulation of a different set of receptors, or it may be the effect of a different central response to more intense stimulation of the same population of receptors, as is suggested by the effects of ammonia vapour. Weak ammonia vapour (less than one part in 10^4) caused coughing only in one of ten trials, whereas strong ammonia vapour caused coughing in four of eight trials. We are studying the response of single afferent fibres in the superior laryngeal nerve in order to determine whether two or more populations of mucosal receptors respond to the stimuli we have used. Phenyl diguanide, which Paintal (1955) has shown to stimulate juxta-pulmonary capillary receptors (J-receptors) more than other intra-pulmonary receptors when given intravenously, had significantly more effect than saline only in slowing the respiratory frequency. A greater number of trials could show significance

in the other variables as well but, even if this were the case, the response to topical phenyl diguanide is not qualitatively different from that seen with other weak chemical irritants.

The other patterns of immediate response, apnoea and sustained simultaneous inspiratory and expiratory activity, were seen less frequently. The pattern of phrenic discharge in the latter response (Fig. 3) is similar to that seen in the 'aspiration reflex' (Ivanco & Korpas, 1954; Ivanco, Korpas & Tomori, 1956; Nail, Sterling & Widdicombe, 1972) where bursts of activity at a frequency of 8–12 Hz are seen in the phrenic nerve. Unlike the aspiration reflex, however, expiratory activity and bronchoconstriction accompany this activity.

The late response of slowing and deepening of breathing was seen with remarkable consistency. This is in contrast to the effect of insufflation of ammonia vapour into the trachea and lungs, which causes an increase in frequency with a decrease in tidal volume (Banister, Fegler & Hebb, 1950). The threshold of the response appears to differ, as reflex responses were seen with as little as 1 part per million of ammonia vapour in the larynx, whereas we noted no response to intratracheal insufflation until 1 part in 100 was used in the single cat in which we made careful comparison.

The time for inspiration, the time for expiration and the slope of the integral of phrenic activity all change after laryngeal irritation. The drop in the rate of increase of phrenic activity (decrease in phrenic slope) indicates that the slowing of breathing is not due to a change in the central response to stretch receptor activity, since the latter does not influence the rate of build-up of inspiratory discharge but only the duration before 'cut-off' (Larrabee & Knowlton, 1946; Clark & von Euler, 1972) and, in any case, the changes in these variables were still seen after vagotomy.

The finding of bronchoconstriction (increase in total lung resistance) after mechanical or chemical irritation of the larynx may help to resolve a controversy over the bronchomotor response to nasal irritation. Dixon & Brodie (1903) and Ellis (1938) both reported that chemical irritation of the nasal mucosa caused bronchoconstriction. Nadel & Widdicombe (1962) found no change in total lung resistance after mechanical irritation of the nose, and noted that the earlier investigators had used strong chemical irritants and had not localized the stimulus carefully. They speculated that chemical irritation of the larynx might have been responsible for the earlier findings. Tomori & Widdicombe (1969) reported that irritation of the nose caused bronchodilation. This study provides direct evidence that chemical irritation of the larynx does indeed cause bronchoconstriction.

Previous workers (Nadel & Widdicombe, 1962) have noted an increase in blood pressure after mechanical laryngeal irritation. This was most pronounced in decerebrate cats and was less striking in cats with chloralose-

urethane anaesthesia. The difference in our observations may therefore be due to differences in anaesthetic. The change in pulse rate after intense laryngeal irritation (Fig. 5) has been noted by earlier workers (Franck, 1876).

Recent reports of slowing of breathing in man and cats after exposure to CS gas (Cotes, Evans, Johnson, Martin & Reed, 1972; Brimblecombe, Green & Muir, 1972) might be explained by reflexes arising from irritation of the laryngeal mucosa, although the reflex response to nasal irritation is an equally plausible explanation (Angell James & Daly, 1972; Kratchmer, 1870). We have studied the effects of 2×10^{-4} M-CS in saline applied to the laryngeal mucosa of one cat, and noted a dramatic response similar to that seen after veratrine. We will carry out further studies of this action of CS on the larynx.

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