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THE EFFECT OF TRANSIENT STIMULATION OF LUNG IRRITANT RECEPTORS ON THE PATTERN OF BREATHING IN RABBITS

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SUMMARY

1. 100 ms pulses of inflation and deflation were applied to the lungs of anaesthetized rabbits before and during inactivation of pulmonary stretch receptors.

2. Pulses of either sign given in inspiration often produced augmented breaths, whether or not stretch receptors were inactivated. Inflation pulses were more effective than deflation pulses.

3. After an augmented breath it was impossible to produce another for at least 1 min (refractoriness).

4. Pulses of deflation always shortened expiration. Pulses of inflation early in expiration shortened expiration. Later in expiration they lengthened expiration when stretch receptors were active and shortened expiration when stretch receptors were blocked. No refractoriness was observed for the effects on expiratory time.

5. Pulses in paralysed animals caused a burst of phrenic activity of fixed duration, usually with brief latency. There was no refractoriness.

6. We suggest that the duration of inspiration is governed by the activity of pulmonary stretch receptors, except during an augmented breath, and that the duration of expiration is governed by a balance of stretch and irritant receptor activity.

INTRODUCTION

Augmented breaths, whether spontaneous or triggered by inflation of the lungs, have been ascribed at least in part to the excitation of lung receptors (Reynolds, 1962), probably 'irritant' receptors (Sellick & Widdicombe, 1970; Glogowska, Richardson, Widdicombe & Winning, 1972). However, in cats histamine, which stimulates irritant receptors when given either intravenously or as an aerosol, accelerates breathing (Karczewski & Widdicombe, 1969) with a decrease in inspiratory (T_I) and expiratory durations (T_E) (Widdicombe & Winning, 1976), which suggests that irritant receptors shorten both T_I and T_E. Knox (1973) reported a decreased T_E due to pulses of deflation

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given during expiration; he ascribed this effect to the excitation of irritant receptors, a conclusion in agreement with the decrease of T_E produced by histamine. However, part of this response to deflation could be due to decreased stretch receptor activity (Knox, 1973; Bartoli, Bystryzcka, Guz, Jain, Noble & Trenchard, 1973).

Since the majority of lung stretch receptors and all their reflex effects can be blocked by inhalation of SO_2 (Callanan, Dixon & Widdicombe, 1975; Davies, 1976), we re-investigated the responses to irritant receptor stimulation by pressure pulses in intact and SO_2-treated rabbits.

METHODS

We used seven New Zealand White rabbits weighing between 2·0 and 4·0 kg. Anaesthesia was induced and maintained with sodium pentobarbitone (40 mg/kg, Nembutal, Abbot). Three rabbits were in addition paralysed with 60 mg of gallamine triethiodide, and artificially ventilated. A polyethylene cannula was tied into the trachea, and polyethylene catheters were tied into a femoral vein and artery. Blood pressure was monitored from the arterial catheter by a strain-gauge transducer (Consolidated Electrodynamics).

Tidal volume (V_T) was measured by electronically integrating air flow measured by a Fleisch pneumotachograph head connected to the tracheal tube.

Phrenic activity was recorded from multifibre strands of the upper cut root of the right phrenic nerve, placed in a trough of liquid paraffin; two platinum electrodes and a Tektronix 122 amplifier were used. The raw signal was integrated by a non-leaky amplifier (Davies & Wise, 1978). T_I and T_E were measured from the initial increases and the starts of the rapid decreases of phrenic activity. Activity from nerve fibres with discharge patterns which identified them as lung irritant or stretch receptors was recorded from 'single fibre' preparations of the right vagus nerve in three rabbits. The left vagus was intact. Instantaneous frequency of discharge of receptors was calculated by measuring the time interval between successive spikes.

Pulses of inflation and deflation of the lungs were obtained by briefly connecting the tracheal cannula to a large (20 l) drum, which was maintained at positive or negative pressure, by means of solenoid-operated valves which opened for the required pulse duration. The valves were triggered manually and the distribution of pulses throughout the respiratory cycle was randomized and explored all parts of the cycle. Pulses of 100 ms and $\pm 2{\cdot}0$ kPa pressure were found to be effective and produced inflations of $+20{\cdot}85 \pm 5$ ml (mean $\pm$ S.E.M.) above end-expiratory volume ($n = 34$, two rabbits) and deflations of $-6{\cdot}19 \pm 0{\cdot}4$ ml ($n = 34$, two rabbits) when tidal volume was $18{\cdot}87 \pm 4{\cdot}9$ ml ($n = 68$, two rabbits). End-tidal P_{CO_2} was monitored by a Beckman infra-red analyser and kept near the control value ($38{\cdot}2 \pm 1{\cdot}8$ torr) in intact and paralysed animals.

In some experiments stretch receptor activity was blocked by causing the animal to breath 200 parts per million SO_2 in air for 10 min (Callanan *et al.* 1975). Complete abolition of the Breuer–Hering inflation reflex (the prolongation of T_E caused by inflation of the lungs with a constant pressure of 1·5 kPa) was taken as evidence of stretch block. The responses to pulses of inflation and deflation were compared before and during stretch receptor block. The variables in each experiment were recorded on an ultraviolet recorder (Southern Electronics 6008) and on a seven-channel magnetic tape recorder (Ampex). Results are given as mean $\pm$ S.E. of the mean unless otherwise stated. Student's t test was used to evaluate the significance of differences. N-values refer to numbers of tests.

RESULTS

Spontaneously breathing rabbits

Pressure pulses during inspiration

Pulses of inflation or deflation given during inspiration often caused an augmented breath with an increase in V_T and T_I and a decrease in T_E (Fig. 1). 36 % of inflation pulses and 7 % of deflation pulses caused augmented breaths. In fifty-seven measured

augmented breaths in seven rabbits, T_I was $0{\cdot}73 \pm 0{\cdot}09$ s compared with immediately previous controls of $0{\cdot}41 \pm 0{\cdot}115$ s ($P < 0{\cdot}001$), a ratio of $1{\cdot}85 \pm 0{\cdot}22$. The response was all-or-none, no gradation occurring when the pulse characteristics were varied. In most cases the V_T and phrenic integral slopes were clearly biphasic.

The T_E immediately following augmented breaths was decreased (from $0{\cdot}72 \pm 0{\cdot}04$ s to $0{\cdot}52 \pm 0{\cdot}1$ s), the ratio to the preceding control being $0{\cdot}72 \pm 0{\cdot}17$ ($P < 0{\cdot}001$). Both

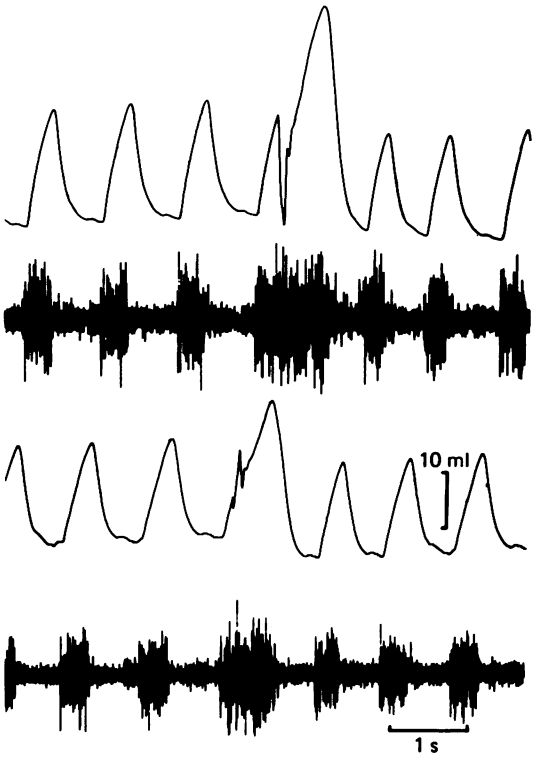

Fig. 1. Augmented inspiratory responses triggered by pulses of deflation (top trace) and inflation (lower trace). In each case tidal volume is shown above phrenic discharge.

T_I and T_E of the next subsequent breath were reduced (T_I ratio, $0{\cdot}87 \pm 0{\cdot}1$; T_E ratio, $0{\cdot}85 \pm 0{\cdot}1$), and returned to control values over two or three breaths.

Once an augmented breath had been elicited it was impossible to trigger another within 1 min; but after 2 min augmented breaths could usually be obtained. An augmented breath was more readily triggered by a pulse in the first half than by one in the second half of inspiration (Table 1). Spontaneous augmented breaths were never observed less than 1 min after a triggered augmented response. This refractoriness is thought to explain the absence of augmented breaths after many of the pulses in the whole series of experiments.

When a pulse produced no augmented breath, there was no significant change in T_I; however measurements in four rabbits showed that the following T_E was reduced (inflation pulses; T_E from $0{\cdot}66 \pm 0{\cdot}06$ s to $0{\cdot}54 \pm 0{\cdot}12$ s, $n = 51$, $P < 0{\cdot}01$; deflation

pulses: T_E from $0{\cdot}66 \pm 0{\cdot}12$ to $0{\cdot}58 \pm 0{\cdot}18$ s, $n = 40$, $P < 0{\cdot}01$). The following T_I was not statistically significantly different from the control.

Pulmonary stretch receptors were blocked by administering SO_2 (200 p.p.m. in air) for 10 min (Callanan *et al.* 1975; Davies, 1976). The block was assessed by the complete disappearance of the Breuer–Hering reflex. In receptor-blocked rabbits,

TABLE 1. Numbers of triggered augmented breaths (t.a.b.s) produced by pulses to the lungs of four rabbits. Equal numbers of inflation and deflation pulses were applied, but more were given in the first half of inspiration. * $P < 0{\cdot}01$ for the difference in ratio between the first and second half of inspiration (χ^2 test)

	Stretch receptors intact	
	First half	Second half
Pulses	120	41
T.a.b.s	48	4
Ratio	0·4	0·1*
	Stretch receptors blocked	
	First half	Second half
Pulses	110	21
T.a.b.s	18	1
Ratio	0·16	0·05

pressure pulses still caused augmented breaths (control T_I, $0{\cdot}63 \pm 0{\cdot}10$ s; augmented T_I, $1{\cdot}02 \pm 0{\cdot}18$ s; ratio $1{\cdot}67 \pm 0{\cdot}17$; $n = 19$, $P < 0{\cdot}01$); however the responses were more difficult to elicit, only 15% of inflation pulses being effective compared with 36% without block. Refractoriness after augmented breaths was still present. Pulses in the first half of inspiration were more effective in causing augmented breaths, although the difference was not statistically significant (Table 1). During stretch receptor block T_E after the augmented breath was decreased (ratio $0{\cdot}66 \pm 0{\cdot}17$; $n = 19$, $P < 0{\cdot}01$).

During stretch receptor block, when no augmented breath was obtained, pressure pulses did not significantly change T_I; however they decreased T_E (ratio $0{\cdot}77 \pm 0{\cdot}16$, $n = 47$, $P < 0{\cdot}01$).

No responses were obtained in rabbits without stretch receptor block when pulse pressure was set to atmospheric (twelve tests in six rabbits), or after cervical vagotomy (six rabbits).

Pressure pulses during expiration

Pulses of deflation decreased T_E. Pulses early in expiration usually reduced T_E by 80–90%. To quantify this effect we calculated $(T_{E,p} - T_p)/(T_{E,c} - T_p)$ where $T_{E,p}$ is the duration of the expiration containing the pulse, T_p is the delay between the end of the previous phrenic discharge and the beginning of the pulse and $T_{E,c}$ is the control expiratory duration (Fig. 2); thus the term is the ratio of the duration of expiration after the pulse to the potential duration of expiration after the pulse if the pulse had had no effect, calculated from the previous expiration. If the term is greater than unity then T_E has been increased, if less than unity, then T_E has been decreased. The term is plotted against $T_p/T_{E,c}$, the position of the pulse in expiration. If the pulses terminated expiration with a constant latency, i.e. with a constant $(T_{Ep} - T_p)$, the

plot would describe a segment of a hyperbola (Fig. 2, interrupted lines), the effect of this termination being most conspicuous with pulses at the beginning of expiration. Assuming a latency of $(T_{E,p}-T_p) = 0{\cdot}1\ T_{E,c}$, (a value frequently obtained experimentally) we constructed the interrupted lines of Fig. 2. Shortening of T_E produced by pulses of deflation gave values close to the curve indicating that the pulses

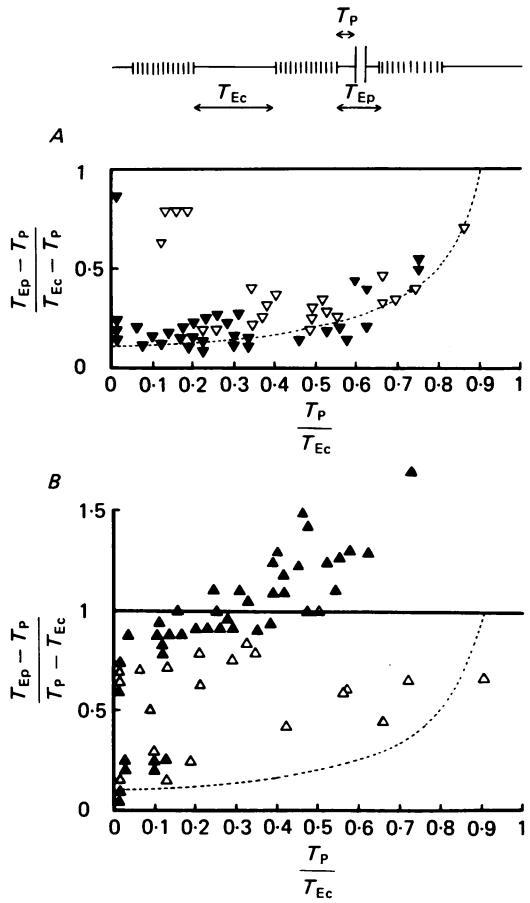

Fig. 2. Effect on T_E pulses of deflation (*A*) and inflation (*B*) given during expiration. The interrupted line was calculated assuming that the shortening of T_E measured as T_E-T_p was constant and equal to $0{\cdot}1\ T_{E,c}$. In both cases the filled triangles were obtained with intact animals and the open triangles in animals with lung stretch receptors blocked by SO_2.

triggered the next inspiration with near-constant latency (Fig. 2*A*) (other latency isobars (omitted for clarity) may be drawn and have similar shape). During block of pulmonary stretch receptors by SO_2 the responses to pulses of deflation were not very different.

In four deflations during stretch receptor block and one deflation without block the shortening of T_E was small (Fig. 2*A*). The pressure pulses were in a phase of rapidly decreasing lung volume and may have produced little receptor stimulation.

Pulses of inflation at the beginning of expiration usually shortened T_E (Fig. 2*B*), sometimes with a latency as short as 0·1 s. Pulses later in expiration had little effect on T_E, and even later the response reversed to an increase in T_E. After block of pulmonary stretch receptors with SO_2 only shortening of T_E was obtained with pulses of inflation, the values sometimes being near to the curve of constant latency (Fig. 2*B*).

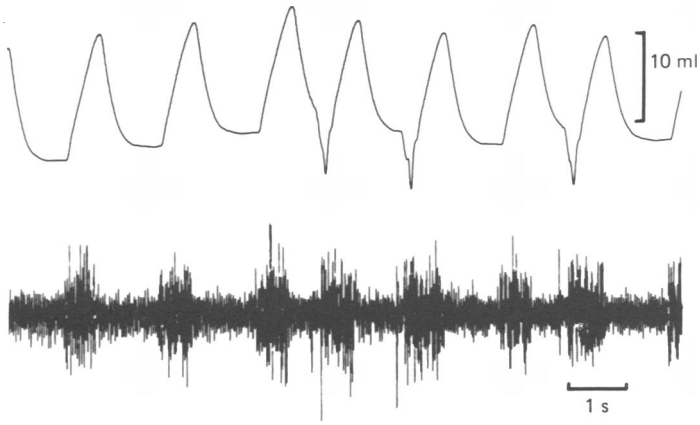

Fig. 3. Three pulses of deflation given in rapid succession in expiration. There is each time a shortening of expiration. Top trace = tidal volume. Bottom trace = phrenic discharge. The horizontal bars indicate pulse timing.

Pulses repeated in consecutive expirations, with stretch receptors blocked or intact, repeatedly produced a shortening of T_E (Fig. 3), demonstrating the absence of refractoriness.

When T_E was shortened by pressure pulses the following T_I was decreased except on rare occasions when a pulse of deflation late in expiration triggered an augmented breath. The size of the change in T_I was not closely correlated to the change in T_E.

Recordings from lung receptors

We recorded activity from twelve vagal fibres which showed patterns typical of pulmonary stretch or lung irritant receptors (Adrian, 1933; Mills, Sellick & Widdicombe, 1969, 1970). They all responded to changes in volume of the lungs and were unlikely to be in the extrathoracic trachea since the tracheal cannula was inserted as low as possible in the neck. Those designated 'stretch receptors' had low-volume thresholds, slowly adapting discharges to maintained lung inflations and decreases in any spontaneous activity with lung deflations. Those designated lung 'irritant receptors' responded to maintained lung inflations and deflations with rapidly adapting irregular discharges.

Seven stretch receptors briefly increased discharge during pulses of inflation (mean +47 %, $n = 12$ pulses) and decreased discharge during pulses of deflation (−45 %, $n = 12$) (Table 2). When the pulse triggered an augmented breath there was a large increase in firing frequency during the second part of the breath coincident with the increase in tidal volume. When the pulse did not trigger an augmented breath the total number of spikes in a respiratory cycle was little affected (about 5–10 % change).

Five irritant receptors responded to both pulses of inflation (+487 %) and deflation (+463 %) with intense burst of activity (Table 2, Fig. 4). Pulses of deflation produced the largest excitations when given at functional residual capacity (f.r.c.), during the expiratory pause. For example, a receptor studied in this respect discharged 17·5±2·8 impulses in the 0·1 s of the pulse of −2 kPa at f.r.c., compared

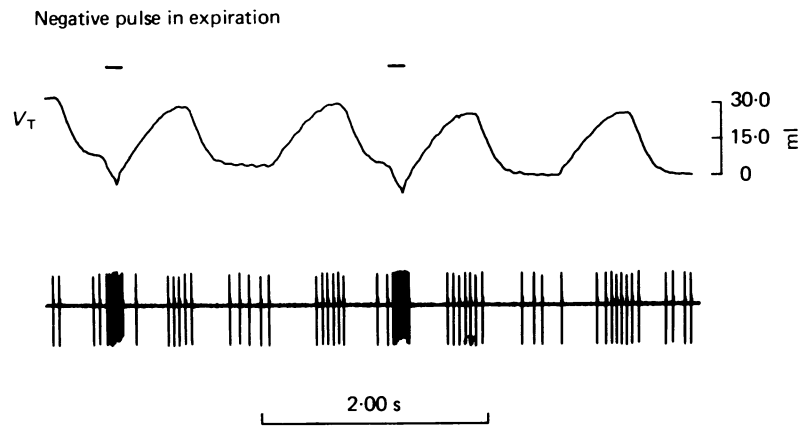

Fig. 4. Tidal volume and activity of a single lung irritant receptor when pulses of negative pressure were applied during expiration. The horizontal bars indicate pulse position.

TABLE 2. Number of impulses produced by stretch and irritant receptors during pulses of inflation and deflation compared with the number of impulses in the same time interval of the previous breath (control period)

Receptor type	Pressure pulse	No. of impulses in control period	No. of impulses in pulse	Change
Stretch: 12 tests	Positive	6·8±0·45	10·0±0·69	+3·2 (+47 %)
7 receptors	Negative	8·2±0·69	4·5±0·33	−3·7 (−45 %)
Irritant: 11 tests,	Positive	1·67±1·0	9·8±2·0	+8·13 (+487 %)
5 receptors	Negative	1·83±1·0	10·3±2·6	+8·47 (+463 %)

with 0·5±0·5 impulses in the corresponding control period (Table 3); at 70 % V_T the same receptor was not affected by equivalent pressure pulses. On the other hand, pulses of inflation at the peak of tidal volume were highly effective in producing activity. Thus five inflation pulses of 2 kPa given at 90 % tidal volume produced 9·2±0·71 impulses in the 0·1 s of the pulse, compared with a control value of 1·5±0·9 impulses.

During augmented breaths irritant receptor discharge was increased in amount and duration; for five augmented breaths the mean total number of impulses was 74·4±22·3 compared with a control of 14·6±8·0 (five receptors).

During the period after an augmented breath, corresponding to refractoriness, irritant receptors were still excited by pressure pulses, with no clear changes in sensitivity.

Spontaneous augmented breaths

In all spontaneously breathing rabbits, spontaneous augmented breaths had similar characteristics to the triggered responses. The ratio T_I to control was $1{\cdot}88 \pm 0{\cdot}21$ ($n = 24$), not significantly different from the ratio of triggered responses ($1{\cdot}85 \pm 0{\cdot}22$). In any particular animal, the tidal volumes of spontaneous and triggered augmented breaths were similar. Although the following T_E was usually decreased, it was occasionally longer, and the mean was not significantly different from control.

TABLE 3. Effect of positive and negative pulses on the activity of an irritant receptor at different lung volumes

Lung volume	Pressure pulse	Impulses during pulse
F.r.c.	None (control)	$2{\cdot}5 \pm 0{\cdot}9$
	Positive	$3{\cdot}6 \pm 1{\cdot}0$
90% V_T	None (control)	$1{\cdot}5 \pm 0{\cdot}9$
	Positive	$9{\cdot}2 \pm 0{\cdot}7$
F.r.c.	None (control)	$0{\cdot}5 \pm 0{\cdot}5$
	Negative	$17{\cdot}5 \pm 2{\cdot}8$
70% V_T	None (control)	$2{\cdot}9 \pm 0{\cdot}6$
	Negative	$2{\cdot}9 \pm 1{\cdot}3$

Five pulses of inflation and five of deflation were given at high and low lung volumes. The number of impulses during the pulse are compared with the number during the same time interval, at the same level of tidal volume in the previous (control) breath.

The spontaneous augmented breaths occurred, but were not usually recorded, at intervals of about 5 min. During block of pulmonary stretch receptors, frequency decreased to one or two augmented breaths per hour. They were never seen in bilaterally vagotomized rabbits.

In three rabbits we applied pressure pulses to the lungs during inspiration as soon as possible after spontaneous augmented breaths. In none of seventeen tests was an augmented breath produced. The refractoriness lasted 1–2 min.

Artificially ventilated rabbits

Three paralysed anaesthetized rabbits were ventilated with tidal volumes and frequencies as near as possible to their spontaneous patterns of breathing. Phrenic discharge locked to the pump frequency and occurred during deflation of the lungs.

Pulses of deflation given during the phrenic pause triggered a burst of phrenic activity lasting about 0·31 s, or $0{\cdot}6 \pm 0{\cdot}02$ ($n = 8$) times the control T_I, and starting 0·08–0·09 s from the beginning of the pulse (Fig. 5). The burst was all-or-none, not depending on pulse characteristics. Pulses of inflation during the phrenic pause produced a similar burst of activity but always at peak tidal volume (Fig. 5).

Pulses given during phrenic activity lengthened the discharge (Fig. 6), the effect being greatest with pulses towards the end of the discharge. This is consistent with the pulse causing a burst of phrenic activity of constant duration after a very short latency either within the spontaneous activity or else prolonging it.

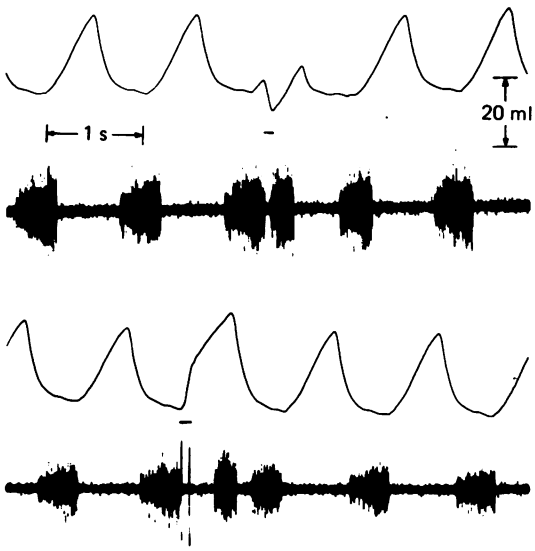

Fig. 5. Effect of pulses of deflation (above) and inflation (below) given during phrenic 'expiration' in an anaesthetized paralysed artificially ventilated rabbit. The artifact produced by the opening and closing of the magnetic valves is clearly seen on the phrenic record during the inflation pulse. In both cases the upper trace is tidal volume and the lower phrenic discharge; the horizontal bar indicates pulse timing.

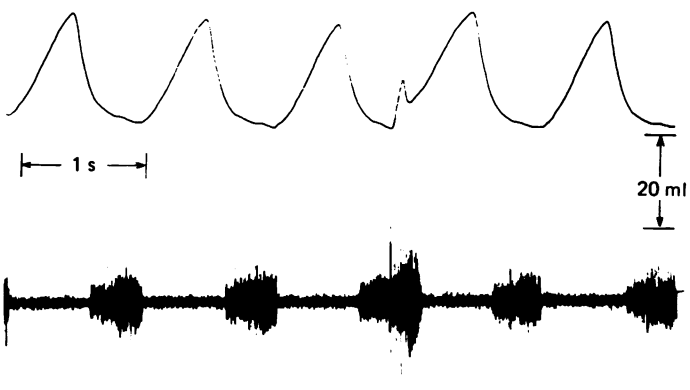

Fig. 6. Effect of a pulse of inflation given during phrenic 'inspiration' in an anaesthetized paralysed artificially ventilated rabbit; the horizontal bar indicates pulse timing.

Phrenic responses to pressure pulses in paralysed rabbits could be repeated in consecutive cycles, i.e. there was no refractoriness. In the paralysed animals only three phrenic discharges with patterns characteristic of an augmented breath were seen. They seemed to occur during the rare occasions when phrenic discharge was coincident with peak inflation volume.

DISCUSSION

In spontaneously breathing rabbits the inspiratory augmenting responses to pressure pulses were generally indistinguishable from spontaneous augmented breaths. Only the subsequent decrease in T_E was more consistent in the triggered responses. Consequently we shall refer to 'spontaneous' and 'triggered' augmented breaths. Our method of measuring end-tidal P_{CO_2} and the absence of a method of rapidly following blood-gas tensions prevented us from observing any transient changes in these variables. Whether or not pulses of inflation and deflation caused transient alterations in blood–gas tensions, the changes in arterial chemoreceptor activity that might result would not occur until one or two breaths later (Leitner, Pagès, Puccinelli & Dejours, 1965) and could not have influenced the characteristics and generation of the triggered augmented breaths. Since the latter were not seen when pulse pressure was set to zero or after vagotomy they were presumably due to excitation of lung receptors (see below and Introduction). Our few experiments with single-fibre recording are incomplete (for example the receptors were not localized or fully characterized) and were only intended to test receptor activity in our experimental conditions.

Of the known lung receptors, pulmonary stretch endings seem unlikely to be the agent. Firstly, pulses of either inflation or deflation in inspiration triggered augmented breaths similar in all respects, while recordings from stretch fibres showed that they were excited only by pulses of inflation. Their excitation in inspiration would decrease T_I. Furthermore, block of stretch receptors by SO_2 did not suppress triggered augmented breaths, although they were less frequently produced.

With regard to type J receptors (Paintal, 1969) and C fibre endings (Coleridge & Coleridge, 1977), we have not directly tested their activity during pulses. However, in cats inflations of up to four times tidal volume fail to excite J receptors (Paintal, 1969), and in rabbits they are not stimulated, or only very weakly, by large maintained inflations or deflations (Sellick & Widdicombe, 1970).

Lung irritant receptors in rabbits are strongly excited both by inflation and deflation (Mills, Sellick & Widdicombe, 1969; Sellick & Widdicombe, 1970). They are not blocked by SO_2 inhalation (Davies, Dixon, Callannan, Husczuk, Widdicombe & Wise, 1978). We therefore agree with Sellick & Widdicombe (1970) and Glogowska *et al.* (1972) that rapidly adapting lung 'irritant' receptors are responsible for augmented breaths. The capacity of pulses in one respiratory cycle to affect subsequent cycles has been described by us (Davies & Kohl, 1979) and by Karczewski, Budzinska, Gromysz, Herczynski & Romaniuk (1976) for a slightly different situation. We cannot say whether this effect is due to a central neural delay or some other factor, but the similarity of our results to those of Karczewski who produced his effects by electrical stimulation suggests the involvement of vagal pulmonary receptors.

In spontaneously breathing animals the triggered augmented breath was 'all-or-none'. In paralysed rabbits, the bursts of phrenic discharge triggered by pulses given during the phrenic pause were also all-or-none, with mean duration 0·31 s or 0·6 times the control T_I. The graded increase in T_I produced by pulses given during phrenic activity can be explained by the introduction with a very short latency, of such a burst of phrenic activity; i.e. the increase in T_I depended on the overlap of

the spontaneous phrenic activity and the stimulated burst. If an augmented breath in a spontaneously breathing rabbit were due to a normal phrenic discharge (0·41 s duration) followed immediately by a reflexly induced discharge of 0·31 s, the T_I of the augmented breath would be 1·75 times contol. This value is close to that observed experimentally (1·85 ± 0·22). This description of an augmented breath could explain both the all-or-none and the biphasic characteristics of the augmented response.

In paralysed rabbits pulses of deflation given during phrenic inactivity triggered bursts of phrenic discharge with very short latencies. Pulses of inflation given at the same phase produced bursts of phrenic activity at the time of the next peak of inflation volume; this would correspond to the peak of irritant receptor discharge induced by the pump inflation. Our hypothesis is that a deflation pulse during phrenic inactivity (i.e. early during lung inflation) is a more powerful stimulus to lung irritant receptors than an inflation pulse; the latter is only able to provoke phrenic discharge when the induced afferent activity is added to that caused by lung inflation by the pump. This hypothesis has yet to be tested, but it could explain why in spontaneously breathing animals any augmentation of phrenic activity always occurred at the end of a normal inspiration (and therefore peak tidal volume) independent of the timing of the pulse. However it would not explain why, in spontaneously breathing rabbits, pulses were less effective in triggering augmented breaths when given towards the end of inspiration (see below).

One of the striking features of our results was the existence of a refractory period after an augmented breath. A similar refractoriness was reported by Reynolds (1962) after the augmented breaths produced by the ventilation of cats with large tidal volumes, and by Glogowska *et al.* (1972) after augmented breaths triggered by chemoreceptor stimulation in cats and rabbits. These authors did not describe whether the refractoriness they produced affected T_I and T_E or whether, as in this study, it was restricted to T_I. The refractory period lasted for 1–2 min in our experiments. Although spontaneous irritant receptor discharge was decreased during this period, as found by Sellick & Widdicombe (1970), irritant receptors were still excited by pulses of inflation and deflation. Refractoriness was absent during paralysis. This may indicate that it is not a purely central mechanism, following an extended inspiration.

It is impossible to say whether the lack of response to a pulse in inspiration sometime after an augmented breath was due to this refractoriness or some other factor. We therefore have no clear base line against which to measure refractoriness and restrict ourselves to reporting its presence.

Pressure pulses were less able to produce an augmented breath during the second half of inspiration; however, the irritant receptors were more sensitive to inflation pulses and less sensitive to deflation pulses during this time. We must conclude that, towards the end of a spontaneous inspiration, irritant receptor activity is prevented from causing an augmented breath. It follows that a spontaneous augmented breath must be caused by the summation of the inspiratory drive with the reflex effects of irritant receptor activity early in inspiration, at a time when the receptors would be sensitized by collapse of the lungs (Sellick & Widdicombe, 1970).

Respiratory frequency increased for a few breaths following an augmented breath. During this period activity of arterial chemoreceptors was probably reduced by a

transient increase in arterial P_{O_2} (Biscoe & Purves, 1967). However, transient reduction in chemoreceptor activity by inhalation of a few breaths of oxygen decreases both tidal volume and respiratory frequency (Leitner *et al.* 1965) and cannot account for the acceleration of respiration reported here. Reduction of airways P_{CO_2} after an augmented inspiration may increase activity of CO_2 sensitive stretch receptors, but this would also be expected to cause an increase in T_E. It is therefore possible that the effects of irritant receptor stimulation during an augmented breath extends over a few respiratory cycles.

Pulses of deflation in expiration always decreased T_E. The change in T_E was not altered by block of stretch receptors by SO_2. Pulses of inflation early in expiration sometimes shortened T_E by as much as that due to pulses of deflation. Later in expiration pulses of inflation produced either less shortening or lengthening of T_E (Fig. 2). Block of stretch receptors reversed any lengthening to a shortening. Our results are consistent with the view that excitation of irritant receptors during expiration shortens T_E; and that if stretch receptors are simultaneously excited they could dominate the response and lengthen T_E. D'Angelo (1978), using a differential d.c. block of the vagus, demonstrated a 'shortening effect on T_E exerted by rapidly adapting or "irritant" receptors'.

Knox (1973) used deflation pulses throughout expiration in cats, and observed shortening of T_E with constant latency except for a graded effect with pulses early in expiration (Fig. 8 in Knox, 1973). He did not observe any shortening of T_E with pulses of inflation, possibly because he used 200 ms pulses which would stimulate stretch receptors more than our 100 ms pulses. The response to a pulse presumably depends on the relative balance of excitation of stretch and irritant receptors.

A pulse of deflation given late in expiration occasionally produced an augmented breath in addition to shortening T_E. With these exceptions, when a pulse shortened T_E the following T_I was shortened, whether or not stretch receptors were blocked. This shows that T_I need not be independent of the previous T_E, as suggested by Clark & von Euler (1972) and Knox (1973). Karczewski *et al.* (1976) reported that electrical stimulation of the vagi in bilaterally vagotomized rabbits produced a smaller decrease in T_I than in T_E, and that the changes in T_E preceded the changes in T_I by one respiratory cycle.

We conclude that irritant receptor stimulation during inspiration produces an augmented breath followed by a refractory period for such breaths; their stimulation in inspiration or expiration shortens expiration without refractoriness.

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