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THE CAT LUNG STRIP AS AN *in vitro* PREPARATION OF PERIPHERAL AIRWAYS: A COMPARISON OF β-ADRENOCEPTOR AGONISTS, AUTACOIDS AND ANAPHYLACTIC CHALLENGE ON THE LUNG STRIP AND TRACHEA

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1 A new *in vitro* preparation, the isolated lung strip of the cat, is described for investigating the direct effect of drugs on the smooth muscle of the peripheral airways of the lung. The preparation comprises a thin strip of lung parenchyma which can be mounted in a conventional organ bath for isometric tension recording. Its pharmacological responses have been characterized and compared with the isolated tracheal preparation of the cat.

2 The lung strip exhibited an intrinsic tone which was relaxed by catecholamines, aminophylline and flufenamate. It was contracted strongly by histamine, prostaglandin $F_{2\alpha}$, acetylcholine, compound 48/80, potassium depolarizing solution and alternating current field stimulation. In contrast, the cat trachea was unresponsive to histamine and prostaglandin $F_{2\alpha}$ and did not exhibit an intrinsic tone.

3 (–)-Isoprenaline and (–)-adrenaline were much more potent in relaxing the lung strip than the trachea. The potency order of relaxation responses to isoprenaline, adrenaline and (±)-noradrenaline in the lung strip was isoprenaline > adrenaline > noradrenaline but in the trachea was isoprenaline > noradrenaline ⩾ adrenaline.

4 β_2-Adrenoceptor selective agonists salbutamol and terbutaline were more potent in the lung strip than the trachea, suggesting β_2-adrenoceptors predominated in the lung strip. Propranolol was equipotent in inhibiting isoprenaline relexations of the lung strip and trachea, whereas practolol was much less effective in inhibiting lung strip than trachea, further supporting a predominance of β_2-adrenoceptors in lung strip and β_1-adrenoceptors in trachea.

5 Strong Schultz-Dale type contractions were elicited in both lung strips and trachea by *Ascaris lumbricoides* antigen in actively sensitized cats. The initial phase of the contractile response of the lung strip following challenge was shown to be due to histamine release and was absent in the trachea. The delayed phase of the contraction which took several minutes to develop in both the mepyramine-treated lung strip and trachea was not due to prostaglandins E_1, $F_{2\alpha}$ or bradykinin, the probable mediator being slow reacting substance of anaphylaxis (SRS-A).

6 It is concluded that the isolated lung strip of the cat is useful as an *in vitro* model for investigating the effect of drugs on the smooth muscle of the peripheral airways of the lungs.

Introduction

Techniques available for investigating the direct actions of drugs on smooth muscle of the lung chiefly use preparations of the large central airways. Tracheal rings tied together (Castillo & De Beer, 1947) or opened before tying together (Akcasu, 1959) and intraluminal pressure recorded from whole trachea (Farmer & Coleman, 1970) are examples. However, *in vivo* measurements of lung compliance or airways resistance suggest that the principal site of action of some drugs is at the level of the fine peripheral airways (Colebatch, 1970; Drazen & Austen, 1974). Direct evidence for such an action requires an *in vitro* preparation of the peripheral airways and we describe here a simple technique using strips of isolated lung parenchyma of the cat for investigating the direct effect of drugs on the small airways. Some of the pharmacological characteristics of this cat isolated lung preparation are described. A preliminary report

of this work was presented at the 6th International Congress of Pharmacology (Sparrow & Mitchell, 1975).

Methods

Adult cats of either sex were lightly anaesthetized with halothane, the chest opened, the lungs carefully excised and placed in modified Krebs solution at 37°C and aerated with 95% O_2 and 5% CO_2. The composition was (mM): NaCl 119, KCl 5.6, $NaHCO_3$ 14, $CaCl_2$ 2, dextrose 11 and KH_2PO_4 1.2. The solution was buffered to pH 7.3 with NaMOPS (morpholinopropane-sulphonic acid titrated with NaOH to pH 7.3) 5 mM; K_2H_2EGTA (ethyl-eneglycol-bis-(β-amino-ethylene ether) *N,N'*-tetra-acetic acid) 0.05 mM was included as a sequestering agent as a safeguard against heavy metal contamination. In potassium depolarizing solution the NaCl in the above solution was replaced by K_2SO_4 80 mM.

Preparation of isolated trachea from cats

From tracheal rings about 3 mm in width, most of the cartilage was removed before attaching threads to the small pieces of cartilage remaining at each end of the trachealis muscle. The tissues were stretched to a tension of 0.3 g and where appropriate, tone was induced with 0.4 μM carbachol.

Preparation of isolated lung strips of cats

Sections of lung tissue, about 3 mm in width, were dissected quickly from a lower lobe with the longitudinal axis of the strip cut parallel to the bronchus. This was then divided into two or more thin strips with approximate dimensions of 20 × 3 × 3 mm. (Figure 1).

In some experiments, strips were dissected from either the peripheral margin of a lobe or from across the lobe at right angles to the bronchus, but not including it. There was no detectable difference in the pharmacological responses of these strips compared with those routinely cut as in Figure 1.

With threads attached to each end, strips were mounted in organ baths containing aerated Krebs at 37°C. A load of between 2.0 to 2.5 g force was applied by gently stretching and the tissues were allowed to equilibrate for 1 h with the solution changed at 15 min intervals.

Usually two-organ baths, each containing a pair of strips, were run simultaneously to permit the testing of various drugs in differing order and dose and with adequate controls. Consistent responses could be obtained at 37°C for at least 6–8 h and the responsiveness to drugs was unimpaired after storage overnight at 4°C. Concentration-response relationships were obtained using a cumulative dose schedule

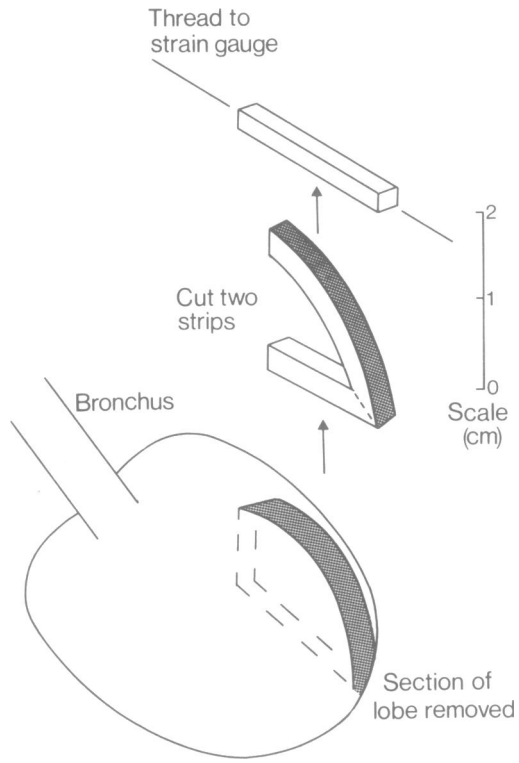


Figure 1 Preparation of isolated strips from cat lung.

after which the organ bath was flushed and the tension allowed to return to its original value. Changes in tension were measured isometrically with a Grass FTO3C force-displacement transducers.

Preparation of antigenic extract from Ascaris lumbricoides

Ascaris lumbricoides were removed from pigs; 200 g of the fresh worms were finely homogenized with 20 mM sodium phosphate buffer pH 7.4 at 4°C and made up to 500 ml. An equal volume of 0.85 M phenol solution was added, the mixture stirred for 1 h, centrifuged at 12,000 *g* for 10 min, and the supernatant dialysed for 48 h against running water and then for a further 12 h against distilled water containing 5 mM phosphate buffer at pH 7.4. The dialysed solution was then freeze-dried and yielded approximately 2 g of solid residue. This was stored under N_2 at −20°C.

Sensitization of cats to Ascaris lumbricoides

Cats were injected subcutaneously with 5 mg of Ascaris extract in an equal volume of Freund's

complete adjuvant every third day for 3 weeks. The cats were either manually restrained or lightly anaesthetized with halothane for this procedure. The animals were killed and the isolated lung strips and trachea prepared as above.

Calculations

Mean concentration-response curves for the relaxing drugs were obtained by determining the concentration of drug which elicited a given percentage of the maximal response to (–)-isoprenaline. These concentration values for individual tissues were averaged and the standard error of the mean determined (Chahl & O'Donnell, 1967). The EC_{50} value for a relaxing drug was calculated as the mean concentration giving 50% of its maximal response. Figures 2, 3 and 5 show examples of a typical experiment, a similar result being obtained in at least 4 other cats. pA_2 values were obtained by the method of Arunlakshana & Schild (1959) where at least 3 concentrations of antagonists were used for 20 min exposures in not less than 3 preparations. Statistical evaluation was performed using Student's t test, $P < 0.05$ was regarded as significant.

Drugs

The following drugs were used: (–)-isoprenaline hydrochloride (Sigma), (–)-adrenaline hydrochloride (Sigma), (±)-noradrenaline bitartrate (Sigma), histamine acid phosphate (Koch-Light), acetylcholine chloride (Roche), carbachol (Abbot Labs, injection), salbutamol sulphate (Allen & Hanbury's), terbutaline sulphate (Astra), compound 48/80 (Sigma), prostaglandins E_1 and $F_{2\alpha}$ (Upjohn), atropine sulphate (DHA), mepyramine maleate (May & Baker), methysergide (Sandoz), propranolol hydrochloride (ICI), practolol (ICI), phentolamine (Ciba), aspirin, indomethacin (Merck, Sharp & Dohm), flufenamate (Parke-Davis), bradykinin (Sigma), cocaine hydrochloride, normetanephrine hydrochloride (Calbiochem), Freund's complete adjuvant (CSL) and aminophylline (DHA).

Concentrations are expressed as either the free acid or base unless otherwise stated.

Results

Isolated lung strip tone

Isolated lung strips exhibited an intrinsic tone which was maintained for at least 6 hours. This tone could be relaxed by either aminophylline (10 μM to 10 mM) or catecholamines. Figure 2 shows examples of relaxation responses to (–)-isoprenaline. Relaxation was usually slow in onset, taking 5–10 min to reach completion. Following washout, the tissues recovered their initial tone within 30 minutes. Consistent responses could be elicited repeatedly at 30 min intervals.

Lung strips were contracted by histamine (0.1 μM to 0.1 mM) and prostaglandin $F_{2\alpha}$ (0.1 μM to 0.1 mM), examples of which are shown in Figure 2. Similar responses were elicited by acetylcholine (0.1 μM to 1.0 mM), compound 48/80 (0.01–1 mg/ml), potassium depolarizing solution and alternating current field stimulation (10 V/cm, 50 Hz for 0.8 seconds). Prostaglandin E_1 (0.1 μM to 10 μM) did not affect the tone of the lung strip (Figure 2).

The intrinsic tone of the lung strip depended on the initial tension applied to it (Figure 3). When the preparation was lightly stretched to give an initial tension of 1 g, (–)-isoprenaline (1 μM) elicited a small relaxation, typically of approx. 0.3 g in magnitude, but with greater stretch applied (–)-isoprenaline elicited a much larger relaxation. At tension of 5.0 g, the (–)-isoprenaline-induced relaxation was 2.3 grams. Since adequate responses to both contracting and relaxing durgs could be obtained with an initial tension of 2.0 g, this value was used for subsequent experiments.

The steady tone of lung strip was unaffected following exposure to atropine (1 μM), mepyramine (1 μM) or methysergide (10 μM) for 20 minutes. The tone of the preparation was not influenced by incubation for 1 h with aspirin (3 mM) or indomethacin (0.3 mM). However, sodium flufenamate from 50 μM to 0.5 mM produced a slow decrease in tone within 1 min of exposure. This relaxation was incomplete and in 4 preparations tested an average of 75% reduction in tone occurred after 30 min compared with the relaxation elicited by a maximal concentration of (–)-isoprenaline (1 μM).

Sensitivity of the isolated lung strip compared with the isolated trachea

The pharmacology of the lung strip was different from that of the trachea. Histamine (0.1 μM to 0.1 mM) and prostaglandin $F_{2\alpha}$ (0.1 μM to 0.1 mM) strongly contracted the lung strip but the trachea was insensitive at these concentration ranges (Figure 2). Pretreatment with mepyramine (10 μM) completely prevented these histamine responses. Similarly, contractions induced with histamine (0.1 mM) were abolished by the subsequent addition of 10 μM mepyramine. Whereas prostaglandin E_1 (0.1 μM to 10 μM) had no effect on the intrinsic tone of the lung strip it relaxed the carbachol-induced tone of trachea. Bradykinin had no effect on either the lung strip or the trachea at concentrations up to 10 μg/ml.

(–)-Isoprenaline and (–)-adrenaline were much more potent in relaxing the lung strip than the trachea. The differences in the relaxant potencies of catecholamines on lung strip and trachea are shown in the concentration-response curves (Figure 4). (–)-Adrenaline was

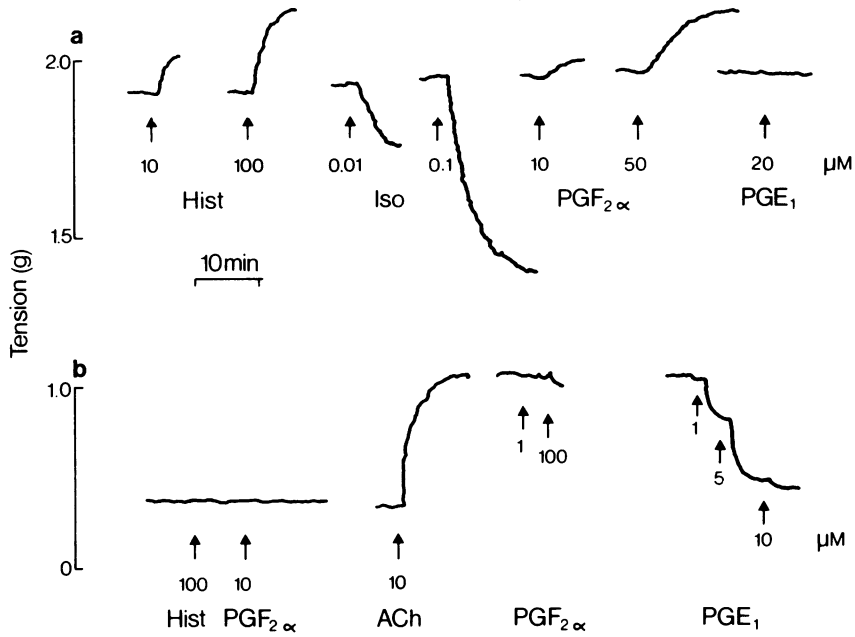
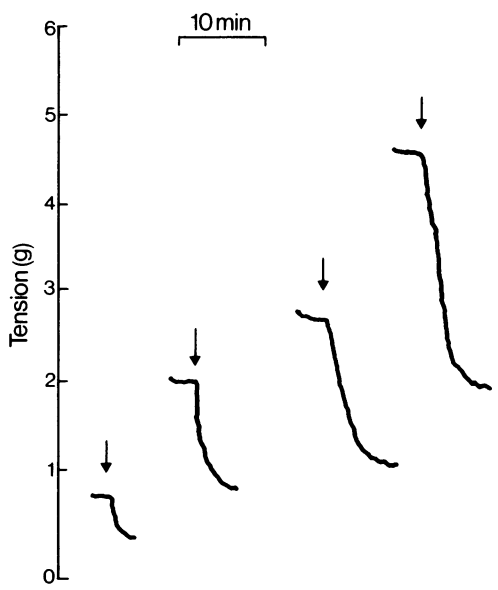


Figure 2 Isometric tension responses of (a) isolated lung strip and (b) trachea of the cat; (a) lung strips: consecutive responses of one strip to histamine (Hist), (–)-isoprenaline (Iso), prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and prostaglandin E_1 (PGE_1). An initial tension of 1.9 g was applied to the tissue by gently stretching. After each drug treatment the tissue was washed frequently and allowed to return to baseline tension before the next treatment. (b) Trachea: no response to histamine and prostaglandin $F_{2\alpha}$. When partially contracted by acetylcholine (ACh 10 μM) prostaglandin $F_{2\alpha}$ is still without effect, but prostaglndin E_1 causes relaxation. Concentrations μM.



72 times more potent than (±)-noradrenaline in lung strip whereas in trachea they were equipotent. The similar potencies of (–)-adrenaline and (±)-noradrenaline could not be explained by a dominant $Uptake_1$ mechanism occurring in the lung strip since cocaine (10 μM) did not significantly affect the pD_2 of (±)-noradrenaline (4 strips from 2 cats). Nor could an enhanced $Uptake_2$ mechanism in the trachea explain the similar potencies of (–)-adrenaline and (±)-noradrenaline since normetanephrine (10 μM) did not significantly shift the pD_2 values of (–)-adrenaline in

Figure 3 The relationship between the initial tension applied to the isolated lung strip of the cat and the relaxation response to (–)-isoprenaline 1 μM (at arrow). A typical experiment in which a relaxation to (–)-isoprenaline was elicited and after washout the tissue was allowed to return to baseline then stretched to a greater resting tension. When this had stabilized the tissue was again challenged. The approximate initial tensions shown are 1,2,3 and 5 grams. Duplicate responses were elicited at the beginning and end of the experiment to check reproducibility.

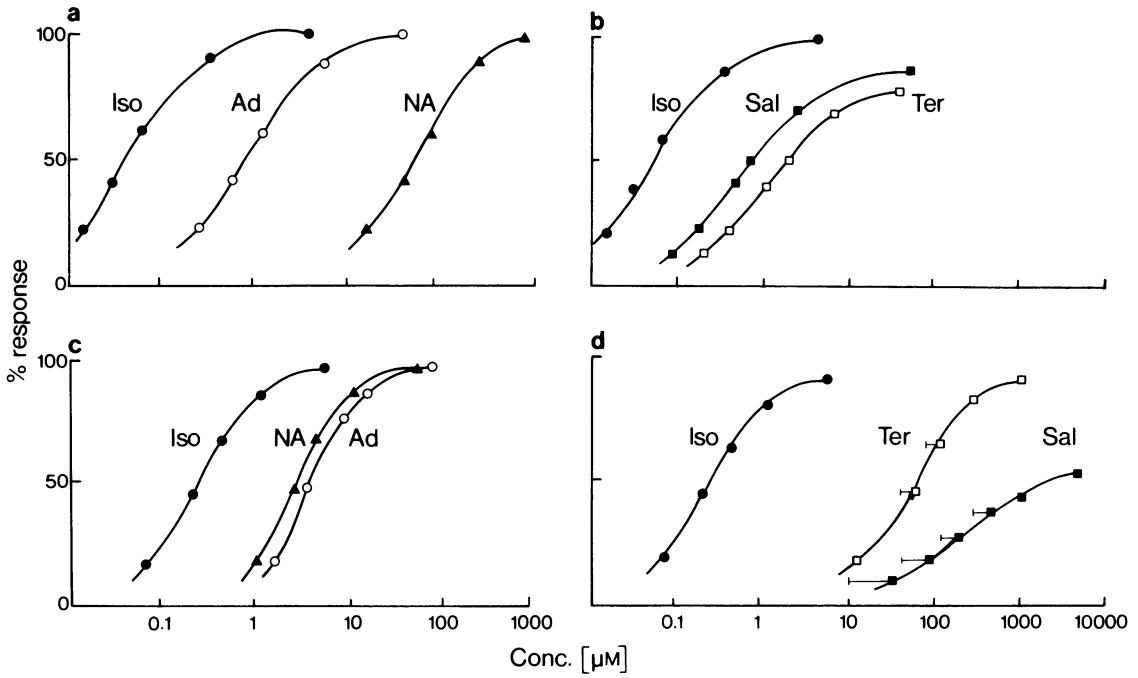


Figure 4 Mean concentration-response curves of the isolated lung strip (a & b) and the trachea (c & d) of the cat to the catecholamines (–)-isoprenaline (Iso), (–)-adrenaline (Ad) and (±)-noradrenaline (NA) and the β_2-adrenoceptor selective agonists salbutamol (Sal) and terbutaline (Ter). Relaxation responses are plotted as percent of relaxation to a maximal concentration of (–)-isoprenaline on the intrinsic tone of the lung strip, and of the carbachol-induced tone in the trachea using carbachol (0.4 μM). Each point is the mean of at least 5 different tissues and the standard error bars are only shown when they exceed the dimensions of the symbols used.

trachea (4 tissues from 2 cats). pD_2 values, relative potencies and intrinsic activities of the catecholamines, terbutaline and salbutamol are shown in Table 1.

The different potencies of (–)-adrenaline and (±)-noradrenaline in lung strip, compared with trachea, suggested a difference in the type of β-adrenoceptor present and support for this was obtained by the use of the β_2-adrenoceptor selective agonists, salbutamol and terbutaline and the β-adrenoceptor antagonists, propranolol and practolol. For a 50% response the dose of salbutamol was about 10 times greater than that of isoprenaline when the lung strip was used, and

Table 1 Table showing potency, pD_2, and intrinsic activity (α) of (–)-isoprenaline, (–)-adrenaline, (±)-noradrenaline, terbutaline and salbutamol on isolated lung strip and trachea of the cat

	Lung strip			*Trachea*		
	*Potency**	*pD_2†*	*α‡*	*Potency*	*pD_2*	*α*
(–)-Isoprenaline	1000	7.34 ± 0.02 (16)	1	1000	6.74 ± 0.25 (26)	1
(–)-Adrenaline	52.2	6.07 ± 0.03 (5)	1	43.5	5.46 ± 0.02 (13)	1
(±)-Noradrenaline	0.75	4.22 ± 0.04 (5)	1	72.5	5.53 ± 0.03 (16)	1
Terbutaline	49.7	6.05 ± 0.08 (10)	0.77 ± 0.02	4.5	4.59 ± 0.15 (12)	1
Salbutamol	93.4	6.34 ± 0.06 (7)	0.83 ± 0.02	0.9	4.11 ± 0.23 (9)	0.62 ± 0.05

*Potencies are the ratio of pD_2 values compared with that for (–)-isoprenaline which has been arbitrarily assigned a value of 1000. † The pD_2 value is defined as the negative log EC_{50}. Mean ± s.e. mean. Number of tissues shown in brackets. ‡ Intrinsic activity for an agonist (Van Rossum, 1963) is expressed as the maximum response relative to that for (–)-isoprenaline. Mean ± s.e. mean.

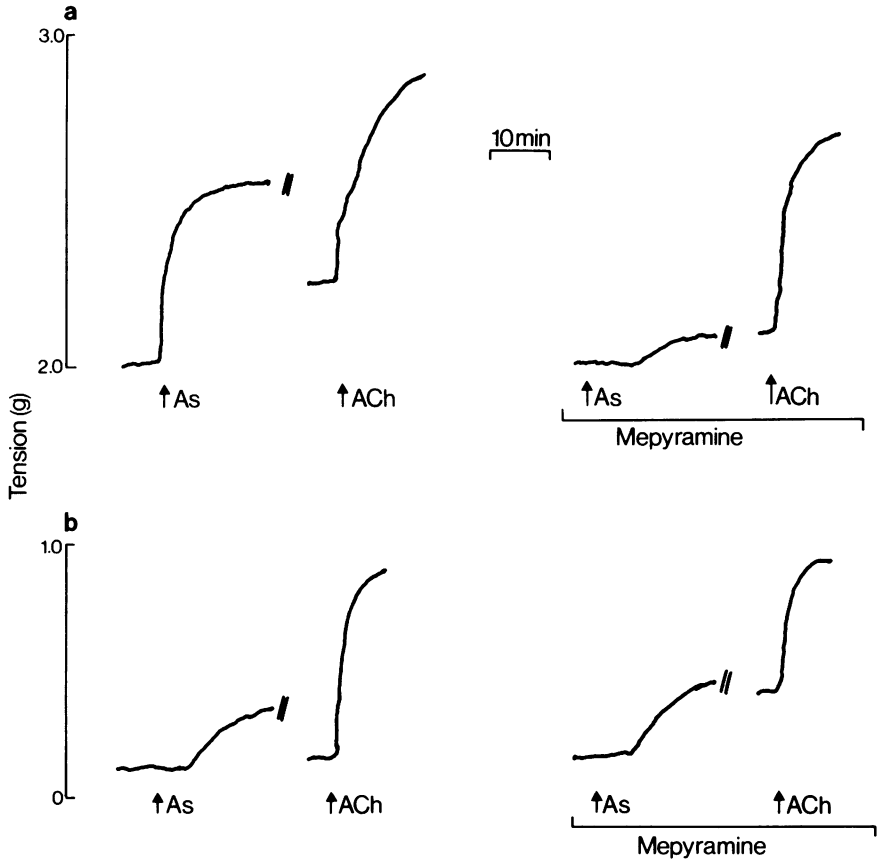


Figure 5 Contractions elicted by *Ascaris* extract (1 mg/ml) of (a) the isolated lung strip and (b) trachea from a cat sensitized with *Ascaris* antigen (As). The upper and lower figures on the left show control responses to *Ascaris* extract. The lung strip contracts immediately to *Ascaris* extract but there is a delay of 5 min before the tracheal response is seen. On the right another pair of tissues is shown which were pre-treated for 5 min with mepyramine (100 μM). The immediate response of the lung strip is abolished and a smaller delayed contraction is seen but the tracheal response is maintained. In each case the magnitude of the contractile responses is compared with the tension developed to a maximal concentration of acetylcholine (ACh 100 μM) injected 10 min after washout of the *Ascaris* extract.

about 430 times greater for the trachea (Figure 4). Propranolol showed about equal potency in inhibiting (−)-isoprenaline responses of both the lung strip and trachea (pA_2 values of 8.0 and 8.1 respectively), whereas practolol was much less effective in inhibiting lung strip than trachea (pA_2 of 5.4 and 6.4, respectively).

The presence of α-adrenoceptors in the lung strip could not be readily demonstrated with α-adrenoceptor blockers. In four preparations, relaxation caused by (±)-noradrenaline (0.1 mM) was unchanged by the presence of phentolamine (30 μM). However, after β-adrenoceptor blockade using 20 min exposures of propranolol (10 μM) the response to (±)-noradrenaline (0.1 mM) was changed to a contraction averaging about 40% of the maximal response to acetylcholine (1 mM) (14 preparations from 5 cats). By contrast, tracheal preparations from the same cats gave contractions of only 10 to 15% of the acetylcholine maximum, and only 8 of the 14 tissues responded. Excitatory α-adrenoceptor participation in the trachea therefore seemed to be of minor significance, a finding which is in agreement with Fleisch, Maling & Brodie (1970).

Anaphylaxis of isolated lung strip and trachea

Ascaris extract (1 mg/ml) elicited strong contractions (Schultz-Dale) in both lung strips and trachea from actively sensitized cats (Figure 5), but tissues from

unsensitized animals were unresponsive. The response of the lung strip occurred immediately following challenge, but there was a consistent 2–8 min delay before the trachea contracted. This delay period was observed at all concentrations of *Ascaris* used (0.01–10 mg/ml).

The immediate phase of contraction of the lung strip could be abolished by exposure to mepyramine (1 to 100 μM) for 5 min prior to challenge (Figure 5). Response was then delayed for several minutes and resembled the tracheal contraction in this characteristic. Mepyramine (1 to 100 μM) added when anaphylactic concentrations had reached a plateau resulted in a 50–68% ($n=3$) reduction in tension in the lung strip in the ensuing 5 min, whereas the tracheal contractions were unchanged.

The Schultz–Dale contraction relaxed to baseline tension within about 20 min after washout of antigen. After contact with antigen, the tissue did not respond to compound 48/80 (50–100 μg/ml), but still responded normally to acetylcholine. Desensitization developed rapidly to the *Ascaris* extract, so that it was only possible to challenge each tissue once. Considerable variation in the magnitude of the anaphylactic responses to the *Ascaris* extract was found among the actively sensitized cats. Table 2 shows concentration-response data from three cats where a marked difference in the sensitivities of the tissues is seen to *Ascaris* extract in concentrations from 0.01–10 mg/ml.

Discussion

We have described a new preparation whereby the direct effect of drugs on the small airways of the lungs can be examined *in vitro*. It seems probable that the contractile responses of the lung strip were due principally to activation of the airways smooth muscle. The lung strip chiefly comprises the spongy respiratory tissue of the lung lobe where the smooth muscle is present in alveolar ducts, respiratory bronchioles, bronchioles and blood vessels. Low power microscopic examination showed that the bronchioles had diameters of approx. 0.1 mm. From the sparsity of these bronchioles in the parenchyma, usually less than 2 per mm^2 cross section, it would appear that the smooth muscle of the alveolar ducts and respiratory bronchioles may make the major contribution to the contractile responses of the lung strip, transmitting tension throughout the strip via connective tissue linkages. A component of tone from vascular smooth muscle could not be demonstrated because firstly, (±)-noradrenaline caused relaxation which would not have been expected had the drug been acting principally on pulmonary vascular smooth muscle (Houghton & Phillips, 1975), and secondly, blockade of α-adrenoceptors with phentolamine did not enhance this (±)-noradrenaline-induced relaxation. After β-adrenoceptor blockade, (±)-noradrenaline in high concentration caused contraction of lung strips from which the existence of α-adrenoceptors may be inferred, but the extent to which they are located on bronchial or vascular smooth muscle is unknown.

The isolated lung strip preparation responded to a variety of stimuli. The responses were reproducible over several hours at 37°C and were slow to reach completion, resembling those of the isolated tracheal chain preparation (Castillo & De Beer, 1947). The presence of intrinsic tone was demonstrated by the ability of drugs such as the catecholamines and flufenamate to cause relaxation of strips. The fenamates in concentrations from 1–20 μg/ml have been shown to antagonize the actions of spasmogens such as slow reacting substance of anphylaxis (SRS-A) and prostaglandin $F_{2\alpha}$ on human bronchi (Collier & Sweatman, 1968), concentrations which are 10 times less than that required to relax cat lung strip. Indomethacin did not relax the intrinsic tone of cat

Table 2 Comparison of anaphylactic contractions elicited by *Ascaris* extract on the isolated lung strip and trachea of three actively sensitized cats

	Cat 1		*Cat 2*		*Cat 3*	
Ascaris *extract (mg/ml)*	*Lung strip*	*Trachea*	*Lung strip*	*Trachea*	*Lung strip*	*Trachea*
0.01	43*	63	0	0	10	2
0.1	50	57	14	2	15	6
1.0	68	61	42	17	14	7
10.0	106	62	74	31	17	11

*Response expressed as the percentage of the peak isometric tension elicited by a maximal concentration of ACh (1 mM).

lung strip although at concentrations of the order of 1 μM, it relaxes guinea-pig isolated trachea (Farmer, Farrar & Wilson, 1974). This may reflect a different profile of mediators responsible for the intrinsic tone of lung strip. The lack of effect of atropine, mepyramine and methysergide indicated that acetylcholine, histamine or 5-hydroxytryptamine were not involved in the maintenance of resting tone in the cat lung strip.

Histamine did not affect cat trachea, whereas contractions were elicited in lung strips. These histamine responses were abolished by mepyramine, indicating that the receptors were of the H_1 type (Black, Duncan, Durant, Gannelin & Parson, 1972). These results with lung strip provide *in vitro* evidence for an action of histamine on peripheral airways consistent with the observations of Colebatch (1970), who demonstrated a reduced lung compliance to histamine in anaesthetized cats. We have also observed differential sensitivity of the cat airways to the prostaglandins, prostaglandin $F_{2\alpha}$ contracting lung strips but not trachea, and prostaglandin E_1 relaxing trachea but not lung strip. It will be of interest to see whether this differential sensitivity of the central and peripheral airways to prostaglandins is seen using *in vivo* techniques which measure airways resistance and dynamic compliance (Widdicombe, 1963).

(–)-Isoprenaline, (–)-adrenaline and (±)-noradrenaline relaxed both trachea and lung strip preparations. The order of potency of the catecholamines on lung strip was found to be (–)-isoprenaline > (–)-adrenaline > (±)-noradrenaline, and this is the same order of potency as found in the guinea-pig isolated trachea, a β_2-adrenoceptor preparation (Farmer & Coleman, 1970; O'Donnell, 1972; O'Donnell & Wanstall, 1974). However, on the cat isolated trachea the order of potency was found to be (–)-isoprenaline > (±)-noradrenaline ≥ (–)-adrenaline. It was reported by Lands, Arnold, McAuliff, Luduena & Brown (1967) and Furchgott (1967) that (±)-noradrenaline is equipotent or more potent than adrenaline in eliciting a β_1-adrenoceptor response, so that the order of potencies of the catecholamines on the cat trachea is consistent with a β_1-adrenoceptor preparation. In support of this, the selective β_2-adrenoceptor agonists terbutaline and salbutamol were found to be, respectively 7 and 43 times more potent in relaxing the lung strip than the trachea. With propranolol, the non-selective β-adrenoceptor antagonist, identical pA_2 values were obtained against isoprenaline on both the lung strip and trachea, whereas practolol, the selective β_1-adrenoceptor antagonist (Dunlop & Shanks, 1968) was 10 times more active on trachea than the lung strip. These results support the conclusion that the adrenoceptors in the lung strip are predominantly the β_2 type and those of cat trachea β_1.

The ability to actively sensitize cats, in this instance to *Ascaris* extract, has not to our knowledge been reported elsewhere. Previous workers using antigens such as horse serum were unable to obtain active sensitization (Akcasu, 1962). We have consistently found both lung and trachea contract following antigen challenge *in vitro* with the *Ascaris* extract. The early part of the response of the lung strip was abolished with mepyramine, indicating that this phase was due to the release of histamine. The late response of the trachea and the mepyramine-treated lung strip demonstrated the release of a non-histamine component which is tentatively attributed to slow reacting substance of anaphylaxis (SRS-A), since prostaglandins E_1 and $F_{2\alpha}$ and bradykinin did not provoke contraction of the trachea. This differential sensitivity of the isolated lung and trachea of the cat may be useful for following the temporal release of mediators during anaphylaxis.

The isolated lung strip preparation has several advantages over conventional *in vitro* methods. It uses that part of the tracheobronchial tree which contributes most to the changes in compliance observed using *in vivo* techniques (Konzett & Rossler, 1940; Widdicombe, 1963). Furthermore, the preparation exhibits an active tone against which bronchodilator drugs may be tested, whereas the cat isolated trachea does not. The size of the organ permits a dozen or more tissues to be obtained from a set of lungs, thereby providing an adequate number of control and test strips. Insofar as this preparation has been tested to date, its usefulness as a model for investigation of pharmacological control of small airway function is indicated.

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