Stimulation of the vagal nerves resulted in a contraction of the stomach and a displacement of McEwen's solution from the lumen of the stomach into the reservoir. Hyoscine (0.3 μM) converted the contraction into a relaxation; the increase in volume of the stomach following vagal stimulation (5 Hz for 10 s) was 2.0 ± 0.4% (s.e. mean, $n=13$; resting volume 29 ± 6 ml). In the presence of hyoscine, relaxations were consistent for 30 hours.

Drugs, dissolved in 0.1 ml McEwen's solution, were injected via the coeliac axis and followed by 0.4 ml McEwen's solution. Relaxations induced by (−)-noradrenaline (0.1–10 nmol) and ATP (0.1–10 μmol) were rapid in onset and produced a maximum effect within 10 seconds. The relaxations resembled the responses to vagal stimulation the presence of hyoscine. The drug-induced relaxations were not tachyphylactic and were not antagonized by tetrodotoxin (0.3 μM). The preparation was more than 80 fold more sensitive to noradrenaline and more than 30 fold more sensitive to ATP when the drugs were injected via the coeliac axis than when added to the McEwen's solution in the organ bath.

Reference

BEANI, L., BIANCHI, C. & CREMA, A. (1971). Vagal non-adrenergic inhibition of guinea-pig stomach. *J. Physiol., Lond.*, **217**, 259–279.

Regional perfusion of the airways of guinea-pig lung: a selective action of histamine on the smooth muscle of the small airways

SUSAN P. BESWICK,
JACQUELINE S. DAVIES & P. GOADBY

Department of Pharmacology, School of Pharmacy, Sunderland Polytechnic, Sunderland SR1 3SD

The direct actions of drugs on the smooth muscle of lung have usually been investigated using muscle of the larger airways (Castillo & de Beer, 1947; Coleman & Farmer, 1970) despite evidence from experiments *in vivo* that the principal site of action is the fine peripheral airways (Drazen & Austen, 1974). The actions of histamine and acetylcholine on the perfused airways of guinea-pig lungs have been investigated using modifications of the preparation of Sollman & Von Oettingen (1928).

Lungs were removed from guinea-pigs (350–650 g) and washed free of blood with Krebs solution (NaCl, 119; KCl, 4.7; $CaCl_2$, 2.5; MgCl 1.2; $NaHCO_3$, 25.0; NaH_2PO_4 1.2; glucose 11.5 mM) via a cannula in the pulmonary artery. Whole lungs were perfused via a polythene cannula tied into the trachea, the tip lying about one-third of the distance from the larynx to the bifurcation of the major bronchi. The fluid escaped from fine scarifications on the surface of the lobes. Half lungs were cannulated through the lower trachea and the cannula tied into the bronchus so that the tip lay 2–4 mm beyond the bifurcation. Single lobes were perfused via a fine cannula introduced through the bonchus such that the tip lay in the centre of the lobe; all other lobes were tied off and removed. Preparations were suspended in a constant temperature chamber and perfused with Krebs solution gassed with 5% CO_2 in O_2 at 5, 2.5 and 2 ml/min respectively. Perfusion pressure was measured by a transducer attached to a side arm above the cannula. Agonists were injected into the perfusion fluid in volumes of 0.1 ml through a thick-walled elastic tubing between the side-arm and the cannula.

Acetylcholine (100 ng–200 μg) and histamine (10 ng–100 μg) caused dose-dependent increases in perfusion pressure in all preparations. The order of sensitivity to both agonists was left lower lobe > right lower lobe and upper lobes ≥ half lungs > whole lungs (ED_{50} for histamine = 25 : 141 : 141 : 4000 ng respectively and for acetylcholine = 0.63 : 3 : 14 : 18 μg respectively). Also the maximum pressure attained with left lower lobes (mean ± s.e. = 155 ± 18 mm Hg; $n=14$) was greater than that attained with other preparations (66 ± 10 mmHg; $n=20$).

The greater sensitivity of perfused lobes compared with whole lungs to histamine (ratio ED_{50} $s=16$) against acetylcholine (ratio ED_{50} $s=2.9$) suggests that histamine has a relatively greater effect on smaller airways. In addition, the perfused single lobe provides a very sensitive simple preparation for the study of drugs on the smooth muscle of small airways.

References

CASTILLO, J.C. & de BEER, E.J. (1947). The tracheal chain. *J. Pharmac. exp. Ther.*, **90**, 104–109.

COLEMAN, R.A. & FARMER, J.B. (1970). A new preparation of the isolated intact trachea of the guinea-pig. *J. Pharm. Pharmac.*, **22**, 46–50.

DRAZEN, J.M. & AUSTEN, K.F. (1974). Effects of intravenous administration of slow reacting substance of anaphylaxis, histamine, bradykinin and PGF on pulmonary mechanics in the guinea pig. *J. clin. Invest.*, **53**, 1679–1685.

SOLLMAN, T. & von OETTINGEN, W.F. (1928). Bronchial perfusion of isolated lung as a method for studying pharmacological reactions of bronchiolar muscle. *Proc. Soc. exp. Biol.*, **25**, 692–695.