1/intercept (Furchgott, 1966). The K_a values for isoprenaline (n = 8), orciprenaline (n = 4) and terbutaline (n = 4) were 6.25×10^{-8}, 7.57×10^{-6} and 11.31×10^{-4} M on rate and 8.96×10^{-8}, 5.48×10^{-6} and 7.67×10^{-4} M respectively on tension. There was therefore no difference in affinity of these agonists for the β-adrenoceptors mediating rate and tension responses.

The efficacy of orciprenaline and terbutaline relative to isoprenaline were determined by replotting the initial dose-response curves for the agonist compared with isoprenaline. The response to each concentration of agonist was plotted against the negative logarithm of the fraction of active receptors (RA/Rt) occupied by the agonist ($RA/Rt = A/K_a + A$). The relative efficacy was the antilogarithm of the distance between the agonist curve and corresponding isoprenaline curve along the RA/Rt axis. Terbutaline (1.33) and orciprenaline (1.78) had greater relative efficacy values than isoprenaline on rate, in spite of their lower affinities. Indeed, in the presence of carbachol, orciprenaline produced a greater maximum response than isoprenaline. This confirms the suggestion of O'Donnell & Wanstall (1977). On tension, their relative efficacies were lower than isoprenaline (orciprenaline 0.56; terbutaline 0.21) and this may explain their lower maxima on tension than on rate. The replotted rate curves for all agonists were to the left of those for tension which may indicate that their rate selectivity is due to a greater efficacy.

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A study on potassium-depolarized trachael chain preparations from guinea-pigs

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The extraneuronal uptake (ENU) inhibitor drugs phenoxybenzamine (PHB) and metanephrine (MN) potentiated responses to isoprenaline on guinea-pig tracheal chain preparations (O'Donnell & Wanstall, 1976) but not on guinea-pig uterine preparations (Anning, O'Donnell & Wanstall, 1978). The uterine preparations, unlike the tracheal preparations, were depolarized by immersion in K^+-Krebs solution (Krebs solution in which all the sodium was replaced by the equivalent amount of potassium) in order to induce tone. Fluorescence histochemical experiments indicated that the smooth muscle of both trachea and uterus could accumulate isoprenaline extraneuronally, but in both tissues the accumulation was markedly reduced if K^+-Krebs solution was used instead of normal Krebs solution (Anning *et al.*, 1978). Thus it was postulated that the failure of ENU inhibitor drugs to potentiate isoprenaline responses on K^+-depolarized uterine preparations was due to the use of the K^+-Krebs solution. The present study was carried out to see if data to substantiate this hypothesis could be obtained on trachea. Therefore pharmacological experiments have been carried out using K^+-depolarized tracheal chain preparations from guinea-pigs. In particular the effects of PHB or MN on responses to isoprenaline on K^+-depolarized tracheal

preparations have been compared with the effects of PHB on intrinsic tone preparations (preparations allowed to gain tone spontaneously) and the effects of MN on carbachol-contracted preparations (carbachol, 1 μM) respectively.

All tracheal chain preparations were taken from reserpinized guinea-pigs and set up in the appropriate Krebs solution at 37°C and aerated with 95% O_2 and 5% CO_2. Cumulative concentration-response lines to isoprenaline were obtained. From each line the molar concentration producing 50% of the maximum response in that line was determined (EC_{50}). Changes in sensitivity to isoprenaline are expressed as the mean (±s.e. mean) of differences between paired values of log EC_{50} for isoprenaline before and after ENU inhibitor drug. K^+-depolarized preparations, like carbachol-contracted preparations, were less sensitive to isoprenaline than intrinsic tone preparations. The maximum responses to isoprenaline and the slopes of concentration-response lines were lower on K^+-depolarized preparations than on intrinsic tone or carbachol-contracted preparations. The pA_2 values for propranolol and butoxamine against isoprenaline on K^+-depolarized preparations were 8.30 (slope = 0.95 ± 0.06, $n = 15$) and 5.81 (slope = 0.81 ± 0.18, $n = 16$) respectively. There was no potentiation (−0.07 ± 0.10 log units, $n = 5$) of isoprenaline responses by PHB (50 μM for 30 min followed by washout) on K^+-depolarized preparations compared with significant ($P < 0.001$) potentiation (0.49 ± 0.05 log units) on paired intrinsic tone preparations. There was also no potentiation (−0.13 ± 0.03 log units, $n = 5$) by MN (10 μM for 30 min) on K^+-depolarized preparations compared with significant ($P < 0.001$) potentiation (0.32 ± 0.04 log units) on the paired carbachol-contracted preparations.

The results support the hypothesis that when K^+-Krebs solution is used ENU is reduced and, as a result, ENU inhibitor drugs no longer potentiate responses to isoprenaline. Thus, the inclusion of a drug to inhibit ENU would not be necessary when using K^+-depolarized tracheal preparations in β-adrenoceptor studies.

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Evidence for a vagosympathetic bronchodilator reflex initiated by prostaglandin $F_2\alpha$

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The broncho-constricting action of intravenous prostaglandin $F_2\alpha$ (PG $F_2\alpha$) can be enhanced following β-adrenoceptor blockade, induced with propranolol, in the guinea pig (James, 1969). But Frey & Schäfer (1974) failed to demonstrate such potentiation in vagotomised cats.

In an attempt to identify a vago-sympathetic bronchodilator reflex, we have investigated the bronchomotor reactions of PG $F_2\alpha$ under normal and vagotomised conditions, with and without β-adrenoceptor blockade induced with propranolol (1 mg/kg). Experiments were performed to test the actions of injected PG $F_2\alpha$ intravenously and to compare the broncho-reactivity of this substance with histamine under identical physiological conditions.

Male Dunkin Hartley guinea pigs (450–530 g) were anaesthetized with a combination of diazepam (3 mg/kg i.p.) and fentanyl and fluanisone (0.5 ml/kg i.m.), paralysed with gallamine (4 mg/kg i.v.) and maintained under artificial respiration after tracheostomy. Respiratory resistance was measured by a forced oscillation technique (Goldman, Knudson, Mead, Peterson, Schwaber & Wohl, 1970). An oscillation frequency of 6 Hz was used; resistance was measured during 20 s periods of apnoea at end expiration and was commenced 5 s after histamine injection and 10 s following PG $F_2\alpha$.

Intravenous administration of PG $F_2\alpha$ (1–4 μg) in normal animals produced a 15% increase in respiratory resistance (307 ± 19 to 356 ± 24 cm H_2O l^{-1} s) (14 tests in 5 animals); following bilateral cervical vagotomy, PG $F_2\alpha$ produced a 36% increase in resistance (302 ± 19 to 410 ± 32 cm H_2O l^{-1} s; $P < 0.05$).