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; $P < 0.05$).

A dose of PG $F_2\alpha$ (500 ng – 2 μg), which was necessary to produce a 9% increase in resistance in normal animals (248 ± 10 to 271 ± 11 cms H_2O l^{-1} s), produced a 38% increase following β-adrenoceptor blockade (411 ± 10 to 567 ± 36 cm H_2O l^{-1} s) (10 tests in 4 animals; $P < 0.001$). However, following vagal section and in the presence of β-adrenoceptor blockade, there was only an 18% increase in respiratory resistance following an identical dosage of PG $F_2\alpha$ (346 ± 31 to 410 ± 35 cm H_2O l^{-1} s; $P < 0.001$).

Histamine induced broncho-constriction (2–10 μg), in marked contrast to PG $F_2\alpha$, produced less increase in respiratory resistance following bilateral cervical vagotomy. The potentiated increase in resistance produced by histamine in animals treated with propranolol persisted after the vagi were cut.

In conclusion, we suggest that prostaglandin $F_2\alpha$ initiates a vago-sympathetic reflex which modifies airway tone. This is shown by (1) its greater bronchoconstrictor action in vagotomised animals and (2) a potentiation of broncho-constriction with β-adrenoceptor blockade only when the vagi were intact.

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Differential inhibition by PGE_1, PGE_2 and endoperoxide analogue U46619 of secretion from the rat isolated gastric mucosa stimulated by histamine, pentagastrin and methacholine

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Prostaglandins of the E-series inhibit secretory responses to various stimuli including histamine, pentagastrin and vagal stimulation *in vivo* (Nezamis, Robert & Stowe, 1971). We have investigated the direct effects of these agents and the endoperoxide analogue U46619 (Bundy, 1975) on the rat isolated gastric mucosa stimulated by various secretogogues.

Paired mucosae were obtained from each rat (Main & Pearce, 1978a). Drugs were added to the serosal bathing solution and four responses were obtained in each preparation (30 min contact) separated by 60 min washout periods. Randomly allocated to control and test groups, one preparation was used to monitor time-dependent changes in responses and the other treated with inhibitor for 30 min preceding the second response.

In the presence of PGE_2 (2×10^{-6} M) the response to histamine (H, 5×10^{-5} M, $n = 7$) was reduced to 20 ± 6% (mean ± s.e. mean) of that in the parallel controls. The third and fourth responses recovered to 38 ± 7% and 92 ± 13% respectively. In contrast, PGE_2 did not inhibit the response to pentagastrin (P, 1.8×10^{-8} M, $n = 5$) during contact, but decreased the third response to 52 ± 10%. Prolonged contact with PGE_2 (2×10^{-6} M, 240 min, $n = 4$) caused progressive inhibition of P, decreasing to 53 ± 15% and 24 ± 7% at the third and fourth responses. A higher concentration (2×10^{-5} M, $n = 4$) caused a fall to 18 ± 6% at the third response. PGE_2 (2×10^{-6} M) had no immediate effect on methacholine (M, 5×10^{-7} M, $n = 6$), although the third response was reduced to 41 ± 14%. When added 15 min after H or M, PGE_2 (2×10^{-6} M, $n = 6$ for all groups) decreased the response to H at 30 min but had no effect on M over the same period. Responses to dibutyryl cyclic-AMP were unaffected.

Similar effects were observed with PGE_1 (2×10^{-6} M, $n = 4$) and U46619 (2×10^{-5} M, $n = 3$). Second responses to H were reduced to 19 ± 11% and 11 ± 6%, while no inhibition of P was observed until the third response (62 ± 19% and 37 ± 15%, respectively).

These results show that PGE_2, E_1 and U46619 are qualitatively similar in their inhibitory effect on acid secretion and confirm that the latter substance is less potent (Frame & Main, 1977). In a concentration which caused immediate inhibition of histamine, PGE_2 had only a delayed effect on pentagastrin. This differential effect has not been reported for the rat (Main & Whittle, 1973) or other species *in vivo*. In this *in vitro* preparation, metiamide (10^{-5} M), which abolishes responses to histamine, only partially inhibits pentagastrin (Main & Pearce, 1978b), although *in vivo* it has similar activity against both secretogogues.