The effect of prostaglandin E_1 on isolated bronchial muscle from man

SIR,—The prostaglandins are a family of closely related hydroxy unsaturated C_{20} fatty acids which have been isolated from various mammalian tissues and whose biological properties have been reviewed by Horton (1965). They were originally discovered in semen and in the prostate gland by virtue of their vasodepressor and intestinal smooth muscle stimulating properties (Goldblatt, 1933; Euler, 1934). More recently they have been shown to have inhibitory action *in vivo* on both the reproductive smooth muscle of the rabbit (Horton, Main & Thompson, 1963) and the respiratory smooth muscle of the rabbit and guinea-pig (Main, 1964). *In vitro*, prostaglandins have been shown to relax tracheal muscle from the monkey, cat, rabbit, guinea-pig and ferret (Main, 1964) and myometrial strips from non-pregnant human females (Bygdeman & Eliasson, 1963). There has been no report of the action of prostaglandins on human respiratory smooth muscle and accordingly such a study has been made using prostaglandin E_1 (PGE_1).

Human bronchi were obtained from macroscopically normal parts of human lung which had been removed in surgery for carcinoma of the lung. The lung specimens were transferred to the laboratory in ice-cold oxygenated Tyrode solution. Suitable secondary (lumen diameter 6–8 mm) or third order (lumen diameter 4–6 mm) bronchi were dissected and were used after 24 or 48 hr storage in oxygenated Tyrode solution at 4°. A bronchus was sectioned into rings, the rings cut open, and two or more of these opened rings were tied together in series to form a bronchial strip. The strip was mounted in a 10 ml isolated organ bath and attached to a lever with a magnification of 14 : 1 writing on a smoked drum. The tissue was bathed in oxygenated Krebs (1950) solution containing double strength glucose at a temperature of 37°. The tension on the tissue was about 100 mg, and the tissue was allowed to rest for 30 min before the addition of drugs.

Using the inherent tone of the bronchial strip *in vitro* it was found that PGE_1 produced inhibition of this tone. The threshold concentration was usually 0·25 μg/ml. A typical experiment is illustrated in Fig. 1, when concentrations of 2, 4 and 8 μg PGE_1/ml caused relaxations represented by falls on the tracing of 13, 15 and 25 mm respectively. For comparison, 5 and 10 ng isoprenaline/ml produced falls of 20 and 29 mm respectively.

A similar inhibitory action was seen when PGE_1 was added to the organ bath during a sustained contraction of the bronchial muscle produced by histamine acid phosphate (4 μg histamine base/ml). Fig. 2 shows a typical experiment when concentrations of 1 and 2 μg PGE_1/ml caused 36 and 100% inhibition of

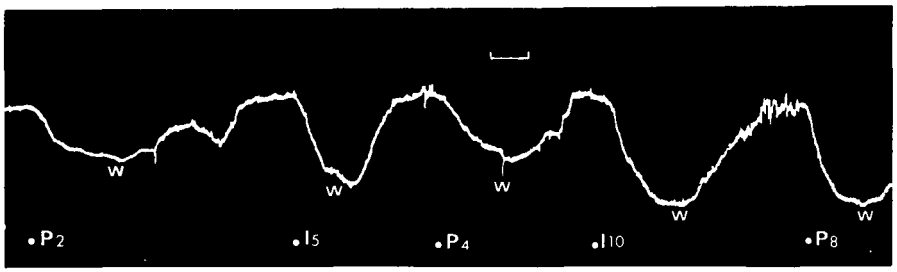

FIG. 1. The inhibitory effect of PGE_1 (P) and isoprenaline (I) on the inherent tone of isolated human bronchial muscle. Doses of P in μg/ml and of I in ng/ml. W: wash. Time scale: 5 min.

the contractile response respectively. For comparison, 2 and 5 ng isoprenaline/ml caused 32 and 100% inhibition respectively.

It was also demonstrated that although the inhibitory effect of isoprenaline was abolished in the presence of the β-adrenergic blocking agent propranolo (0·1 μg/ml), the inhibitory effect of PGE_1 was not affected. Nor did the α-adrenergic blocking agent phenoxybenzamine (10 μg/ml) affect the response to PGE_1.

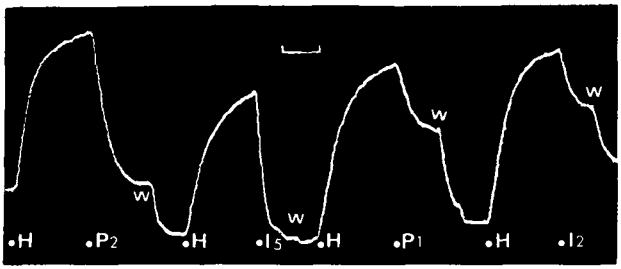

FIG. 2. The inhibitory action of PGE_1 (P) and isoprenaline (I) on contractile responses of human bronchial muscle induced by histamine (H): 4 μg/ml. Doses of P in μg/ml and of I in ng/ml. W: wash. Time scale: 5 min.

Of the isolated tracheal muscle tissues examined by Main (1964), cat preparations were the most sensitive, their tone being inhibited by concentrations as low as 1 ng PGE_1/ml. Pig and sheep preparations were least sensitive and responded irregularly only to doses of 0·25 to 3 μg/ml. In the experiments reported here, isolated human bronchial muscle was inhibited by PGE_1, but the sensitivity was low, concentrations of 0·25 μg/ml and more having to be used. Experiments with adrenergic blocking agents indicate that the inhibitory effect of PGE_1 on human bronchial muscle is not produced by an action on adrenergic receptors.

The prostaglandins found in human bronchi and lung parenchyma by Karim, Sandler & Williams (1967) were F_{2a} (1–50 ng/g) and E_2 (1–8 ng/g). Qualitatively, PGE_1 is similar in its action on cat tracheal smooth muscle to PGF_{2a} and PGE_2, while quantitatively it is at the very least equi-active (Horton, 1965). It is difficult therefore to envisage a physiological role in normal human lung from such small concentrations of prostaglandins.

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