contrast, papaverine and isoprenaline inhibited methacholine in doses approximately 15 times greater than those required to inhibit tone. In both situations the effects of isoprenaline were reversed by washing, as were the effects of papaverine, although the latter were more persistent. The effects of all doses of indomethacin (10 to 320 μg/ml) on methacholine-induced contractions were quickly reversed by washing. However, its effect on intrinsic tone was very persistent, and in many cases could not be reversed at all.

It therefore seems unlikely that the inhibition by indomethacin of tracheal smooth muscle tone is due to non-specific smooth muscle relaxation.

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Anti-inflammatory property of 401, a peptide from the venom of the bee (Apis mellifica L)

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Breithaupt & Habermann (1968) isolated a twenty-two residue peptide from bee venom, which they referred to as a mast cell degranulating peptide. Its primary sequence was reported by Haux (1969) in agreement with that found by Hanson & Vernon (1969), who also determined the position of the disulphide bridges in this peptide which they refer to as 401. These latter workers also observed that this peptide showed anti-inflammatory activity in both the carageenin oedema test and in adjuvant arthritis (Billingham, Hanson, Shipolini & Vernon, unpublished results).

Accumulation of ^{125}I-labelled serum albumin has been used as an indicator of increased vascular permeability in inflammatory responses in skin, joints and paw tissue of the rat. By this method it was demonstrated that subcutaneous injection of 401 (1 mg/kg) markedly reduced increased vascular permeability in response to subplantar injections of carageenin and to intra-articular injections of turpentine. Its efficiency in these tests exceeds that of the conventional non-steroidal anti-inflammatory agents; indomethacin, salicylate and phenylbutazone.

Both 401 and another peptide from bee venom, melittin cause increased vascular permeability following subcutaneous or intradermal injection, and mast cell degranulation *in vivo* and *in vitro*. However, comparable doses of melittin do not result in demonstrable anti-inflammatory activity in these tests, suggesting that the anti-inflammatory activity of 401 is not merely a consequence of its inflammatory and mast cell degranulating properties. 401 is not specific in its anti-inflammatory activity, since responses to intradermal injections of substances such as bradykinin,

histamine, 5-hydroxytryptamine, serum or glandular kallikrein and prostaglandins are reduced or abolished, providing that there is a delay of an hour or more between the subcutaneous injection of 401 and the intradermal skin tests. The anti-inflammatory activity is not markedly affected by denervation of the inflammatory test site; administration of phenoxybenzamine (10 mg/kg) or adrenalectomy. These results indicate that 401 acts by making the peripheral microvascular bed unresponsive to phlogistic agents.

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The fate of salbutamol administered by intermittent positive pressure breathing

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Salbutamol is a selective β_2-adrenoceptor stimulant drug used as a bronchodilator in the treatment of asthma. It is normally given orally (2 mg tablet) or from a pressurized aerosol (0·1 mg/puff). It has become common practice in several centres to treat inpatients by administering a large dose, up to 10 mg, of salbutamol by intermittent positive pressure ventilation and nebulization. It was decided to investigate the fate of tritiated salbutamol (10 mg) given from a 'Bird' respirator, in four asthmatic patients who were receiving this form of treatment. There was an average increase in forced expiratory volume in 1s of 45% (23–67%) and there were no significant side-effects.

Eighty per cent of the dose administered was recovered either from the 'Bird' nebulizer or from the patient's expired air, which was collected during administration of the salbutamol. Of the remainder, the majority was excreted in the urine within 24 h; 50% of this was free salbutamol and the rest was metabolite. This metabolite is the same as that recovered after other routes of administration (Evans, Paterson, Richards & Walker, 1971; Evans, Richards, Walker & Paterson, 1971).

The maximum plasma level ranged from 50–120 nM. There was an initial rapid rise of plasma radioactivity, which at 30 min was greater than half the peak level eventually seen. In this initial phase, the major proportion of plasma radioactivity was free salbutamol. The pattern of absorption and the metabolic data suggest that proportionately more salbutamol reaches the lung when given by intermittent positive pressure breathing than when taken by pressurized aerosol.

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