statistically significant ($P<0.05$). The physiological significance of this observation is obscure.

From the results it can be calculated that the repletion of the plasma kininogen stores proceeded about three times faster in the pregnant group than in either of the non-pregnant groups. This increase in the rate of regeneration of plasma kininogen in 22 day pregnant rats may help to account for the rapid increase in the plasma kininogen towards the end of gestation.

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The effect of indomethacin on the tracheal smooth muscle of the guinea-pig

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Farmer & Coleman (1970) described a preparation of the isolated intact guinea-pig trachea in which alterations in muscle tone were recorded as changes in intraluminal pressure. A high resting intraluminal pressure can be obtained in this preparation (Coleman & Farmer, 1971) and this may be due either to the intrinsic tone of the smooth muscle or to mediators released as a result of the experimental technique.

In the present study, indomethacin (0·05 to 0·8 μg/ml) was found to produce a dose-related relaxation of the tracheal preparation. As indomethacin has been shown to inhibit the synthesis of prostaglandins (Vane, 1971) the possibility was considered that prostaglandins may be involved in the maintenance of the tone of the preparation. However, Northover (1967) showed that indomethacin could inhibit smooth muscle in a non-specific manner, and experiments were carried out to determine whether the observed relaxation of the trachea could be explained in this way. The effects of indomethacin on responses of the trachea to methacholine were therefore compared with its effects on intrinsic tone. The responses to methacholine were inhibited by indomethacin, but only in concentrations approximately 270 times higher than those which inhibited tone (Table 1). In

TABLE 1. *ED_{50} values of the inhibitory effects of isoprenaline, papaverine and indomethacin on (A) the intrinsic tone and (B) methacholine-induced contractions of the guinea-pig tracheal tube preparation*

	(A) Intrinsic tone			(B) Methacholine-induced contractions			Ratio of ED_{50}'s
Drug	No. of tissues	ED_{50} (μg/ml)	95% Confidence limits	No. of tissues	ED_{50} (μg/ml)	95% Confidence limits	B / A
Isoprenaline	7	0·0016	0·0013 – 0·0018	6	0·031	0·022 – 0·042	19·4
Papaverine	8	0·29	0·26 – 0·34	16	3·7	3·1 – 4·4	12·8
Indomethacin	17	0·45	0·33 – 0·63	22	121	106 – 137	269

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,