film whose π-A characteristics have first been established in the absence of the gases. The rates of compression should be slow enough to allow the molecules in the monolayer to maintain "equilibrium" orientations at all areas at which measurements are made. Furthermore, the film should never be compressed beyond the collapse pressure when further expansion-compression cycling of the film is desired.

We have found that when these experimental conditions are adhered to, effects of gases on films that result in small surface pressure changes can be easily detected.

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The effect of bradykinin and anti-inflammatory agents on isolated arteries

SIR,—Bradykinin constricts isolated perfused arteries from guinea-pig lung (Moog & Fischer, 1964) and from rabbit lung (Hauge, Lunde & Waaler, 1964). This vasoconstrictor effect is abolished by phenylbutazone (Klupp & Konzett, 1965), acetylsalicylic acid (Greeff & Moog, 1964), and flufenamic and mefenamic acids (Bauer, Gmeiner & Konzett, 1965) although the antagonism has been shown to be non-specific (Hauge, Lunde & Waaler, 1966). We have now examined the responses of other arteries to these drugs by the method of de la Lande & Rand (1965). Bradykinin and its antagonists were injected through the cannula into the perfusion fluid (McEwen's solution, 1956) which supplied the isolated artery preparation. Histamine, 5-hydroxytryptamine, acetylcholine, noradrenaline and kallidin were our standards of comparison. On occasions, the upper ends of the vessels were stimulated electrically (pulse width 1 msec, strength 10–20 V, frequency 1–20/sec) using bipolar platinum electrodes.

In our hands, also, bradykinin (1–10 μg) constricted the isolated pulmonary artery of the rabbit and the anti-inflammatory agents (sodium phenylbutazone, sodium mefenamate, sodium flufenamate, sodium meclofenamate and calcium acetylsalicylate) antagonised the response when administered by slow infusion (0·1–2·5 mg/min). The same concentrations of antagonists also antagonised the vasoconstrictor responses to histamine (0·1–0·5 μg), 5-hydroxytryptamine (5-HT) (0·1–0·5 μg), acetylcholine (0·2–10 μg) noradrenaline (0·1–0·5 μg) and kallidin (0·2–2 μg), and so it was proved that the antagonism was non-specific. The effects of electrical stimulation were also greatly reduced by the anti-inflammatory agents. In some experiments, tachyphylaxis to repeated doses of bradykinin was noted.

Bradykinin had little or no effect on the ear, femoral, mesenteric, brachial and carotid arteries of the rabbit unless these had been constricted during electrical stimulation. Under these circumstances, bradykinin (1–10 μg), kallidin (0·5–5 μg) and acetylcholine (0·1–1 μg) were all vasodilator in action (see Fig. 1). On the other hand, histamine, 5-HT and noradrenaline were always vasoconstrictor, the contractions they produced being superimposed on those already present when electrical stimulation was applied. Doses of atropine (0·01–0·2 μg) which completely abolished the response to acetylcholine did not modify the responses to bradykinin and kallidin. The ear and mesenteric vessels were the most sensitive of the rabbit arteries responding with dilatation to bradykinin, and tachyphylaxis was not found in any of these preparations. The anti-inflammatory agents did not modify the vasodilator action of bradykinin.

All the seven corresponding arteries of the guinea-pig were constricted by bradykinin (0·1–10 μg), the brachial, femoral and carotid vessels being the most sensitive (see Figs 1 and 2). Histamine (5–20 μg), 5-HT (5–20 μg) and noradrenaline (0·4–10 μg) also constricted the vessels and often markedly potentiated the subsequent bradykinin effect. Doses of mepyramine, bromolysergic acid diethylamide and phentolamine which blocked the responses to histamine, 5-hydroxytryptamine or noradrenaline did not affect those of bradykinin.

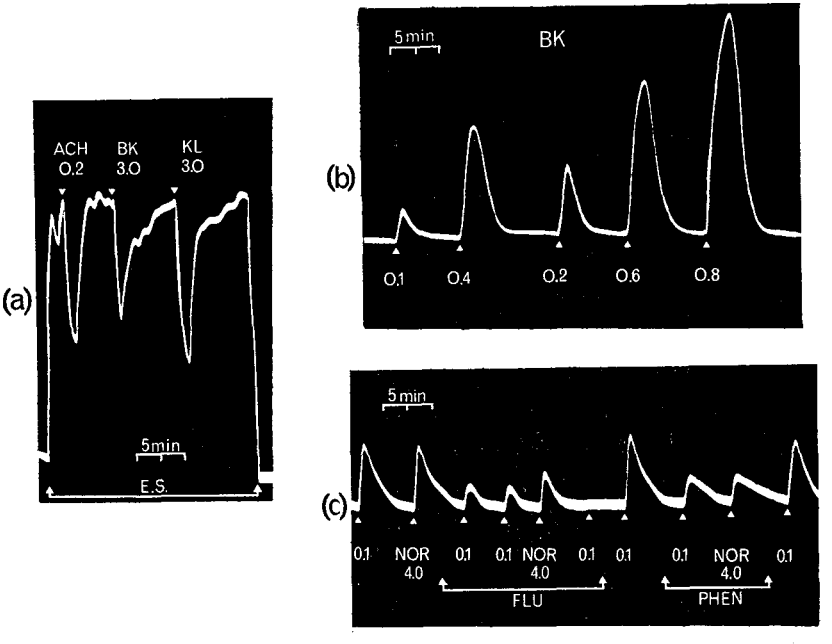

FIG. 1 (a). Effect of bradykinin (Bk, μg) on the isolated rabbit ear artery. Continuous stimulation (E.S.) shown between the arrows. The effects of acetylcholine (ACH, 0·2 μg) and kallidin (KL, 3 μg) are also shown.

(b). Responses of the isolated artery from guinea-pig leg to various doses of bradykinin. Note that bradykinin relaxes the rabbit ear artery but constricts the guinea-pig femoral artery.

(c). Effects of the anti-inflammatory drugs, sodium flufenamate (FLU, 0·64 mg/min) and sodium phenylbutazone (PHEN, 0·64 mg/min), on the responses of the guinea-pig mesenteric artery to bradykinin (0·1 μg) and noradrenaline (NOR, 4 μg).

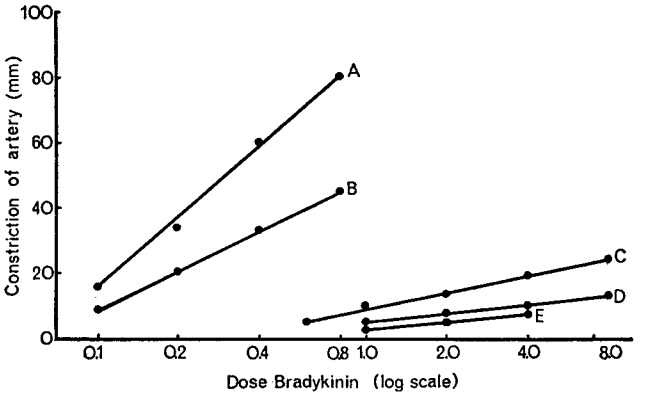

FIG 2. Log-dose response curves for bradykinin (μg) using brachial (A), femoral (B), carotid (C), mesenteric (D) and renal (E) arteries of the guinea-pig.

However, as with rabbit arteries, infusions of the anti-inflammatory agents which blocked the response to bradykinin also blocked responses to the other constrictor agents, and when the infusions ceased, recovery of all the vasoconstrictor actions was immediate (see Fig. 1). On many guinea-pig artery preparations, bradykinin was often 10–50 times more active than noradrenaline. Except on the pulmonary artery, tachyphylaxis to repeated doses of bradykinin was not found.

The seven corresponding arteries of the rat responded to bradykinin like those of the rabbit, only the pulmonary artery constricting. Kallidin was usually about twice as active as bradykinin in these preparations.

It is evident that the vasoconstrictor action of bradykinin on isolated mammalian arteries is antagonised in a non-specific manner by these anti-inflammatory agents. All artery preparations from guinea-pigs were constricted by bradykinin but only those of the pulmonary vessels of the rat and rabbit responded in this way.

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