decreased MBF (by 30 ± 4% of basal, $n = 3$) but had no consistent effect on acid-loss or PD, and a low erosion 'score' was observed after 3 hours. However, during taurocholate perfusion, indomethacin reduced the elevated MBF (to 244 ± 17% of basal, $n = 4$) and led to a high incidence of erosions. The total acid-loss during taurocholate perfusion was 360 ± 50 μEq 3 h^{-1} ($n = 5$), and was 460 ± 40 μEq 3 h^{-1} ($n = 4$) following simultaneous administration of indomethacin (20 mg/kg s.c.).

The acid back-diffusion during combined taurocholate and indomethacin administration was reduced (20 ± 5%, $n = 8$) by the (15S)-15 methyl analogue of prostaglandin E_2 (5 μg $kg^{-1}h^{-1}$ s.c.), in a dose causing 53% inhibition of the erosions (Whittle, 1975). Intravenous infusion of the prostaglandin analogue (5 μg kg^{-1} over 1 h) increased PD (by −6.7 ± 0.9 mV, $n = 3$) and MBF (by 66 ± 13% of basal, $n = 3$) following taurocholate or indomethacin administration, and during resting conditions. Exogenous prostaglandins may therefore prevent erosions by actions on both MBF and mucosal permeability. However, the failure of parenteral indomethacin, alone, to markedly alter resting PD or acid-loss, in doses reducing mucosal prostaglandin levels (Main & Whittle,1975) may argue against a local role for endogenous prostaglandins in the maintenance of the rat mucosal barrier.

These results in the rat suggest that although a reduction in MBF, as observed with parenteral indomethacin, or an increased acid back-diffusion as seen with taurocholate, can lead to a low incidence of mucosal erosions, a combination of both produces extensive mucosal damage. Since several aspirin-like drugs are known to cause acid back-diffusion following intragastric administration, their potency in producing gastric erosions may be related to their concurrent effects on mucosal blood flow.

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The pro-inflammatory activity of E-, A-, D- and F-type prostaglandins and analogues 16, 16-dimethyl-PGE_2 and (15S)-15-methyl-PGE_2 in rabbit skin; the relationship between potentiation of plasma exudation and local blood flow changes

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Potentiation of inflammatory exudation by locally-injected prostaglandins has previously been described in guinea-pigs (Williams & Morley, 1973) and in rats (Moncada, Ferreira & Vane, 1973; Thomas & West, 1973). It was suggested (Williams & Morley, 1973) that this potentiation may be a consequence of the vasodilator activity of prostaglandins (PGs). This possibility has been investigated using a technique for the simultaneous measurement of local plasma exudation and blood flow changes in rabbit skin (Williams, 1975). The technique consists of intravenous injection of [^{131}I]-albumin, followed by intradermal injections of inflammatory agents mixed with ^{133}Xe in saline. After a fixed interval the animal is killed, skinned and punched-out lesions counted in a γ-counter. The ^{131}I counts then give a measure of plasma exudation and $\log_e$ ^{133}Xe counts are inversely proportional to local blood flow. Using this technique it was found that intradermal injections of prostaglandins alone produced insignificant

plasma exudation, as in the guinea-pig, but that addition of PGE_1 or PGE_2 to bradykinin or histamine before i.d. injection produced marked potentiation, in doses of prostaglandin down to a few nanograms. PGE_1 and PGE_2 had similar potentiating potency, as did the analogues 16, 16-dimethyl PGE_2 and (15S)-15-methyl-PGE_2. PGA_1 and PGA_2 showed less potentiating activity. Potentiation was produced by PGD_2 and $PGF_{2\alpha}$ but only at high doses (1 μg/dose). The evidence linking potentiation with vasodilatation is as follows. Firstly, the ranking order of the exudation potentiating activity of the prostaglandins studied, correlated with their vasodilating potency. Secondly, other vasodilators, e.g. adenosine diphosphate (1 μg/dose), produced significant potentiation of histamine responses. Thirdly, PGEs, in spite of their lability, produced prolonged dilatation in skin, and when histamine was administered as a supra-injection (i.d.) 30 min after PGE_2 injection, potentiation was still in parallel with the observed increased blood flow. This was also the case with the more persistent effects of the methylated analogues. Fourthly, addition of vasoconstrictors, e.g. angiotensin II, to histamine/prostaglandin mixtures before intradermal injection reduced local blood flow and reduced exudation potentiation in parallel.

Thus it would appear that in rabbit skin, vasodilatation (perhaps by increasing transmural hydrostatic pressure gradients and vessel wall area), may be responsible for the potentiation of inflammatory exudation produced by prostaglandins.

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The effects of anti-inflammatory steroids on levels of prostaglandin in adipose tissue *in vitro*

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Lewis and Piper (1975) have postulated that anti-inflammatory steroids inhibit the prostaglandin mediated vasodilatation accompanying lipolysis in adipose tissue by preventing the release of prostaglandin (PG). This hypothesis has now been tested further using an *in vitro* system.

Female New Zealand white rabbits were killed and the epigastric fat depots removed. The fat tissue was rinsed in Krebs medium and divided into portions (5g), chopped into pieces about 2 mm^3 and washed three times with Krebs medium. The chopped fat was placed in fresh Krebs medium to a final volume of 10 ml. Each portion was pre-incubated for 20 min at room temperature with or without the anti-inflammatory drug before the addition of $ACTH_{1-24}$ (0.1 μg/ml) and then incubated for a further 120 minutes. After incubation, the Krebs medium was separated by filtration; a fresh volume was added to the chopped fat and again filtered. The two filtrates were combined. The chopped fat was placed in ice-cold ethanol (10 ml) and both the fat and supernatant extracted into ethyl acetate. Since only small amounts of PG were released on incubation with $ACTH_{1-24}$, radioimmunoassay (Hennam, Johnson, Newton & Collins, 1974) using an antiserum which cross-reacted 100% with PGE_2 and 44% with PGE_1, was used to measure the PG content.

In order to provide further evidence of identification of the PG, pooled ACTH stimulated extracts were subjected to thin layer chromatography in the AII system. The plate was then divided into 1 cm zones, silica gel scraped off and PGs estimated on rat stomach strip, chick rectum and rat colon. The activity recovered from the plates corresponded to PGE_2.

The release of glycerol, measured by the method of Eggstein (1966), was used to monitor the lipolytic action of ACTH. The increase of