Prostaglandin production contributes to the contractions of the rat isolated uterus

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Prostaglandins (PGs) can be released by the uteri from several species, including women at term (Karim, 1968), guinea-pigs (Horton, Jones, Thompson & Poyser, 1971) and pregnant rats (Tothill, Rathbone & Willman, 1971). Indomethacin and other non-steroidal anti-inflammatory drugs are potent inhibitors of PG synthesis (Vane, 1971). We have now studied the effect of indomethacin upon spontaneous contractions of the rat isolated uterus and those elicited by agonists.

Uterine horns from virgin rats of the Wistar strain were superfused at 10 ml/min with Krebs solution at 37° C or bathed with De Jalon's solution at 35° C in a 15 ml bath. Submaximal contractions of the uteri were induced by oxytocin or $PGF_{2\alpha}$; indomethacin (0·25–1 μg/ml) was then added to the bathing fluid. Whereas the effects of $PGF_{2\alpha}$ were relatively unchanged (dose ratio $1{\cdot}6 \pm 0{\cdot}5$ (mean $\pm$ S.E.M.; 12 experiments)) the activity of oxytocin was reduced (dose ratio 5 ± 1; 18 experiments).

Prostaglandin output into the bathing fluid (15 ml organ bath Krebs solution 37° C) was also measured using uteri from rats which were 17–22 days pregnant. Bath fluid was withdrawn at 15 min intervals, extracted into acidified ethyl acetate and the acetate phase evaporated in vacuo at 40° C. PG-like activity was assayed in terms of $PGF_{2\alpha}$ on the rat isolated stomach strip, rat colon and chick rectum superfused with Krebs solution containing antagonists (Gilmore, Vane & Wyllie, 1968). PG-like activity (2·1–6·5 (ng/g)/ml of fluid over 15 min) was present in the bath fluid and the output was maintained over a three hour period. Indomethacin (1–4 μg/ml) reduced the output to undetectable amounts within 45 min. At the same time the spontaneous activity of the uteri was abolished.

These results suggest that intramural generation of a PG in the rat isolated uterus contributes to the maintenance of spontaneous activity and to the contractions induced by oxytocin.

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Inhibition of prostaglandin synthesis and functional hyperaemia in rabbit adipose tissue

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When rabbit epigastric adipose tissue is activated by close arterial injection or infusion of fat mobilizing substances, the release of free fatty acids is accompanied by a prolonged vasodilatation (Lewis & Matthews, 1968). In addition it was found

that extracts of activated adipose tissue contained a vasodilator substance (Lewis & Matthews, 1970), and that this substance closely resembled, prostaglandin E_2 (Bowery, Lewis & Matthews, 1970). It was therefore suggested that PGE_2 might be the mediator of functional vasodilatation in adipose tissue.

More recently Vane (1971) has found that prostaglandin synthesis is inhibited by certain anti-inflammatory agents of which indomethacin is one of the most active. This finding has enabled us to test the hypothesis that functional vasodilatation in rabbit epigastric adipose tissue is mediated by a prostaglandin. Bowery *et al.* (1970) had shown that alcohol and ether extracts of stimulated fat pads contained the equivalent of up to 250 ng/g of PGE_2. In the present experiments it was found that after close arterial infusion of indomethacin 10 μg/min for 15 min less than 20 ng/g was detectable in the extracts of stimulated fat depots. Since this level was often found in control unstimulated fat depots the finding showed that this dose of indomethacin inhibited prostaglandin synthesis during lipolysis.

ACTH 1 μg/min infused into the epigastric artery towards the fat depot caused a prolonged vasodilatation ; when the ACTH was infused for 5 min the vasodilator response continued for 30–60 min. If an interval of approximately 1 h was left between infusions, the response was reproducible and little or no tachyphylaxis developed.

When an infusion of indomethacin was made before the infusion of ACTH there was a marked reduction in the vasodilatation. After a 5 min infusion of indomethacin 10–20 μg/min the response to ACTH was reduced to about 45% of the control response, while after a 10 min infusion the response was reduced to 10–20%. Partial recovery of the response occurred 1–2 h after the infusion of indomethacin.

The vasodilator response to PGE_2 itself in the fat depot was not much reduced by a single infusion of indomethacin. After several infusions there was a reduction in the response to several vasodilator substances including PGE_2.

It is concluded that indomethacin not only reduces prostaglandin synthesis in rabbit adipose tissue but also reduces functional vasodilatation in the tissue, lending further support to the view that PGE_2 is mediator of functional vasodilatation in rabbit adipose tissue.

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The effect of some prostaglandins on respiration in rats and cats

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It has been noted that certain prostaglandins can stimulate respiration in humans (Bergström, 1967) and dogs (Said, 1967 ; McQueen & Ungar, 1969). This report is on preliminary experiments performed on four cats and ten rats, anaesthetized with pentobarbitone sodium 36 mg/kg, in order to investigate the actions of prostaglandins on respiration.