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.

Prostaglandins were administered by intravenous or intra-arterial infusion and changes in respiratory rate, tidal volume, respiratory minute volume (RMV) and mean arterial blood pressure during and following prostaglandin administration were calculated. Figure 1 shows the response obtained following I.A. administration of prostaglandin E_1 (PGE_1) to a cat.

The increases in RMV began about 15 sec after an infusion of prostaglandin and the effect persisted for up to 5 min in both rats and cats; PGE_1, PGE_2, PGA_1, all produced increases in RMV. $PGF_{2\alpha}$ and PGA_2 produced variable effects.

Bilateral vagotomy in cats and rats produced very little change in the size of the respiratory response, and in two cats bilateral cutting of the sinus nerves after vagotomy also produced no diminution in the respiratory response to prostaglandin infusion. In one cat, blood pressure compensation (maintaining arterial blood pressure within a few percent of the mean value) did not greatly affect the respiratory response to PGE_1.

Ganglion blocking drugs (hexamethonium bromide 1 mg/kg I.V.; pentolinium tartrate 0·2 mg/kg I.V.) reduced the respiratory effect following administration of PGE_1 and PGE_2 in rats. In some rats the respiratory response to PGE_2 was reduced before that to PGE_1.

It is concluded that prostaglandins can increase respiratory minute volume in rats and cats, and that the mechanism of action does not appear to involve either the arterial baroreceptors or chemoreceptors. The site of action may be within the central nervous system.

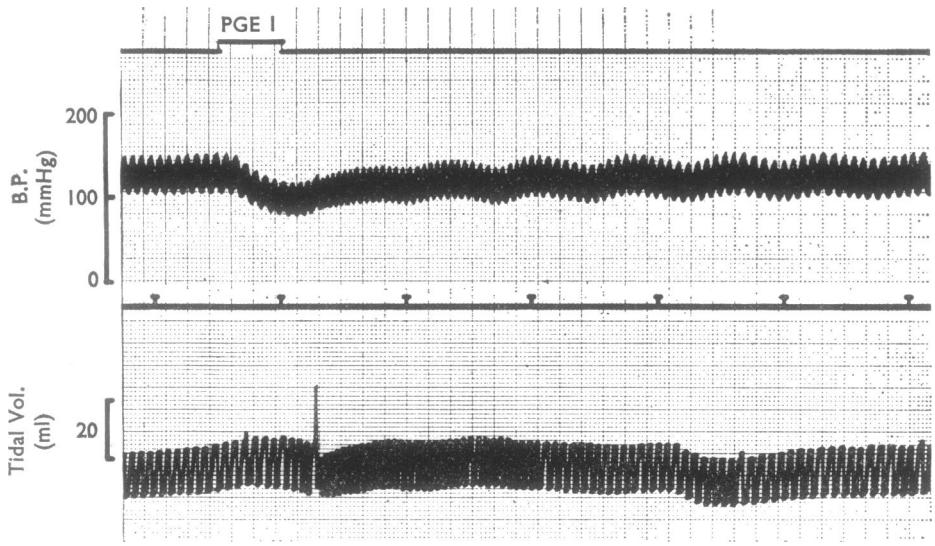

FIG. 1. Cat ♂ 3·6 kg. From above downwards the record shows: marker, I.A. administration of PGE_1, 2·1 μg/kg over a period of 30 sec; arterial blood pressure; one min time marker; and tidal volume.

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