aggregation in order to distinguish between PGE_1 and PGE_2, and to investigate the possible presence of 6-oxo-$PGF_1\alpha$, the stable end-product of prostacyclin (PGX) which would be expected to be produced by these cultured cells (Moncada, Gryglewski, Bunting & Vane, 1976). The 'PGE' fraction did not inhibit platelet aggregation, showing that PGE_1 was not present in significant amounts. Some inhibitory activity was detected in the 'PGF' fraction indicating that 6-oxo-$PGF_1\alpha$ might be present.

Bradykinin (1 μg/ml) increased PGE production during 1 h from a basal level of 5.2 ± 0.7 ng/ml to 13.7 ± 4.0 ng/ml (measured as PGE_2 by RIA, means of four separate cell culture batches). This is a similar phenomenon to that observed with human endothelial cells stimulated with angiotensin II (Gimbrone & Alexander, 1975). Lower doses of bradykinin (1 ng/ml) also significantly increased PGE from 3.9 ± 0.3 ng/ml to 6.6 ± 0.5 ng/ml ($P < 0.01$, Students t-test) (1 experiment, $n = 5$ replicate cultures). Indomethacin (1 μg/ml) reduced PGE production by $33 \pm 5\%$ when given with bradykinin (1 μg/ml) and, in another experiment, by $83 \pm 1\%$ when given as an additional 30 min pretreatment ($n = 5$ replicate cultures in each experiment).

The production of the vasodilators, PGE_2, and possibly prostacyclin, by endothelial cells in culture, may be analogous to situations *in vivo* where the endothelium is regenerating, e.g. in graft vascularization where we have been measuring elevated blood flow by ^{133}Xe clearance (Lewis, Peck, Williams & Young, 1976).

The increase in prostaglandin production in cultured endothelial cells induced by vasoactive substances such as bradykinin, may be related to prostaglandin production in inflammatory responses *in vivo*, and to prostaglandins detected in perfusates from tissues *in vitro*. (Results: mean ± s.e. mean)

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The cardiovascular and uterine effects of labetolol in conscious normotensive pregnant rats

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Labetolol, an antagonist at both α- and β-adrenoceptors (Farmer, Kennedy, Levy & Marshall, 1972) has been shown to be an effective hypotensive agent in hypertensive dogs and rats (Brittain & Levy, 1976) suggesting a clinical use in hypertension. This work investigates the effects of labetolol in the conscious, normotensive pregnant rat on blood pressure and uterine activity.

Pregnant rats (Sprague-Dawley) were prepared with an intrauterine microballoon and jugular cannula on Day 19 of gestation (Day 1 = Day of mating) as described previously (Whalley & Riley, 1977). A polyethylene cannula (PP50 tubing) was also placed in the carotid artery for recording blood pressure. The three tubes were exteriorized through a stainless steel template sewn subcutaneously in the back of the neck. Uterine activity and blood pressure were recorded by Bell and Howell pressure transducers and displayed on a Grass polygraph recorder. Uterine activity was quantified by means of a polygraph integrator (model 7P10B). Cardiovascular effects were recorded on Day 20 and uterine activity recorded continuously from Day 20 up to parturition.

The maximum fall in blood pressure after giving labetolol as a bolus dose intravenously on day 20 of gestation was 18.0 ± 5.1 mmHg ($n = 6$) after 1 mg/kg and 26.4 ± 3.4 mmHg ($n = 6$) after 10 mg/kg. No effect on uterine activity was observed on Days 20, 21 or 22 of gestation (given daily from day 20) with 1 mg/kg labetol ($n = 6$). Small transient increases in uterine activity were observed on each day after labetolol (10 mg/kg).

In a separate group of rats having only a intrauterine balloon and jugular cannula parturition was allowed to commence.

Labetolol was given as a bolus injection intravenously after the 2nd or 3rd pup had been delivered. Parturition was arrested and prolonged in 2 out of 4 rats with 1 mg/kg and in 3 out of 4 rats with 10 mg/kg labetolol. These preliminary results suggest that labetolol in normotensive conscious pregnant rats is an effective hypotensive agent with little effect on uterine activity pre-partum, but which can interfere with the parturient process.

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Action of bradykinin on isolated rat whole uterus and longitudinal myometrial strip

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Bradykinin has been shown to release prostaglandins in a variety of organs including canine kidney (McGiff, Terragno, Malik & Lonigro, 1972), cat spleen (Ferreira, Moncada & Vane, 1973) and rat intestine (Crocker & Willaroys, 1976). Prostaglandins have been suggested to play a key role in myometrial contractility (Vane & Williams, 1973). The endometrium at least in the pregnant rat appears to be the major source (Williams, Sneddon & Harney, 1974).

This study describes a technique for obtaining a longitudinal myometrial preparation and investigates the action of bradykinin on the uterus. Virgin oestrous rats, 150–200 g were used. Uterine horns were mounted in a 15 ml organ bath containing Garcia de Jalons solution at 31°C and bubbled with 95% O_2 and 5% CO_2. A resting tension of 0.5 g was applied to each tissue, and isometric contractions recorded on a pen recorder. Myometrial preparations were obtained as follows. Uteri were everted and a glass rod placed in the lumen. With fine forceps, endometrial tissue was carefully removed intact. Histological studies demonstrated good separation with cleavage occuring mainly in the circular muscle band, resulting in a myometrial preparation consisting mainly of longitudinal muscle fibres. Myometrial preparations were set up as for whole uteri. Concentration-effect curves obtained with acetylcholine and prostaglandin $F_{2\alpha}$ were similar on both preparations, with the same maximal tensions being developed. The concentration-effect curve to bradykinin on the myometrial preparation was shifted to the right with a mean reduction of 12.9% of the maximal tension produced compared to that seen on the whole uterus. Indomethacin (10 μg/ml) depressed the maximal response of the whole uterus to acetylcholine by $9.9 \pm 2.2\%$ ($n=5$), to prostaglandin $F_{2\alpha}$ by $6.0 \pm 2.5\%$ ($n=6$) and to bradykinin by $18.3 \pm 3.3\%$ ($n=6$). The antagonism of bradykinin by indomethacin was significantly greater ($P<0.05$) from that of acetylcholine and prostaglandin $F_{2\alpha}$.

After obtaining constant maximal responses of the myometrial preparation to bradykinin and acetylcholine, prostaglandin $F_{2\alpha}$ (10 ng/ml) was added to the bath for 1 min and then washed out. Bradykinin and acetylcholine were then repeated. The maximal response to bradykinin was potentiated by $11.6 \pm 2.8\%$ ($n=4$) whereas that of acetylcholine only by $1.3 \pm 0.8\%$ ($n=4$).

These results suggest that the action of bradykinin on the uterus involves both a direct action on the myometrium and an indirect action via release of prostaglandin(s) from the endometrium.

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