Stimulation of uterine activity by administration of 
prostaglandin F-2α during parturition in sheep

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In sheep, prostaglandin (PG) F-2α concentrations rise in uterine venous plasma and in myometrium 
and maternal cotyledons before dexamethasone-induced parturition (Liggins & Grieves, 1971). 
As in many other species these high PGF-2α concentrations are thought to play a role in stimulating 
uterine contractions (Thorburn, Nicol, Bassett, Shutt & Cox, 1972). The experimental evidence to 
date does not support an acute effect of PGF-2α in the pregnant ewe (Liggins, Grieves, Kendall & 
Knox, 1972; Oakes, Mofid, Brinkman & Assali, 1973; Keirse et al., 1973). However, a positive effect 
of chronic PGF-2α administration on uterine contractility has been reported (Liggins, Fairclough, 
Grieves, Kendall & Knox, 1973); in this case the myometrial sensitivity to oxytocin was greatly 
increased after PGF infusion for 12 hr and spontaneous uterine contractions were observed after 
24 hr of treatment. This report describes experiments designed to determine whether PGF-2α can 
exert an acute effect on uterine activity during parturition in sheep.

Aortic, amniotic, fetal and uterio-ovarian venous catheters were established in 5 ewes between 
Days 128 and 137 of gestation. All animals gave birth to live lambs. Intra-fetal dexamethasone 
administration was used to induce parturition in 4 of these animals; in such ewes the endocrine 
changes are similar to those associated with spontaneous parturition at term (Liggins et al., 1972; 
Thorburn et al., 1972). Dexamethasone was infused at a rate of 1–3 mg/24 hr into the fetal vena cava 
through a catheter inserted via a tarsal vein. For these 4 animals the mean (±S.D.) time from 
induction to parturition was 41±9 hr. The fifth animal gave birth spontaneously on Day 144 of gesta-
tion. The concentrations of progesterone, total unconjugated oestrogens and PGF were measured 
by radioimmunoassays as previously described (Flint, Anderson, Patten & Turnbull, 1974; Mitchell, 
Flint & Turnbull, 1975). Serial infusions of PGF-2α were performed via the maternal aorta, with 
PGF-2α (THAM salt) being infused at a rate which resulted in uterine venous plasma PGF levels 
similar to those found previously at term (Table 1).

| Table 1. | Hormone levels in the utero-ovarian venous plasma of Ewe 1 during and 4 hr after 
(figures in parentheses) experiment |
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<td>Exp.</td>
<td>Time before induced parturition</td>
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<td></td>
<td>(hr)</td>
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<tr>
<td></td>
<td>Progesterone (ng/ml)</td>
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<tr>
<td></td>
<td>Total unconjugated oestrogens</td>
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<tr>
<td></td>
<td>(pg/ml)</td>
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<td></td>
<td>PGF (ng/ml)</td>
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<tr>
<td>1</td>
<td>48</td>
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<tr>
<td>2</td>
<td>28</td>
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<td>3</td>
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The response to intra-aortic infusion of PGF-2α was similar in all 4 treated ewes (3 induced parturi-
tions and one of natural onset). The results for one of these animals are shown in Plate 1 and Table 1. 
In the fifth animal the infusion catheter was inserted to a point posterior to the junction of the iliac 
and uterine arteries: infusion of PGF-2α (125 µg/min) in this animal and intra-aortic saline infusion 
in another produced no change in uterine contractility (results not shown). There were no changes in 
the concentrations of progesterone and total unconjugated oestrogens in uterine venous plasma 
samples taken during the first infusion in Ewe 1 (Plate 1). The pressure recordings were analysed
manually in terms of Montevideo units as defined by Caldeyro-Barcia et al. (1957), i.e. the product of intensity (rise in pressure in mmHg each contraction produces in the amniotic fluid) and frequency (number of contractions/10 min). The results for the total experimental period were averaged for comparison with the total control period. The amplitude of contraction was taken as the distance between peak and base of each contraction. Intrauterine pressure changes in response to PGF-2α showed a characteristic pattern in all 4 treated animals, an initial hypertonus being followed by increased uterine contractility. Closer to parturition there was an apparent increase in response in all the ewes, the effect being both greater and longer lasting. There was a mean tenfold stimulation of uterine activity during the infusions compared to the relevant control periods ($P < 0.005$, one-tailed $t$ test).

The immediate effect of PGF-2α on uterine activity may have been missed by previous investigators because too low a dose was given. From this study it appears that, apart from an indirect effect on the ovine myometrium by a lowering of the oxytocic threshold, PGF-2α can also exert an acute effect on uterine contractility. This is consistent with the idea that the surge of PGF-2α at term is the final impetus for fetal expulsion in the sheep.

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References


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Intra-amniotic pressure recordings during five experiments in Ewe 1, which gave birth to twin lambs 53 hr after the start of intra-fetal dexamethasone infusion. Intra-aortic infusion of PGF-2α at 94 μg/min began at A and ended at B. The pattern of contractility shown before starting PGF-2α infusion was typical of that observed during the preceding 30 min.