Equine Reproduction V

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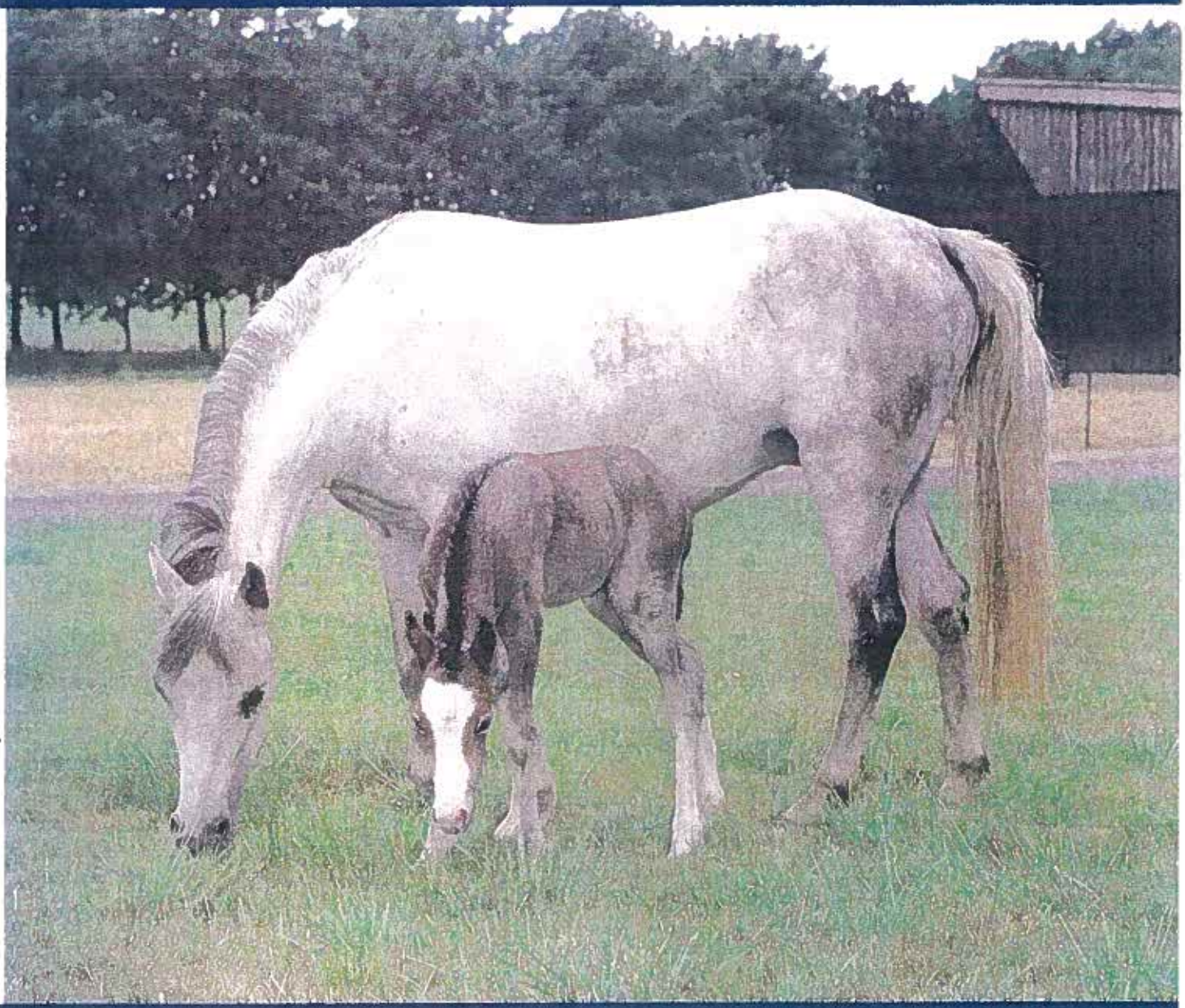

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The role of endogenous prostaglandin release in abortion in mares induced by $PGF_{2\alpha}$ analogue administration

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Introduction

The aim of this study was to examine the role of endogenous $PGF_{2\alpha}$ secretion in abortion induced by a $PGF_{2\alpha}$ analogue (cloprostenol). During the period of equine chorionic gonadotrophin (eCG) secretion, the termination of pregnancy can be affected by the administration of $PGF_{2\alpha}$ or an analogue (Varner *et al.*, 1988; Kasman *et al.*, 1988). Because progesterone of luteal origin is no longer required for maintenance of pregnancy after Day 80 of gestation, it appears that luteolysis plays only a minor role in prostaglandin-induced abortion at this time. We postulated that repeated administration of $PGF_{2\alpha}$ or an analogue, during the fourth month of pregnancy results in stimulation of secretion of endogenous prostaglandin, which promotes relaxation of the cervix and contraction of the uterus resulting in expulsion of the fetus.

Material and methods

Six mares, at 82–102 days into pregnancy were injected with a prostaglandin analogue (cloprostenol, 250 μg, i.m.) every 24 h until they expelled the fetus. Two additional mares, at 96 and 110 days into pregnancy, were treated with non-steroidal anti-inflammatory drug, flunixin meglumine, to block endogenous prostaglandin synthesis in conjunction with prostaglandin analogue administration. Flunixin meglumine (500 mg i.v.) was administered every 8 h beginning 15 min before $PGF_{2\alpha}$ analogue injection until the fetus was expelled. Hourly blood samples were collected from the day before $PGF_{2\alpha}$ administration until 6 h after expulsion of the fetus. In addition, hourly blood samples were collected for 60 h from 4 mares, 92, 94, 95 and 97 days into pregnancy, and used as controls. Fetal viability was monitored daily by ultrasonography per rectum. Endogenous $PGF_{2\alpha}$ secretion was monitored by measurement of plasma 15-keto-13, 14 dihydro-$PGF_{2\alpha}$ (Kindahl *et al.*, 1976); progesterone concentration in plasma was measured by enzyme immunoassay (Munro & Stabenfeldt, 1984) and plasma concentrations of conjugated estrogen were measured by radioimmunoassay (Stabenfeldt *et al.*, 1991).

Results and discussion

The 8 treated mares aborted following prostaglandin analogue (n = 6) (average 48·7 h; range 39·5–56 h), or flunixin meglumine plus prostaglandin analogue (n = 2) (28·5 and 29 h) administration. The 4 control mares remained pregnant.

In the 4 control mares, plasma concentrations of progesterone, oestrogen conjugate and PGF-metabolite did not change significantly during the sampling period (60 h). In the 8 treated mares, an increase in $PGF_{2\alpha}$ metabolite concentrations was observed following each $PGF_{2\alpha}$ analogue administration and each rectal palpation after the first $PGF_{2\alpha}$ injection. The amount of $PGF_{2\alpha}$ released was larger (amplitude and duration) after each intervention (prostaglandin administration and palpation per rectum) indicating a cumulative stimulation of endogenous $PGF_{2\alpha}$ secretion. Expulsion of the fetus was preceded by even greater $PGF_{2\alpha}$ secretion, which started several hours before. Flunixin meglumine treatment did not prevent endogenous $PGF_{2\alpha}$ secretion. Oestrogen conjugate values, indicative of the activity of the feto-placental unit, were unchanged until immediately after

expulsion when the levels declined to 0, indicating that prostaglandin treatment did not have a direct deleterious effect on the fetus or placenta. Progesterone concentrations declined during the period of prostaglandin treatment indicating a luteolytic effect of the treatment.

The dosage regime used in 2 pregnant mares was sufficient to block endogenous $PGF_{2\alpha}$ secretion induced by uterine infusion of saline in the non-pregnant mare (Pascoe, 1986), or endotoxin-induced $PGF_{2\alpha}$ secretion in pregnant mares (Daels *et al.*, 1990). Despite the flunixin meglumine treatment, increases in endogenous $PGF_{2\alpha}$ occurred in association with injection of $PGF_{2\alpha}$ analogue, palpation of the uterus and expulsion of the fetus. In fact, abortion occurred about 20 h earlier in flunixin meglumine treated mares as compared to mares injected with $PGF_{2\alpha}$ analogue only. We conclude that the repeated administration of a $PGF_{2\alpha}$ analogue to pregnant mares between 82 and 110 days, results in the secretion of endogenous $PGF_{2\alpha}$ leading to abortion.

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