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STUDIES ON THE ENDOCRINOLOGY OF

PARTURITION IN THE GUINEA-PIG

by

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SUMMARY

A considerable amount of evidence has accumulated in sheep which ascribes to the foetal-pituitary adrenal system an important role in controlling the production of oestrogen, progesterone and prostaglandin F. Similar studies have shown that the foetus plays an important part in parturition in goats and cows but the extent to which these findings can be extended to other species is a matter of conjecture.

The present study investigates the role of the guinea-pig foetus in the endocrinology of late pregnancy and parturition.

The methods used in the study were:

1. Injections of drugs into the immature foetus.
 - (i) Foetal adrenal growth and activity was stimulated by ACTH.
 - (ii) Endogenous levels of glucocorticoids were elevated by corticosteroids.
2. Injections or infusions of drugs into the mother.
 - (i) Maternal adrenal activity was stimulated to investigate the possibility that the site of action of ACTH administered to the foetus is within the maternal compartment.
 - (ii) The effect of raised levels of oestrogen and $\text{PGF}_{2\alpha}$ on myometrial activity and on gestation length was observed. (These hormones mediate the action of cortisol on the sheep myometrium).
3. Observations on foetal adrenal weight.
 - (i) Adrenal weight was measured during normal gestation and after birth to obtain a range with which to compare

the results of hormone treatment.

(ii) Adrenal weight was measured after injections of ACTH, glucocorticoids or oestrogen to mother or foetus.

4. Measurements of levels of hormones circulating in the dam in order to recognise changes reflecting preparation for birth.

(i) The concentration of progesterone, cortisol, prostaglandin F and 15-keto-prostaglandin F were measured during the few weeks before birth in serial samples from chronically cannulated dams. Catheters were placed, using sterile techniques, in either a jugular vein, a carotid artery or the inferior vena cava.

(ii) The pattern of progesterone, prostaglandin F, 15-keto-prostaglandin F and cortisol was measured by competitive protein binding or radioimmunoassay techniques.

5. Estimations of the separation of the pubic symphysis during late pregnancy from x-ray plates.

The results of the study show:

(i) Injection of synacthen (ACTH) into all foetuses of a litter caused adrenal growth and shortened gestation length. Adrenal weight and litter size were possible factors related to premature parturition: Large litters and litters with the greatest combined mass of adrenals tended to deliver earlier. The interpretation of the results, however, were complicated by the use of varying doses of ACTH given to two strains of guinea-pigs. More data are required to relate ACTH-induced delivery to the physiology of parturition in guinea-pigs.

- (ii) Injection of a glucocorticoid (triamcinolone) into all foetuses of a litter was without effect on gestation length. The dose chosen was equivalent in glucocorticoid potency to other analogues effective in causing premature parturition in ruminants and rodents at a similar stage of gestation.
- (iii) Total adrenal weight increased during the last stages of pregnancy. The mean total adrenal weight per litter corrected for body weight declined when plotted against gestational age. In a population of newborns selected for constant litter size, females had larger adrenal glands than males. A population of seven day old guinea-pigs showed no sexual dimorphism in total adrenal weight.
- (iv) Injections of ACTH into nonpregnant, adult guinea-pigs stimulated adrenal growth. The same regimen given to the dam between Day 50 - 54 of gestation did not shorten gestation length. Maternally-administered ACTH did not cause growth of the foetal adrenal glands as seen after intrafoetal injections.
- (v) Injection of a dose of oestrogen greater than the daily production rate of oestradiol in late pregnancy given either at Day 46 - 48 of gestation or just before term did not affect gestation length. Oestrogen injections near term were associated with enlargement of the foetal adrenal glands. The significance of this observation is unknown.
- (vi) Prostaglandin $F_{2\alpha}$ administered as a continuous intra-arterial infusion caused an increase in the sensitivity

of the uterus to oxytocin, an increase in myometrial activity and premature delivery. No sharp fall in progesterone concentration preceded delivery. The number of observations in these experiments was small and the results are only qualitative. Because of the possible importance of $\text{PGF}_{2\alpha}$ in the physiology of parturition more thorough investigations are warranted.

(vii) There was considerable variation both within and between animals in hormone levels.

The mean concentration of progesterone in maternal blood in serial samples collected at the same time of day declined between Day 40 and 55 of gestation and rose during the last ten days of gestation. Progesterone concentration was high (30-450ng/ml) and there was no abrupt fall during the few days preceding birth. Further work is required to establish the pattern on the day of birth.

Prostaglandin F levels rose on the day of birth and at delivery. 15-keto-prostaglandin F levels rose in most animals at delivery. The concentration of the metabolite was lower than prostaglandin F concentration in the same sample. In three animals that aborted post-operatively the levels of prostaglandin F and 15-keto-PGF were high at delivery.

The concentrations of cortisol was very high (1-11 μ g/ml) and showed considerable variation some of which may have reflected responses to environmental conditions.

(viii) During the week before birth the pubic symphysis separated in preparation for delivery of young.

It is concluded that the results of the present study do not resolve the question of the mechanism initiating labour in the guinea-pig. Some evidence was found to suggest that activity of the foetal adrenal was involved but how the products of adrenal secretion might influence uterine contractility remains unknown.

PURPOSE OF THE WORK

The work in this thesis was designed to determine whether the foetal guinea-pig initiates parturition in a way similar to that proposed for the foetal lamb.