

ENDOCRINE REQUIREMENTS FOR IMPLANTATION, MAINTENANCE OF PREGNANCY AND PARTURITION IN THE RABBIT

JONG KUK KWUN

Thesis Submitted for the Degree of Doctor of Philosophy in the University of Sydney

SUMMARY

Experiments were carried out to establish the endocrine requirements for implantation, maintenance of pregnancy and parturition in rabbits ovariectomized the day after induction of ovulation followed by artificial insemination. This was done by replacement therapy and by direct estimation of circulating hormone levels. These were undertaken since, despite considerable literature on the subject, the results of previous workers are contradictory and very few have used adequate numbers of animals.

A series of replacement therapy experiments, using progesterone in varying doses, with or without varying doses of oestradiol, and with variation in the duration of steroid injections, was carried out in rabbits ovariectomized or ovariectomized and adrenalectomized the day after the injection of HCG and artificial insemination. The experiments were designed to observe the percentage implantation on Day 10, the foetal development percentage on Day 30, and the percentage of foetuses alive and the percentage born naturally at term or on Day 38 (Day 1 is the day of ovulation). In addition, the function of 20α -hydroxyprogesterone in early pregnancy and the influence of halothane and pentobarbital sodium anaesthesia were explored.

No implantation occurred without administra-

tion of progesterone on Days 2 to 4 inclusive. 20α -hydroxyprogesterone was a weak inducer of implantation with less than one tenth of the potency of progesterone. Progesterone alone was capable of supporting both implantation and pregnancy, and the absence of the adrenal glands had no effect on such artificially maintained pregnancy.

A low dose of oestradiol produced slight but sometimes significant improvements in implantation and foetal development. The injection of progesterone plus oestradiol beyond Day 29 gave no live births and showed a significantly low percentage of normal parturition. However, the cessation of progesterone injections on Day 29 and continued injections of a low dosage of oestradiol, resulted in normal parturition and gave as good a percentage of live births as in controls. By such replacement therapy, normal implantation, foetal development and near normal parturition has been possible. Halothane anaesthesia did not favour the overall process of implantation or foetal development compared with pentobarbital sodium.

Attempts to measure plasma progesterone and hydroxyprogesterone separately were not successful, so that in natural pregnancy, these compounds were estimated together and called *progestin*. Prior to ovulation, more 20α -hydroxyprogesterone is secreted than progesterone, but others have found that later on, most of the steroid is progesterone.

The blood progestin levels in normal pregnancy and in artificially maintained pregnancy were compared to see how closely the empirically determined replacement therapy copied the natural blood progestin levels. In addition, the preovulatory progesterone secretion rates, the disappearance rate of injected progesterone from the circulatory system of ovariectomized does, oestradiol secretion rates, and the circadian variation of progesterone and oestradiol secretion were investigated.

Circadian fluctuations were observed in oestradiol secretion but not in progesterone. The level of injected progesterone rose rapidly, reached a

plateau in an hour and stayed there for 4~5 hours, thereafter it declined to blank level in 24 hrs. Preovulatory progestin level reached a peak in 2 hrs and declined before ovulation. The mean progestin level in normal pregnancy gradually increased by mid-pregnancy and declined slowly thereafter until term. The progesterone level in artificially maintained pregnancy showed similar patterns to those of progestin in normal pregnant rabbits. The level of oestradiol in normal pregnancy showed a small rise around Days 5 and 6, but remained very low throughout the rest of the gestation period.