

same dose of DL 204 IT administered on Diestrus one to 4-day cycling rats slightly elevate PRL levels when assayed in proestrus or estrus and increased PRL by 350% when assayed in diestrus one or diestrus two. Plasma LH and FSH levels were unchanged by the treatment. Studies in adult male rats were performed using a similar dosage of DL 204 IT and the plasmas were assayed for the same hormones at 24, 48, 72 and 96 h post-injection. LH levels were unaltered but FSH levels were decreased by 26% at the 48 h sampling, although unchanged at other time periods. PRL levels were unaffected during the first 2 post-treatment days but at 72 and 96 h after DL 204 IT injection PRL levels were increased by 200 and 300% respectively. The relationship of these effects on gonadotrophin levels to the biological activities reported previously is unknown, however, it is tempting to speculate that these changes in prolactin and FSH are related to an altered steroid and prostaglandin balance as well as to changes in histamine metabolism induced by DL 204 IT treatment.

18. The influence of hyperprolactinaemia on pulsatile LH and ovarian oestradiol secretion during the follicular phase of the sheep oestrous cycle, A. S. MCNEILLY and D. T. BAIRD, M.R.C. Unit of Reproductive Biology, 2 Forrest Road, and Department of Obstetrics and Gynaecology, Royal Infirmary, Edinburgh

Hyperprolactinaemia, both physiological and pathological, is associated with reduced or absent ovarian cyclicity in the human. Whether prolactin *per se* is directly implicated in this failure of ovarian cyclicity is as yet unresolved although experiments in the ewe [1] suggest that prolactin acts by modulating gonadotrophin release resulting in anovulation, although a direct ovarian effect cannot be ruled out. We have investigated the influence of hyperprolactinaemia on the pulsatile release of LH and subsequent ovarian oestradiol secretion in 12 ewes with ovarian or utero-ovarian transplants [2]. On day 10 of the luteal phase, premature luteal regression was induced by injection of the prostaglandin $F_{2\alpha}$ analogue ICI 80996 (chorprostenol 100 μg i.m.) and blood samples were taken at hourly intervals from both jugular and ovarian veins for the following 108 h. Hyperprolactinaemia was induced by repeated injection of TRH (10 μg i.v.) every 2 h for 58 h after chorprostenol injection in 6 ewes. LH, FSH and PRL were measured in jugular and oestradiol, and progesterone were measured in ovarian vein plasma. Increased secretion of oestradiol during the follicular phase occurred in a pulsatile manner in all ewes studied, and pulses were always preceded by a pulse of LH. Oestradiol secretion in the hyperprolactinaemic group was significantly lower than in controls. However, the time to and duration of oestrus was not significantly different between control and hyperprolactinaemic groups and an ovulatory LH discharge occurred in all animals. No difference in LH pulsatility between hyperprolactinaemic and control ewes was observed, suggesting that the lowered oestradiol secretion may be due to a direct effect of prolactin on the ovary.

References

1. Kann G., Martinet J. and Schirar A.: In *Prolactin and Human Reproduction* (Edited by P. G. Crosignani and C. Robyn) (1977), pp. 140-162.
2. Goding J. R., McCracken J. A. and Baird D. T.: *J. Endocr.* 39 (1967) 37-62.

19. Effects of castration and steroid hormone replacement on the pituitary-thyroid axis in the adult rat, E. ROTT*, A. VAGENAKIS†, D. CHRISTIANSON† and L. BRAVERMAN†, *Istituto di Patologia Medica-Cattedra di Endocrinologia, Universita' di Parma, Italy, and †University of Massachusetts Medical School, Worcester, U.S.A.

We and others have previously reported that the serum TSH response to TRH is greater in women than in men. Studies were, therefore, carried out to determine whether sex-related differences in TSH secretion also exist in the rat. Adult, 75-day-old male (M) and female (F) rats were subjected to sham surgery, orchectomy (Orch), or ovariectomy (Ovar) and sacrificed 10 or 21 days later. In some experiments, castrated rats were treated with physiological doses of sex steroids (E_2 , 0.3 $\mu\text{g}/\text{d}$ or T, 0.3 mg/d) for the final 5 days in the short-term experiments or continuously in the 21 day studies. Baseline serum TSH in all 5 experiments was significantly increased in males (M, 15.7 ± 1.3 , mU/dl vs. F, 5.5 ± 0.6 ; mean \pm S.E.; $P < 0.001$) as was Δ TSH after iv TRH (M, 39.2 ± 3.7 vs. F, 21.9 ± 1.8 ; $P < 0.02$). In contrast, serum T_4 and T_3 concentrations, pituitary TSH, and hypothalamic TRH (RIA) were similar in M and F. Ten days following castration, serum TSH and Δ TSH to TRH were still significantly higher in the Orch males vs. the Ovar females, but were similar 21 days after surgery. Serum TSH and Δ TSH after Orch were significantly decreased as compared to the normal male rat at both 10 and 21 days after surgery. These decreases were partially restored by T. In contrast, ovariectomy, E_2 replacement, and T administration to ovariectomized female rats did not affect TSH or Δ TSH after TRH. Conclusions: Serum TSH concentration is higher in the male rat as compared to the female. This increase is due to enhanced sensitivity of the male pituitary to TRH, probably mediated by T. In contrast, the pituitary-thyroid axis in the female rat is unaffected by ovariectomy and E_2 and T administration.

CENTRAL NERVOUS SYSTEM—II. HUMAN

20. Biphasic action of estrogens in the sensitivity of the anterior pituitary to LH-RH in amenorrhoeic women, J. HORSKÝ, J. HERZMANN and A. ŠTROUFOVÁ, Institute for Care of Mother and Child, Prague, Czechoslovakia

Modulatory action of estrogens on the anterior pituitary appears to be an important and complex problem. This action is dose related and depends on chronic or acute application and other events. Time related changes of estrogen effects were the objects of this study. Sensitivity of the anterior pituitary was tested by serum LH and FSH response (RIA method, kits of Seron, Roma) to 100 μg LH-RH in 9 women with hypoestrogenic amenorrhoea. One week later the retesting was performed 24 h after 5 mg estradiol benzoate i.m. In another similar group of 8 women the retesting was made 48 h after the same dose of estrogen. The maximal increase of LH and FSH in the LH-RH test (Δ LH, Δ FSH) was chosen as the criterion for comparison. We have found a significant decrease of Δ LH i.e. a decrease of sensitivity of the anterior pituitary 24 h after estrogen application. In the second group of experiments a significant increase of Δ LH 48 h after the same dose of estrogen was seen. A similar response (which was not significant) was found in values of Δ FSH. Hence, biphasic time-related phenomenon in the sensitivity of the anterior pituitary to LH-RH after estrogen treatment has been described for the first time in amenorrhoeic women. This fact may have a therapeutical and physiological significance.

21. Comparison of oestradiol and progesterone concentrations in the plasma of infertile women treated with clomiphene and tamoxifen, B. E. SENIOR, M. L. CAWOOD, R. E. OAKLEY, J. M. McRIDDIE and D. R. SIDDLE, Division of Steroid Endocrinology, Department of Chemical Pathology, University of Leeds, and Clayton Hospital, Wakefield, England