

Clomiphene and tamoxifen have both been used in the treatment of infertility but their effects on the concentrations of ovarian hormones in plasma have not been compared. To correct this omission, nine infertile women (three with anovulation and six with suspected luteal phase deficiency) took part in a cross-over trial consisting of one month with placebo treatment, two months with either clomiphene or tamoxifen treatment, a further month with placebo and finally two months with the drug not previously taken. Each drug was administered for 5 days at a low and a high dose level in succeeding months (clomiphene, 50 mg/day and 100 mg/day; tamoxifen, 20 mg/day and 40 mg/day). Blood samples were taken three times in each month (between days 6–8, 11–13, and 18–20) and the concentrations of oestradiol and progesterone were determined by radioimmunoassay. The oestradiol results from all patients while on a given treatment were considered together, irrespective of dose, as there was no significant difference between results at the two dose levels for either drug. The progesterone results were treated in the same way. Both drugs caused a significant shift in the distribution of oestradiol and progesterone concentrations towards values higher than those recorded during placebo treatment (Chi-square,  $P < 0.05$ ). Separate inspection of the data from the anovulatory and the luteal phase deficiency patients revealed that the latter group differed in their response to the two drugs. Treatment with clomiphene, but not with tamoxifen, was associated with excessively high hormone concentrations when compared with values obtained in the normal menstrual cycle, suggesting biochemical hyperstimulation.

**22. Research into any eventual hormonal changes associated with the administration of danazol (D).** C. MAZZI, L. P. RIVA and A. VAILATI, Hospedale Generale Provinciale S. Antonio Abate, 21013 Gallarate, Divisione di Endocrinologia, e Medicina Costituzionale, Italy

This study was carried out to evaluate the levels of certain hypophysial and principal steroid hormones, and the response capacity of the hypophysis to stimulation with Releasing Hormones (GnRH and T&H) following treatment with D.

D was administered in the dose of 600 mg/day for 7 days to 8 women volunteers, aged 32, 33 and 35, suffering from gynecologic disorders. Tests on plasma samples were carried out by radioimmunoassay: FSH, LH, GH, PRL, TSH, oestradiol, progesterone, testosterone and cortisol were evaluated with CEA-IRE-SORIN kits; ACTH using an Amersham, Radiochemical Centre, kit. The following were measured in urine: 17-hydroxycorticosteroids using the Porter and Silber method according to Scholler *et al.*, total 17-keto-steroids with the colorimetric method using the Ketachrome Bio-Rad-kit; androsterone and aetiocholanolone, pregnanediol and pregnanetriol using a gas chromatographic method, total oestrogens using the Ittrich fluorometric method.

Results underlined a decrease in LH secretion; the other prehypophysial hormones, as well as peripheric ones, showed no substantial variations. The response capacity of the hypophysis to stimulation with the RH for FSH, PRL, TSH and GH remained unchanged. This was not so for LH whose level following stimulation with GnRH, is shown below:

Case no.	Before		After	
	Basal	Peak	Basal	Peak
1	1.6	40.0	1.4	26.0
2	3.2	25.4	0.2	14.2
3	2.0	32.3	0.6	19.0

mU · IRP<sub>2</sub>/ml.

On the whole such data does not differ from others to be found in literature. The selective activity of D is confirmed, with particular suppression of the function of the hypothalamo-prehypophysial axis. Wider scale experiments are being carried out in order to obtain more precise verification of the FSH behaviour.

**23. Polycystic ovary syndrome and hyperprolactinemia.** P. FALASCHI, G. FRAJESE, A. ROCCO, V. TOSCANO and F. SCIARRA, Istituto di Patologia Speciale Medica II, University of Rome, Italy

In 1954 Forbes described a syndrome due to a pituitary tumour characterized by oligo-amenorrhoea, galactorrhoea, some degree of obesity, hirsutism and seborrhoea with a high incidence of polycystic ovaries (PCO). More recently Thormer demonstrated that some patients with oligo-amenorrhoea and hyperprolactinemia had polycystic ovaries on gynecography: after bromocriptine treatment gonadal function returned rapidly to normal and the patients became highly fertile. In the present study the behaviour of prolactin (PRL) and sex steroid hormones was evaluated in a homogeneous group of 35 hirsute women with the typical characteristics of PCO. Patients were selected on the basis of the following criteria: oligo-amenorrhoea, enlarged ovaries, high pulsatile LH without mid-cycle peak, normal or low FSH, raised levels of testosterone (T), androstenedione, dehydroepiandrosterone and oestrone but low or-normal levels of oestradiol.

Basal levels of PRL, LH, FSH, T, androstenedione, dehydroepiandrosterone, oestrone and oestradiol were determined on blood drawn at 9.00 a.m. between 6th and 10th day of the menstrual cycle (in those cases presenting dysfunctional uterine bleeding).

PRL levels were elevated in 10 cases ( $29.49 \pm 3.11$  (S.E.) ng/ml, normal range  $< 20$  ng/ml), 28.5% of all subjects studied. In this group a bromocriptine suppression test (2.5 mg  $\times$  3 days, 2.5 mg b.d.  $\times$  3 days and 2.5 mg t.d.s.  $\times$  7 days) was performed. PRL levels dropped to  $3.61 \pm 0.22$  (S.E.) ng/ml after 7 days and to  $1.93 \pm 0.18$  (S.E.) ng/ml after 13 days. T levels during test were:  $107.8 \pm 7.04$  (S.E.) ng/100 ml, in basal conditions,  $57.00 \pm 3.28$  (S.E.) ng/100 ml and  $50.8 \pm 4.66$  (S.E.) ng/100 ml respectively after 7 and 13 days (normal range: 20–70 ng/100 ml).

It is difficult to establish whether in PCO syndrome hyperprolactinemia is primarily due to a hypothalamo-pituitary dysfunction or is a secondary consequence of an abnormal positive feed-back mechanism probably mediated by adrenal and/or ovarian steroids. Hyperprolactinemia could play a role in the pathogenesis of hirsutism probably through a stimulatory action of PRL on androgen biosynthesis, as has been recently postulated by Giusti *et al.*, Besser and Thormer.

The use of bromocriptine in the treatment of some cases of PCO syndrome is proposed. As far as concerns the modifications of hirsutism, however, further studies on the long term administration of the drug are necessary.

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#### OOCYTES AND STEROIDS

**24A.**—see p. xxi.

**24. Short-term culture of mouse Graafian follicles: the effect of steroids on oocyte maturation and atresia.** J. P. P. TYLER and W. P. COLLINS, World Health Organization, Collaborating Centre for Clinical Research on