stood with the exception of cases in which the syndrome is associated with elevated or slightly elevated plasma levels of prolactin.

11 subjects, 7 with the chronic inadequate luteal phase and 4 with a short luteal phase (2 not desiring pregnancy and the others sterile) were studied in detail during a control cycle to define their respective endocrine features. The presence of an LH ovulatory peak was found in 9 cases. All cases demonstrated estradiol (E2) values which, though indicating follicular growth, were slightly lower than expected. The subjects were treated with Epimestrol (3-methoxy-ether-17-epiestriol) at a dose of 5 mg x 2/day for 10 days from the 5th day of cycle. In 7 subjects the treatment induced adequate luteal phase from the first cycle of treatment. One case of inadequate luteal phase gave a short luteal phase. In 2 other subjects an increased daily dose of Epimestrol and/or length of treatment (5 mg x 3/day for 10 days and 5 mg x 4/day for 15 days) induced an adequate luteal phase. Only one case failed to respond. Two subjects became pregnant in the first cycle of treatment. The hormonal assays performed during treatment indicated that E2 levels in the follicular phase were significantly higher than before treatment while no apparent modification was found in basal gonadotropins in 4 cases except for a more marked rise of plasma LH during the ovulatory peak.

Independently of the clear clinical usefulness of Epimestrol treatment for short and inadequate luteal phase, it seems that besides the known effect it has on pituitary gonadotropin secretion in hypogonadic subjects, Epimestrol improves follicular maturation and E2 production probably through a peripheral effect on the response of granulosa cells to endogenous gonadotropins.

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29. Plasma steroid response of pubertal girls to human menopausal gonadotropin (HMG), M. ZACHMANN, B. MANELLA, L. SANTAMARIA, W. ANDLER and A. PRADER, Department of Pediatrics, University of Zurich, Kinderspital, 8032 Zurich, Switzerland, and Department of Pediatrics, University of Essen, Universitätsklinikum, 4300 Essen, Federal Republic of Germany

To study their response to ovarian stimulation, plasma steroids were measured radioimmunologically in 31 girls before and after 5 daily i.m. injections (75 IU of LH and FSH each) of HMG. In normal girls (n = 7; 6 familial tall stature, 1 mild idiopathic hirsutism, age 13 to 18, mean 13.9 years), estradiol (E2) increased from 91 ± 11 (SEM) to 292 ± 26 pg/ml ($P < 0.001$). Estrone (E1, n = 5), testosterone (T), androstenedione, and 17OH-progesterone (17OHP, n = 3) did not change. In XO Turner syndrome (n = 11, age 8-16 years), E2 (47 ± 5 to 55 ± 8 pg/ml), E1 (n = 9) and the other steroids (n = 2) remained unchanged. In XO/XX Turner mosaicism (n = 4, age 12-14 years), there was an insignificant E2- (55 ± 12 to 77 ± 23 pg/ml), and no E1-response. One girl with acanthosis nigricans, virilization, and diabetes mellitus showed no E2-, but a marked T-response (214 to 678 ng/dl). In one girl with congenital adrenal hyperplasia (CAH, 21-hydroxylase deficiency) off treatment, there was no E2-response, and T and 17OHP were high without further increment. In another girl with CAH (3β-hydroxysteroid dehydrogenase deficiency) on adrenal suppression, there was no E2-response, but DHA increased (312 to 450 ng/dl). In 3 patients with isolated gonadotropin deficiency and anosmia, hypergonadotropic hypogonadism, and testicular feminization (gonadectomized) respectively, and in 2 patients with malignancies on cytostatic treatment, E2 and E1 did not respond. It is concluded that this test allows an evaluation of ovarian E2-secretion already in early puberty.

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30. Hyperprolactinemia syndrome, C. ROBYN, Human Reproduction Research Unit, Université Libre de Bruxelles, Hôpital Saint-Pierre, 322 rue Haute, 1000-Brussels, Belgium

Prolactin secretion is normally under permanent inhibitory influence from the hypothalamus. Most of such inhibition, if not all, is due to dopamine. However, hyperprolactinemia is rather frequent. In women, it is associated with menstrual cycle disorders such as amenorrhea, anovulatory bleeding and a short luteal phase. Galactorrhea is a bad marker of the syndrome.

High circulating levels of prolactin are seen in pathological cases (prolactinoma, hyperplasia of the lactotrophs, suppressed inhibition of prolactin release) but also in a physiological condition, i.e. long-lasting lactation. Psychotropic drugs induce hyperprolactinemia by antagonizing the inhibitory effect of dopamine on prolactin release.

Whatever the cause of the syndrome is, it is characterized by anovulation or corpus luteum defect. Prolactin interferes with the control of ovulation both at the hypothalamic and at the ovarian level. Blood flow conveys pituitary hormones to the hypothalamus where the neurones are sensitive to prolactin. The hormone is even found inside some hypothalamic neurones on immunohistochemical staining. There are close relationships between gonadotropin releasing hormone (LH-RH) nerve terminals and dopaminergic nerve terminals in the median eminence. Prolactin inhibits its own secretion, likely by increasing dopamine turn-over in the median eminence. Furthermore, dopamine inhibits LH release.

In hyperprolactinemia, the pulsatile release of LH is suppressed or altered; the positive feedback of estrogens on LH release is abolished; the LH and FSH responses to gonadotropin releasing hormone are enhanced; the basal levels of serum oestradiol are low; and ovarian responsiveness to gonadotropins is not impaired. But in some hyperprolactinemic women, ovulation is not suppressed. In these cases, oestradiol secretion during the follicular phase is normal, with a normal

preovulatory peak. The LH surge is often of reduced amplitude and the peak of serum progesterone is flat and very short. An excess of prolactin during the follicular phase affects more the corpus luteum function than an excess of prolactin during the luteal phase. In vitro, prolactin excess suppresses progesterone secretion by granulosa cells from human graafian follicles.

In conclusion, prolactin plays a key role in physiological and pathological suppression of ovulation.

31. Infertility with normal menstrual rhythm: hormone patterns before and during treatment with bromocriptine (CB 154), A. CRAIG[2], R. FLEMING[1], W.P. BLACK[1], M.C. MACNAUGHTON[1], P. ENGLAND[3] and J.R.T. COUTTS[1], [1]Department of Obstetrics & Gynaecology, University of Glasgow, Royal Maternity Hospital, Rottenrow, Glasgow, G4 0NA, [2]Clinpath Services Ltd., Lane End Rd., High Wycombe, Bucks, and [3]Department of Pathological Biochemistry, Glasgow Royal Maternity Hospital, Rottenrow, Glasgow, G4 0NA, U.K.

Detailed hormonal examination of the menstrual cycles of 17 infertile women with normal rhythm has been effected by means of daily plasma samples for one complete control cycle and at least one cycle during CB 154 treatment (2.5 mg daily) (20 treatment cycles). The hormones assayed were oestradiol (E2), progesterone (P), FSH, LH, prolactin (PRL), using specific radioimmunoassays. Four of the patients were normoprolactinaemic throughout their control cycles, while 13 showed transient hyperprolactinaemia to a variable degree. Other abnormalities observed during the control cycles were: poor follicular maturation (low E2; in 7 patients); short luteal phase (2 patients); deficient luteal phase (poor P surge; in 7 patients). Treatment with CB 154 caused an immediate decline in PRL concentrations to low or low/normal levels. However, three patients were exceptional in that their PRL concentrations rose again to high levels by mid-cycle. All three showed more consistently elevated PRL levels in their control cycles than the other patients. The follicular phases of the whole group were significantly shorter during treatment cycles, but resulting steroid and gonadotrophin profiles were inconsistent. One patient became pregnant during this programme of CB 154 therapy.

32. Hyperprolactinaemia in polycystic ovary syndrome and in pituitary adenoma: prolactin response to pharmacological stimuli, P. FALASCHI, A. ROCCO, P. POMPEI, F. SCIARRA and G. FRAJESE, Clinica Medica V, University of Rome, Italy

A prolactin (PRL) secreting pituitary adenoma is the most common cause of non-pharmacologically induced hyperprolactinaemia.

There is increasing evidence that many patients with polycystic ovary (PCO) syndrome present raised plasma PRL levels (1). The increased PRL response to TRH (200 µg i.v.) and haloperidol (1 mg i.m.) in PCO patients without radiological evidence of pituitary tumours, prompted us to advance the hypothesis that in this syndrome the PRL hypersecretion could be the consequence of an abnormal positive feed-back effect of oestrogens on the pituitary galactotropes (2). Many reports in the literature, in fact, indicate that the PRL response to these stimuli in situations accompanied by increased circulating oestrogens are exaggerated (3,4).

In order to better characterize the cause of hyperprolactinaemia in PCO syndrome we performed the following investigation.

10 female patients with PRL secreting pituitary adenomas and 10 with the hyperprolactinaemic PCO syndrome and normal sella turcica were studied. 10 normal female volunteers of comparable age served as controls. Blood was drawn through an indwelling catheter between 9.00 and 9.30 a.m. during the early follicular phase of the menstrual cycle in all subjects studied for basal determination of testosterone, oestrone, 17β-oestradiol, LH and FSH. At time 0, on different days, all subjects received: nomifensine (Hoechst) 200 mg x per os, deprenyl (Chinion) 10 mg x per os, L-dopa + carbidopa (Merck, Sharp & Dohme) 250 mg + 25 mg x per os, domperidone (Janssen) 4 mg i.v.

In the hyperprolactinaemic PCO syndrome the PRL response to the pharmacological stimuli was similar to that observed in normal subjects. On the contrary patients with PRL secreting pituitary adenoma showed an abnormal PRL response.

The data obtained strongly suggest that in the PCO syndrome hyperprolactinaemia is the functional consequence of an oestrogen effect.

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