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# Regulation of Disorders of the Female Cycle

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The main indication for the application of progestogenic substances is a deficient progesterone production in the second phase of the cycle.

In cases of corpus luteum insufficiency the therapeutic approach consists of the substitution of the missing hormone. The immediate effect of the oral medication of progestogens is very safe. Much less, however, is known concerning the question of whether a permanent cure can be achieved by such a substitution regimen. Up to now we have investigated this question in a total of 98 patients; mostly sterility cases and polymenorrhea with a corpus luteum insufficiency causing disturbances of the cycle and/or sterility. The corpus luteum insufficiency was established by basal body temperature readings and occasional pregnanediol determinations. Half of the cases were treated with placebo tablets for three months and served as controls. As can be seen in Table I the normalizing tendencies of the cycle after discontinuation of the therapy were clearly better following progestogen than following the placebo. It may be added that the administration of chorionic gonadotropin in a dose of 5000 IU on day 15, 18 and 21 is a very effective therapy for corpus luteum insufficiency which seems, moreover, to have a stimulatory effect on the ovulation in the next cycle. In not a few cases, however, spotting occurs during the HCG therapy. This can be prevented by small substitution doses of oral progestogens, so we now use this combined therapy with an apparently additional improvement of the rate of cure.

Table I

Treatment of corpus luteum insufficiency

| Therapy | Number of patients | Corpus luteum phase | |
|---|---|---|---|
| | | normalized | not normalized |
| Placebo[1] | 40 | 14 | 27 |
| Progestogen[2] | 42 | 23 | 19 |
| HCG[3] | 16 | 11 | 5 |

[1] Milk sugar, coated.

[2] 17$\alpha$-aethinyl-oestr-4-en-17$\beta$-ol, 5 mg/die orally.

[3] 5000 IE HCG on day 15, 18 and 21.

Table II

Treatment of dysfunctional bleeding

| Therapy | Number of patients | Cycle | |
|---|---|---|---|
| | | normalized | not normalized |
| Curettage only | 59 | 37 | 22 |
| Curettage and progestogen[1] prophylaxis: | | | |
| 5th–25th day | 31 | 25 | 6 |
| 16th–25th day | 29 | 24 | 5 |
| | 60 | 49 | 11 |

[1] 17$\alpha$-aethinyl-oestr-4-en-17$\beta$-ol, 5 mg/die orally.

Table III

Effect of oral progestogen therapy on disturbances of the cycle (5 mg lynestrenol from 15th to 25th day)

| | Number of cases | Success | | Failure | |
|---|---|---|---|---|---|
| | | immediate | permanent | of immediate effect | of permanent cure |
| Secondary amenorrhoea (>3 months) ..... | 18 | 18 | 1 | 0 | 17 |
| Oligomenorrhoea ..... | 14 | 14 | 2 | 0 | 12 |
| Polymenorrhoea ..... | 7 | 7 | 0 | 0 | 7 |
| Hypermenorrhoea ..... | 8 | 7 | 2 | 1 | 6 |
| Metrorrhagia ..... | 9 | 7 | 2 | 2 | 7 |
| Premenstrual syndrome | 10 | 7 | 2 | 3 | 8 |
| Dysmenorrhoea ..... | 14 | 12 | 3 | 2 | 11 |
| Dysfunctional sterility (corp. lut. insuff.) ... | 16 | 13 | 0 | 3 | 16 |

Following a curettage for dysfunctional bleeding a prophylactic therapy is to be recommended with oral progestogens to avoid a relapse. We have compared a group without prophylaxis with a group receiving progestogens between the 5th and 25th day and the 16th and 25th day (Table II). The results suggest that a prophylactic medication with oral progestogens for three months following curettage improves the lasting therapeutic effect of a curettage and should be considered in each case. In the 4th and following cycles we proceed in such a way that the patient has to measure basal body

temperature. In case this is not elevated until the 21st day the patient takes progestogens from the 21st to 25th day.

We have, moreover, done some investigations with progestogen therapy in different clinical pictures, such as amenorrhea, oligomenorrhea and others (Table III). As can be seen, a permanent cure of disturbances of the cycle is seldom accomplished.

The induction of ovulation by progestogens has gained greater importance. I have so far treated 11 patients with 6-chloro-9$\beta$,10$\alpha$-pregna-1,4,6-triene-3,20-dione (Ro 4-8347) derivative, giving 8 mg/day from 10th to 25th day of the cycle for 1–3 months. In all of the cases anovulatory sterility was present which had not yet been treated by clomiphene or gonadotrophins. In 4 out of the 11 cases an ovulation occurred as judged from temperature and pregnanediol determinations. Of the remaining 7 patients clomiphen was successful in 5 patients. Two patients did only react to a full HMG-HCG cure. With the retrosteroid so far no permanent ovulatory cycle and no pregnancy has been induced in our patients.

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