

## 14. INTRAUTERINE CONTRACEPTION WITH THE PROGESTASERT<sup>®</sup> SYSTEM

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The idea of continuous intrauterine administration of progesterone for contraception, as originally presented by Dr. Antonio Scommegna, is based on four observations:

- The estrogenic component of oral contraceptives is not essential for contraception.
- Progestin-only mini-pills achieve satisfactory levels of contraception without inhibiting ovulation.
- The mini-pill interferes with nidation and may change the cervical mucus, thus interfering with sperm penetration.
- Most contraceptive failures associated with the mini-pill can be traced to poor patient compliance.

These observations suggest low-level, continuous intrauterine administration of progesterone, a naturally occurring hormone with strong antiestrogenic effect, would be an effective contraceptive. Furthermore, this method would not depend on patient compliance, nor would it cause systemic side effects.

The Progestasert intrauterine progesterone contraceptive system (Figure 1) delivers progesterone to the uterus at a rate of 65  $\mu\text{g}/\text{day}$  for one year. The delivery rate was selected after studies with prototype system releasing 5-110  $\mu\text{g}/\text{day}$  of progesterone. A 65  $\mu\text{g}/\text{day}$  release rate significantly reduced the incidence of proliferative endometria as well as maximizing suppression of the endometrium. Dr. Howard Tatum originally designed the system's T shape.

### I. DATA BASE

Studies with the Progestasert system cover 127,580

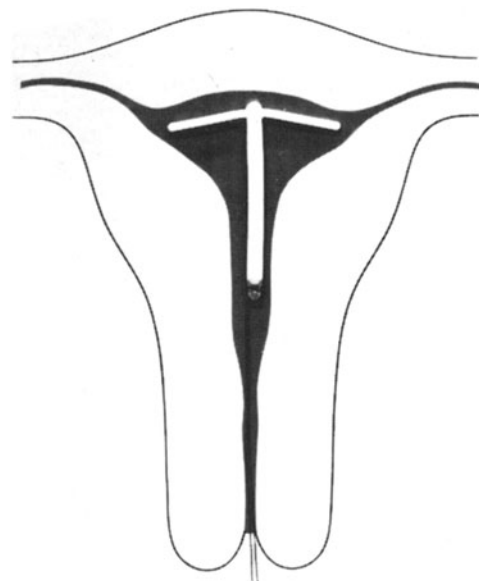


Figure 1. Representation of the Progestasert intrauterine progesterone contraceptive system in the uterus. (Copyright 1976 ALZA Corp.)

woman-months of use in 12,008 women, of whom 3,310 were nulliparous. The studies were conducted in more than forty centers worldwide, and included patients from both public health clinics and private practices.

### II. RESULTS

#### II.A. Systemic effects

The endometrium readily metabolized progesterone. Systems were inserted in women scheduled to undergo hysterectomy (Sievers and Dallenbach-Hellweg 1976); a local progesterone effect was found only in the endometrium. Progesterone and its metabolites were measured in the uterine and

peripheral veins of baboons. Essentially no difference was found between progesterone levels, and mainly progesterone metabolites were found in the uterine vein. Plasma follicle-stimulating and luteinizing hormone levels during the menstrual cycle have been examined to determine the effects of progesterone on the hypothalamic-pituitary-ovarian axis (Tillson et al. 1975). This axis, which is very sensitive to changes in systemic progesterone levels, was essentially unaffected.

In a preliminary report, Spellacy et al. (1978) indicated that changes in prolactin levels occur in patients wearing the Progestasert system; however, further research by the authors did not support these findings (Spellacy and Buhi 1979). Another report from this group indicates a difference from preinsertion levels in second-hour blood glucose following the oral glucose tolerance test in women who had used the system for one year (Spellacy et al. 1977).

## II.B. Bleeding and pain

During our Phase III trials, it became clear that the system – like oral contraceptives, but unlike other IUDs – reduced menstrual blood loss and pain.

Patients who reported having heavy blood loss upon admission to the study later reported a significant reduction in this. Patients with severe menstrual cramps upon admission also reported a lessening of their symptoms (Figure 2). Quantitative studies of blood loss, reported by ourselves and others, indicate that while all other IUDs increase the amount of blood loss by from 50 percent (copper IUDs) to 100 percent (inert IUDs), progesterone-releasing IUDs decrease bleeding by an average of 50 percent (Figure 3).

Three factors observed during use of the system may be responsible for decreases in menstrual bleeding and cramps:

- suppression of the endometrium significantly reduces the endometrial hyperemia that is typical of the secretory phase;
- fibrinolytic activity in the endometrium – an effect known to increase menorrhagia during use of other IUDs – decreases;
- PGF<sub>2α</sub> concentrations in menstrual blood, which affect blood loss and uterine contractility, also fall to significantly below preinsertion levels (Trobough et al. 1978; Zahradnik et al. 1978).

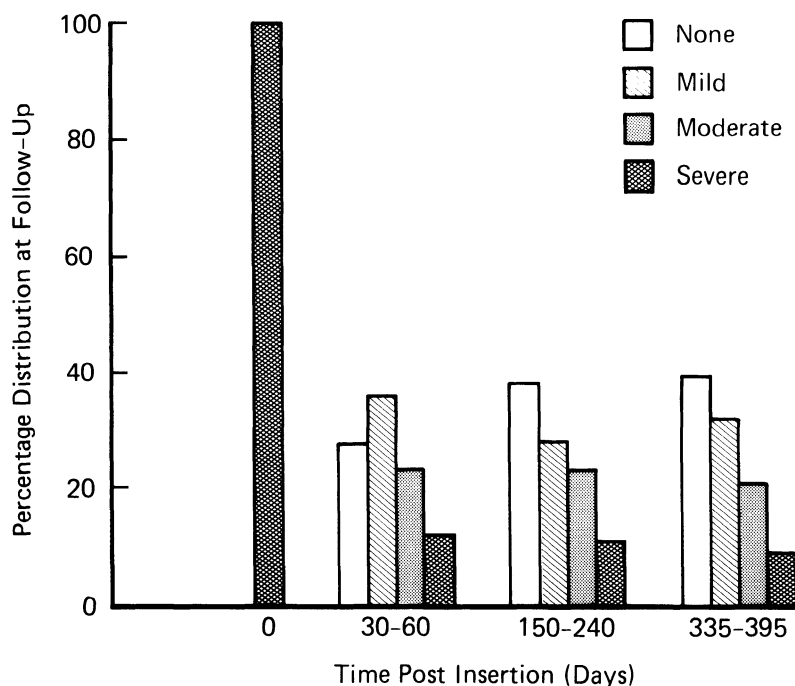


Figure 2. Menstrual cramps in 253 women with severe cramps at insertion of the Progestasert system. (Copyright 1976 ALZA Corp.)