

BRIEF GUIDE TO OFFICE PRACTICE

Progesterone Therapy for Luteal Phase Deficiency

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A woman who is infertile may have a condition known as a luteal phase deficiency (LPD). This deficiency results when a woman produces an inadequate amount of progesterone during the second half of the menstrual cycle (after ovulation). As a result, the endometrium is not adequately prepared for secure implantation of a fertilized ovum. This is a known cause of habitual abortion, but it has not yet been established whether it is a cause of infertility.

Types of luteal phase defects

Luteal phase defects are divided into three separate categories:

1. Women who do not secrete an adequate amount of progesterone due to the inability to form a mature follicle. This leaves them an insufficient number of granulosa-theca cells to produce progesterone, which is determined by a timed endometrial biopsy done in the late secretory phase of the cycle.
2. Women who do not release the egg from the follicle, also known as the luteinized unruptured follicle (LUF) syndrome.
3. Women who produce a ma-

ture follicle from which an egg is released, but who do not secrete an adequate amount of progesterone from the corpus luteum. This is called a pure luteal phase defect.

Efficacy of progesterone therapy

Patients in the first category do not respond well to progesterone alone. Women who are unable to produce a mature follicle usually need an ovulation-inducing drug such as clomiphene citrate, bromocriptine, or human menopausal gonadotropin (HMG). Progesterone, however, is employed in the second half of the cycle to help prevent spontaneous abortion.

Women in the second category require human chorionic gonadotropin (HCG) to release the egg from the follicle first, since improving the endometrium by progesterone is not helpful unless an egg is released.

It is the third category—in which an inadequate amount of progesterone is secreted—that, as a possible cause of infertility, would be expected to respond to progesterone alone.

We therefore researched the efficacy of progesterone as a fertil-

ity drug for women with luteal phase defects at our center, Reproductive and Medical Endocrine Associates. We studied 50 women who had no other cause of their infertility; had a minimum of one and one-half years of infertility; and produced a mature follicle that released an egg, but who had a pure luteal phase deficiency. They were treated with progesterone at a starting dosage of 25 mg bid until the endometrium was dating correctly. The number of pregnancies that would ordinarily occur within a six-month period was calculated. Seventy percent of the women conceived. A 70% pregnancy rate is considered normal for a fertile group of women within a six-month period of time.

To obtain more data, we studied 100 women who presented with the complaint of infertility, and who had been infertile for at least one year. The objective: to determine via ultrasound criteria and estradiol and progesterone assays, whether the woman forms a mature follicle (as defined by a size of 18 mm-24 mm on ultrasound and by a serum estradiol level of greater than 200 pg/ml), releases the egg from the follicle, and has an insufficient amount of progesterone. Interestingly, 86% of these women had a luteal phase deficiency. In this group, 44 other-

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Comparison of therapy in patients with LPD to those with Immature follicles

To determine whether it is truly necessary to differentiate patients with Immature follicles from those with pure luteal phase defects in order to achieve optimal therapeutic results, we did a randomized study in which we treated with progesterone those patients whose social security numbers ended in an even digit, and treated with clomiphene those whose numbers ended in an odd digit. After six months, patients who failed to conceive were given the opposite therapy, with the following results:

Category	Treatment	Patients treated 1st 6 months	Pregnancies	Abortions
Pure LPD	Progesterone suppositories	31	24	1
Pure LPD	Ovulation drugs	27	3	2
Immature follicle	Ovulation drugs and progesterone suppositories	20	14	1
Immature follicle	Progesterone suppositories	12	3	0
Immature follicle	Ovulation drugs	10	7	4

During the second six months, similar data were obtained. For example, 25 of 27 patients with pure LPD who had failed to achieve a successful pregnancy with ovulation drugs, were now treated with progesterone vaginal suppositories; 16 of 25 conceived, and 1 aborted.

wise healthy women had the following ovulation problems: 16 were found to have immature follicles, which caused their luteal phase defect (LPD), three women had the LUF syndrome, and 25 had pure LPD. Twenty-two of the 25 women with pure LPD were able to conceive within eight months by using supplemental progesterone.

Treatment recommendations

The data from our studies strongly suggest the following management for patients with infertility and luteal phase defects:

- Pure LPD: Progesterone support in the luteal phase;

- Immature follicles associated with LPD: Ovulation-inducing drugs in the follicular phase and progesterone support in the luteal phase.

Progesterone is stated in the form of progesterone suppositories 25 mg twice a day; the dosage is increased until correction is apparent via the late luteal phase endometrial biopsy.

The usual choice for an ovulation drug is clomiphene citrate. The dosage is increased until follicular maturation is achieved. Bromocriptine is employed if the prolactin is elevated. If clomiphene causes mucus to be hostile to sperm, human menopausal go-

nadotropin (HMG) is used. Human chorionic gonadotropin (HCG) is given at the time of follicular maturity if the ovum failed to release during the previous cycle.

While we feel quite strongly that progesterone therapy alone can effectively induce fertility, it still remains to be proven. A randomized double-blind controlled study may make this possible. Meanwhile, we encourage physicians to treat their patients with progesterone, but to document first that the patient in question has pure LPD, and does not require improvement of follicular maturation or release of the egg from the follicle.

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