Luteal Phase Support

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Over the past few years, there has been a significant shift from fresh to frozen embryo transfers (FETs) following in vitro fertilization. This shift has occurred in part due to higher pregnancy rates, and also due to the observation that babies born following FET are more likely to be healthy. Whereas, with fresh embryo transfer there is some endogenous progesterone secretion from residual corpora lutea following oocyte retrieval, with FET, there is essentially no endogenous progesterone production. This makes luteal progesterone administration critical to the success of the IVF procedure.

The three most common forms of FET cycles are natural cycles and those stimulated with either estrogen/progesterone combination therapy or letrozole (with or without progesterone). While a large meta-analysis suggested no difference in outcome between natural and stimulated cycles, most programs prefer stimulated cycles due to ease of scheduling, and fewer canceled cycles due to missed LH surges.

Progesterone can be administered orally (PO), intramuscularly (IM), or vaginally (PV). While IM progesterone remains the "gold standard" for luteal phase support, many patients prefer alternative delivery platforms due to the pain caused by IM progesterone. Oral progesterone is not approved by the FDA and is inconsistently absorbed and metabolized. In addition, over 90% of PO P4 is lost due to the first pass effect. Most significantly, studies show lower pregnancy rates with PO compared to IM or PV administration. The one exception to this finding may be dihydrogesterone — a formulation not currently available in the US.

Vaginal progestins appear to cause higher tissue (endometrial) progesterone levels but lower serum levels than IM progestins. This may result in fewer systemic side effects. In addition, while some studies still suggest superiority of IM progesterone, many studies suggest that PV progestins produce comparable pregnancy rates to IM and higher pregnancy rates than PO administration.

Luteal support of IVF cycles is critical, perhaps even more so now that most programs have transitioned to FET from fresh ET. There are several alternative progesterone delivery forms, and while IM progesterone is still a reasonable alternative, recent data suggest that there may well be other, equally successful options for IVF practitioners to consider.