

## Luteal Phase Progesterone Support

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**Mark Perloe, MD:** "I'm Mark Perloe and I'm here at the American Society of Reproductive Medicine reporting for FerCenter, with Dr. James Toner from Atlanta Center for Reproductive Medicine. Jim, you've done some original work on luteal phase support and at this meeting I'm still not sure we have the answers about how to manage the luteal phase in IVF patients. What are your thoughts?"

**James Toner, MD:** "I think we know a few things. I think we know that progesterone supplementation for our IVF patients is essential. We clearly need that. There is a proportion of all of the patients that we have, who will fail to get pregnant or will fail to keep a pregnancy, unless we give progesterone. So it isn't the "yes/no progesterone", it's "how to give it" and there are a few options. In the States, as you know, the standard has always been shots, which is a real inconvenience to our patients and sometimes causes problems besides the discomfort.

So there have been other methods developed such as vaginal replacement and some other work showing that oral, which would be a nice way to go, isn't sufficient. So I think our choice is either intramuscular or vaginal therapy. You know, I think you're right, there's still not a final answer here. The intramuscular I think we know to be the gold standard and to work. I think the evidence is that the vaginal works well but maybe not quite as well. So we're kind of going back and forth but I think we need studies that are a little bit bigger to put an answer to the question."

**Mark Perloe, MD:** "I think one of the things that came out on the presentations was that the vaginal route appears to be associated with a greater incidence of luteal phase spotting. Has this been your experience working with Crino?"

**James Toner, MD:** "And the European experience is the same and they've used vaginal replacement for a decade, almost exclusively, without any intramuscular use and they have just come to accommodate to that difference. It is a difference though and causes some frustration on the part of patients and practitioners in trying to understand why this is happening and whether it means anything."

**Mark Perloe, MD:** "Well, there was conflicting data as to whether this has implications about success during pregnancy. One of the concerns is that vaginal progesterone is absorbed well and that there is a uterine first pass. In a normal luteal phase we're seeing 45 milligrams produced by a single corpus luteum. Do we need more and is there a risk that too much progesterone may be harmful?"

**James Toner, MD:** "I think there is a risk. We know from cycles in which women have high and low response that those with the high response, the high progesterone, do have changes in their lining, uterine lining development that shows you that a high dose of progesterone can have an effect. And I agree with you that the vaginal dosing may, in fact, be a little more than needed or more than desired to get the optimal lining developed."

**Mark Perloe, MD:** "Do we know whether the endometrium wants to see a constant level of progesterone throughout the day or that a three or four hour period of a peak is more physiologic or appropriate to protecting the pregnancy?"

**James Toner, MD:** "I don't think we know whether the uterus cares, the lining cares. We do know,

as you were suggesting, that the mode of delivery does influence how long progesterone circulates, and the product Crinone, which is a vaginal product delivered in a gel form, does have a rather sustained level of progesterone. Whereas suppositories, which had been the earlier way to give progesterone, is much more pulsatile but I don't know that we know for sure whether it matters to the clinical results."

**Mark Perloe, MD:** "Well, thank you for sharing your thoughts on this and hopefully that larger study will get done so we have some direction. I know in our clinic we're always debating this and going back and forth. What are you using right now personally?"

**James Toner, MD:** "Personally we're using intramuscular progesterone until we confirm a pregnancy and then feel comfortable shifting away to a vaginal product."

**Mark Perloe, MD:** "One other issue, do you think that the presence of either a gel or the peanut oil in Prometrium or the base in a suppository could have an adverse affect just because of mechanical irritation when it's used prior to transfer?"

**James Toner, MD:** "Theoretically I think it could but, again, no testing has been done that would confirm or deny that kind of a thinking."

**Mark Perloe, MD:** "Thank you so much and I look forward to seeing you back in Atlanta next week."

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