“Endometrial Shedding Effect on Conception and Live Birth in Women With Polycystic Ovary Syndrome”

(Michael P. Diamond, Michael Kruger, Nanette Santoro, Heping Zhang, Peter Casson, William Schlaff, Christos Coutifaris, Robert Brzyski, Gregory Christman, Bruce R. Carr, Peter G. McGovern, Nicholas A. Cataldo, Michael P. Steinkampf, Gabriella G. Gosman, John E. Nestler, Sandra Carson, Evan E. Myers, Esther Eisenberg, Richard S. Legro, on behalf of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Cooperative Reproductive Medicine Network)


Click Here to Read the Full Article

1. Review the mechanism of action for ovulation induction with clomiphene and compare with the mechanisms of action with letrozole, metformin, and exogenous gonadotropins. Contrast the desirable effects of clomiphene on fecundity with those effects that may reduce its efficiency.

2. Review the protocol for ovulation induction in the “Clomiphene, Metformin, or Both for Infertility in the Polycystic Ovary Syndrome” study. On what basis was the decision made to induce withdrawal bleeding prior to the first course of clomiphene, metformin, or both? What guidelines were used to determine “recent menses”? Were spontaneous menses, anovulatory cycles with progestin withdrawal bleeding, and anovulatory cycles without progestin withdrawal bleeding evenly distributed among all 6 treatment cycles? On what basis was the decision made to induce menses with progestin prior to clomiphene dosage escalation? Were the characteristics of women with spontaneous menses or anovulatory with or without menses similar? Which progestin at what dose and duration was used to induce menses? How might these decisions bias the present study results?

3. Contrast the study protocol with your clinical pattern for ovulation induction with clomiphene. How are they alike? How are they different? Are they sufficiently similar to justify application of the study results to your practice?

4. Review the principal concepts underlying the analysis of variance (ANOVA). Discuss why some variables were analyzed with two-way ANOVA and some with one-way ANOVA. How many statistical analyses were planned? How many were performed? What adjustment, if any, was made in the significance level for multiple comparisons?

5. Using the first-cycle data presented by the authors and the anovulatory women who received progestins as the reference group, derive the relative risk and 95% confidence intervals for live birth for the other two groups. What conclusions do you draw from the calculations?

6. In Dr. Casper's editorial (“Detrimental Effect of Induced or Spontaneous Menses Before Ovulation Induction on Pregnancy Outcome in Patients With Polycystic Ovary Syndrome”), he warns that the authors’ findings need to be confirmed with a prospective trial. Sketch
the design of a study that would confirm or refute a key hypothesis derived from the present study. Include in the study design observations that would support or contradict a mechanism proposed by the author or by Dr. Casper.

7. You and your oligomenorrheic patient with polycystic ovary syndrome (PCOS) agree that she should start on ovulation induction with clomiphene. Her last menstrual period (LMP) was 3 months ago. Discuss how she should be instructed to start the medication. How do you determine that she is not already pregnant? How do you determine that she has not already ovulated spontaneously? How do you know that ovulation is not imminent? How important is it to determine these conditions when starting ovulation induction?

8. Read the ACOG Practice Bulletin #14, "Management of Anovulatory Bleeding" (March, 2000, reaffirmed 2009). Should the section, "What medical therapies are most appropriate for each age group?" be revised?