



## C-Obs 29 (a)

# Progesterone Support of the Luteal Phase and Early Pregnancy

The following statement is based on a literature search for systematic reviews of randomised controlled trials concerning the role of progesterone or progestin luteal support in various contexts.

For **threatened miscarriage**, there is no evidence that vaginal progesterone reduces the risk of pregnancy loss, however this is based on 2 RCTs in which only 84 women were randomised.<sup>1</sup> Further randomised studies are therefore needed. There was no evidence of benefit of progestin for prevention of miscarriage in an unselected population based on 15 RCTs including 2,118 women.<sup>2</sup> However sub-group analysis of 4 of the 15 RCTs which included 223 women with **recurrent miscarriage** ( $\geq 3$  consecutive miscarriages) showed the odds of miscarriage were significantly decreased by progestin treatment (Peto OR 0.38, 95% CI 0.20 to 0.70),<sup>2</sup> however the studies were clinically heterogeneous (varied, particularly in their treatment regimes) - treatments were a composite of oral progestin (dydrogesterone in one RCT; medroxyprogesterone in another RCT) and intramuscular progesterone in two other RCTs. In addition the duration of treatment also being highly variable, ranging from a single dose prior to 10 weeks to continual treatment through to 36 weeks gestation.<sup>2</sup>

For **luteal support in assisted reproductive technologies (ART)**, hCG (human chorionic gonadotrophin) or progesterone gives a significantly higher pregnancy rate than placebo or no treatment; there is no evidence of a difference in pregnancy rate between hCG and progesterone. HCG is associated with significantly higher rates of the complication ovarian hyperstimulation syndrome (OHSS).<sup>3</sup> Limited evidence suggests intramuscular administration of progesterone may be associated with a higher pregnancy rate than vaginal administration<sup>4</sup> and limited evidence that addition of oral oestrogen to progesterone may improve pregnancy rates.<sup>4</sup> Standard current luteal support in most units involves the use of intramuscular hCG or vaginal or intramuscular progesterone and some fertility units use additional oral oestrogen in selected cases.

Use of any hormonal treatment in the luteal phase and in early pregnancy must always be used with great caution owing to the possibility of teratogenesis. Unproven treatments should be avoided. The evidence supporting progestin use for preventing recurrent miscarriage must be viewed cautiously owing to the heterogeneity in treatment regimes that were pooled for this meta-analysis. Ongoing research to provide yet stronger evidence is encouraged.

## References

1. Wahabi HA, Abed NF, Elawad M. Progestogen for treating threatened miscarriage. *Cochrane Database Syst Rev* 2007; 3: CD005943.
2. Haas DM, Ramsey PS. Progestogen for preventing miscarriage. *Cochrane Database Syst Rev* 2008; 2: CD003511.
3. Daya S, Gunby JL. Luteal phase support in assisted reproduction cycles. *Cochrane Database Syst Rev* 2004; 3: CD004830 (withdrawn).
4. Pritts EA, Atwood AK. Luteal support in infertility treatment: a meta-analysis of the randomized trials. *Hum Reprod* 2002; 17: 2287-99.

## ***Links to other related College Statements***

(if any)

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