**Does weekly progesterone prolong gestation in women who have PPROM?**

**NO.** This randomized trial of 69 women who experienced preterm premature rupture of membranes (PPROM) at 20 to 30 weeks’ gestation found no difference in the length of gestation between women given 250 mg of 17-alpha-hydroxyprogesterone (17P) or placebo weekly.

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**Weekly 17-alpha-hydroxyprogesterone did not prolong gestation in women who experienced PPROM at 20 to 30 weeks’ gestation**

All women included in the study received antibiotics according to a protocol from the National Institutes of Health; they also were given betamethasone for fetal maturation. Tocolytics were not used. Because randomization did not occur until after each woman was transferred from the labor and delivery unit to the high-risk floor, we can assume that no participants were manifesting uterine contractions.

Women received weekly injections of 17P or placebo until 34 weeks’ gestation or delivery. The primary outcome was the interval from study entry to delivery.

One woman had a pregnancy of 23.5 weeks’ duration at randomization; the remainder had gestations that were 24 weeks or older. There were no other differences in demographics, cervical dilatation, gestational age at study entry, or reasons for delivery between the two study groups.

**Study design may have been unrealistic**

The authors calculated that they needed a sample size of 56 patients to detect a 50% increase in latency, based on population data from their institution showing that 80% of patients who have PPROM deliver within 7 days. Such a calculation may have set an unrealistic—albeit logistically convenient—goal, rendering the study underpowered to detect smaller effects. Note, for example, that when antibiotics are given to women who...
have PPROM, prolongation of the latency period is only 33% (pooled effect from a recent meta-analysis). Even so, given the findings of Briery and colleagues, latency improvement after 17P administration would appear to be unlikely even in a larger study. There was not even a trend toward a longer interval to delivery (mean of 11.2 days with 17P vs 14.5 days with placebo).

Only secondary prevention of preterm birth is effective
The indications for progesterone supplementation in pregnancy are still evolving as part of a sustained scientific effort to prevent preterm labor and delivery. Strategies to prevent preterm delivery can be categorized as primary, secondary, or tertiary, as can strategies for other public health concerns.

Because any number of variables—known and unknown—may trigger preterm labor, identifying them and providing primary preventive strategies in the entire pregnant population remain elusive tasks.

Tertiary prevention—i.e., treatment given to already symptomatic individuals—is also notoriously ineffective. There are no data supporting the use of progesterone as primary prevention (in low-risk women) or tertiary prevention (e.g., tocolytic). ACOG made note of this in 2003, and its conclusions remain valid today. According to a 2010 Cochrane review, there is insufficient evidence to advocate prophylactic agents as tocolytic agents for women who present with threatened or established preterm labor.

In light of these data, the results reported by Briery and colleagues are hardly surprising. In women who may have already entered the irreversible phase of parturition (manifesting uterine contractions; presenting with advanced, painless cervical dilatation; or after PPROM), progesterone will remain ineffective. The only applicable use of prophylactic progesterone in pregnancy is as secondary prevention. In contrast to primary and tertiary prevention, the secondary level of prevention—i.e., an intervention aimed at minimizing the risk of preterm birth in women who are identified as having an elevated risk—is supported by several systematic reviews of randomized, controlled trials.

According to these reviews, progesterone certainly is effective in high-risk pregnant women who have a short cervix or a history of spontaneous preterm birth. The same cannot be said about women who have PPROM.

**WHAT THIS EVIDENCE MEANS FOR PRACTICE**

Based on the evidence, including this study by Briery and colleagues, administration of antibiotics appears to be the only intervention available to delay delivery and reduce neonatal morbidity in the setting of PPROM. The use of tocolytics is not supported by the data in the clinical context of PPROM.

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**References**


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**FAST TRACK**

The use of tocolytics in the setting of PPROM is not supported by the data.