**Progesterone supplementation shared decision making**

Progesterone may reduce the risk of another preterm birth after a prior preterm birth (20-36&6 weeks) that happened after preterm labor (PTL) or premature preterm rupture of membranes (PPROM). Progesterone can be given in many ways. The most studied form is:

**Hydroxyprogesterone caproate 250 mg intramuscular injections weekly from 16-36 weeks (also known as 17-alpha-hydroxyprogesterone caproate or 17OHP)**

*What do we know about progesterone and recurrent preterm birth?*

In 2003, the Meis trial suggested a 1/3rd reduction in recurrent preterm birth with the use of 17OHP – it was such a powerful effect that the study was stopped early. 17OHP was given provisional FDA approval and was universally recommended/adopted by about 2012. Although the studied name brand drug was expensive (~$10,000 per pregnancy), less expensive compounded alternatives do exist (~$200 per pregnancy) and preterm birth is very expensive in terms of both money and risk to family wellbeing.

In 2019, the PROLONG trial designed to evaluate the FDA’s provisional approval saw no benefit of progesterone supplementation in reduction of recurrent preterm birth. The FDA advisory panel voted 9 to 7 to withdraw provisional approval. The FDA has not taken any such action yet.

*In response, the leading organizations of obstetrics and high risk obstetrics (ACOG and SMFM) made statements:*

**ACOG:** “Consideration for offering 17-OHPC to women at risk of recurrent preterm birth should continue to take into account the body of evidence for progesterone supplementation, the values and preferences of the pregnant woman, the resources available, and the setting in which the intervention will be implemented.”

**SMFM:** “It is reasonable for providers to use 17-OHPC in women with a profile more representative of the very high-risk population reported in the Meis trial.”

*What were the differences between the two study groups?*

The most important difference between the two groups seems to be that the Meis group was much higher risk. What made them higher risk? Many had multiple preterm births, earlier preterm births (<32-35 weeks) and were smokers. Although the Meis study included many more African American women and we know race is a substantial risk factor for preterm birth, subgroup analysis failed to show the strong benefit of 17OHPC for African American women, so it is unclear whether race should be considered an important difference between these two groups.

*Is there other data to consider?*

In 2018, a study was published looking at preterm birth rates before and after use of progesterone and also found about a 1/3rd reduction in preterm birth. As a possible risk, however, patients getting progesterone had almost twice the risk of gestational diabetes. Otherwise, data supports safety in pregnancy but whether there are long term risks, such as metabolic risks to the child (risk of diabetes, obesity, etc) is unknown. Also, presenting for weekly shots from 16-36 weeks during a pandemic may carry additional risks.

*Are there other options to consider to assess or reduce my risk?*

**Natural or micronized progesterone used vaginally nightly from 16-36 weeks**

Preparations include 200mg suppositories (Prometrium), 100mg tablets (Endometrin) and 90mg gel (Crinone)

These may be reasonable alternatives and have been proven beneficial in some patients with short cervix, but data is limited on their impact on recurrent preterm birth risk.

A **transvaginal cervical length** can help assess your risk and **cerclage** is an important intervention for some patients.

*OF NOTE: Subcutaneous progesterone HAS NOT been adequately studied and IS NOT recommended as an alternative.*

What should I do?

Strongly consider progesterone supplementation from 16-36 weeks

Possibly more likely to benefit

Do not initiate progesterone supplementation at 16 weeks

Less likely to benefit

Consider the potential risks and benefits to make your decision

Vaginal progesterone seems to be a reasonable alternative to IM
(SubQ NOT recommended)

If your cervix measures <2.5 cm
Your doctor will talk to you about cerclage
It is unclear whether progesterone helps if you need a cerclage

Provider notes on TVCL:
Low risk patients (no prior deliveries before 34w): universal screening around 20w is reasonable – if TVCL is <2cm at >24w → start vaginal progesterone and refer for high risk consult for reassessment, peri viable counseling, etc.
High risk patients (history of PTL at 32-34w or PPROM): screening indicated, recommend single screen around 20w – if TVCL <5cm → follow-up in 1 week, if TVCL <2.5cm → high risk consult for cerclage
Highest risk patients (history of PTB at <32w for PTL or PPROM): screening indicated, recommend serial screening between 16-22w – if TVCL ≥3cm → reassess in 2-3 weeks, if TVCL <5cm → follow-up in 1 week, if TVCL <2.5cm → high risk consult for cerclage