Spontaneous Preterm Birth Prevention

Approximately 11% of U.S. births occur preterm (< 37 weeks’ gestation), 75% of which are spontaneous. Preterm births contribute disproportionately to childhood morbidity and mortality and societal health care costs. Several strategies may reduce spontaneous preterm birth. In each scenario, the clinician should ensure a viable intrauterine pregnancy and no evidence of lethal fetal anomaly.

1. Sonographic cervical length measurement
   Eligibility
   a. Women with prior spontaneous preterm birth (SPTB)
   b. Women between 18 and 24 weeks without prior spontaneous birth, if performed as part of a universal cervical length screening program. (This approach is an option, not a requirement)
   c. Suspected short cervix during transabdominal ultrasound examination.

   Protocol
   • Cervical length measurement and reporting according to CLEAR guidelines
   • If prior spontaneous preterm birth
     a. every 2 week measurements from 16-24 weeks
     b. weekly measurements up to 24 weeks if shortening to 26-29mm
     c. if singleton gestation and prior SPTB < 34 weeks, offer cerclage for cervical length ≤ 25mm before 24 weeks, after ruling out preterm labor
     d. if twin gestation and cervical length ≤ 25mm after ruling out preterm labor, consider physical examination of cervix and if dilated < 4cm before 24 weeks, may consider cerclage
   • If no prior spontaneous preterm birth
     a. single measurement at either time of suspected short cervix or between 18 and 24 weeks’ gestation
     b. if cervical length ≤ 20mm
       - offer vaginal progesterone (see below), after ruling out preterm labor
       - consider physical examination of cervix and if dilated < 4cm before 24 weeks, may consider cerclage*

2. 17 hydroxyprogesterone caproate (17P)
   Eligibility criteria:
   • Documented previous spontaneous preterm delivery (singleton or twins)
   • Viable singleton pregnancy
   • ≥ 16 weeks’ gestation
Exclusions:
• Heparin therapy
• Hormone sensitive cancer
• Lethal fetal anomaly
• Liver disease
• Multiple gestations
• Thrombocytopenia < 100,000
• Seizure disorder (relative contraindication)
• Uncontrolled hypertension on meds (relative contraindication)
• Allergy to 17P or diluent, peanuts, soy, jam, palm, sesame

Management protocol:
1 ml containing 250 mg 17 alpha-Hydroxyprogesterone Caproate intramuscularly weekly starting no earlier than 16 weeks and continuing through 36 weeks’ gestation.

Once treatment begins, the patient will be seen in the office on a weekly basis for her 17P injection and evaluation of signs of PTL. After one month the patient has the option of giving herself weekly injections at home and schedule her OB office visits as needed.
• If cerclage is placed for cervical shortening, continue 17P or consider switching to daily vaginal progesterone (see below)

Adverse effects:
Redness, pain, bruising or lump at the injection site

Supply:
Apothecary by Design (for compounding) Tel: 207-774-5220
Compounding Pharmacy: 207-899-0886

Makena – commercial form

3. Vaginal progesterone
Eligibility
• Progesterone administered vaginally on a daily basis may reduce the risk of SPTB in the following circumstances
  a. women with a prior spontaneous preterm birth
  b. women with no prior SPTB and a sonographic cervical length ≤ 20mm

Exclusions
• Allergy to progesterone formulation or soy, peanuts, yams, sesame, or palm
• Hormone-dependent cancer

Management
• Daily progesterone administration vaginally
  a. from 16-36 weeks or delivery <36 weeks in women with a prior SPTB
b. from diagnosis of a cervical length ≤ 20mm between 16 and 24 weeks until 36 weeks or delivery < 36 weeks
• Dosing and formulations evaluated include
  a. progesterone gel 90mg
  b. progesterone capsules 200mg

4. Cervical cerclage
   Eligibility
   a. ≥ 3 prior unexplained SPTBs OR
   b. prior delivery consistent with cervical insufficiency OR
   c. prior SPTB and cervical shortening ≤ 25mm between 16-24 weeks without regular uterine contractions in current singleton pregnancy OR
   d. no history of SPTB* short cervix (≤ 20mm) at 16-24 weeks, dilated < 4cm, no regular uterine contractions

*Cerclage efficacy in this situation may be improved with cefazolin 1gm IV immediately pre-operatively followed by doses at 8 and 16 hours postoperatively (dose = 2gm each occasion for patient weight ≥ 100kg) and oral indomethacin 50mg immediately postoperatively, followed by 50mg doses at 8 and 16 hours postoperatively.

Appendix 1
Appendix 2

Initial prenatal visit
Comprehensive obstetrical history
Ultrasoundographic confirmation of gestational age and number of fetuses

Is there a history of spontaneous preterm birth?
(i.e., a singleton live birth at 16\(^{6/7}\)–36\(^{6/7}\) wk of gestation or stillbirth before 24 wk presenting as labor, ruptured membranes, advanced cervical dilatation, or effacement)

Yes
Prescribe 17-OHPC, 250 mg IM weekly from 16\(^{6/7}\)–36\(^{6/7}\) wk of gestation

No
Is this a singleton pregnancy?

Yes
Does the patient have signs or symptoms of parturition (e.g., persistent pelvic pressure, cramps, or spotting or vaginal discharge)?

No
Progestogens are ineffective and cerclage may increase the risk of preterm birth

Yes
Have TVCL performed by credentialed ultrasonographer

TVCL > 25 mm
Provide routine prenatal care

TVCL 21–25 mm
Measure TVCL once more in 7–14 days

TVCL ≤ 20 mm
Prescribe vaginal progesterone daily (200-mg capsules or suppositories or 90-mg gel) until 36 wk of gestation

Yes
If TVCL < 25 mm before 24 wk of gestation:
Consider cerclage suture, especially if patient had prior spontaneous preterm birth at < 28 wk or if membranes are visible

Continue progesterone treatment

No
Use one of the following suggested site-specific screening strategies:
Universal TVCL screening at 18–24 wk of gestation
Universal TA CL screening at 18–24 wk of gestation, until CL < 35 mm
Selective TVCL screening of women with the following risk factors:
Prior preterm birth at < 24 wk of gestation with unknown cause, or twin birth
History of genitourinary infection
Conception with fertility drugs
Black race
Previous cervical surgery
BMI < 19.6 or > 35.0
Periodontal disease
References:


https://clear.perinatalquality.org