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MANAGING WOMEN AT RISK FOR PRETERM BIRTH

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Preterm birth continues to be a major public health concern in the United States. In 2010, according to the March of Dimes' 2012 Premature Birth Report Card, 12% of all babies in this country were born prematurely. This rate has decreased only minimally in the last 10 years. To achieve the federal government's Healthy People 2020 goal of an 11.4% preterm delivery rate, progress in research to identity causes of spontaneous preterm delivery and development of prevention strategies are essential.

Recently, both the Society for Maternal-Fetal Medicine (SMFM) and the American College of Obstetricians and Gynecologists (ACOG) have published clinical guidelines for managing women at risk for spontaneous preterm birth.[1,2] These new guidelines represent a significant change from current practice. This issue of *Perinatal Progress* focuses on up-to-date, evidence-based recommendations for surveillance of and intervention for women at risk for spontaneous preterm birth.

CLINICAL RECOGNITION

Identifying women at risk for preterm birth who would benefit from surveillance and treatment is the first step in preventing this outcome. At-risk women include those with a prior preterm birth due to spontaneous preterm labor or preterm premature rupture of membranes (PPROM). Additional women who may be at risk for preterm delivery include those with a short cervical length in the 2nd trimester, known uterine anomalies, prior cervical surgery or multiple gestation; however, not all at-risk groups have interventions shown to improve outcomes.

CERVICAL LENGTH SURVEILLANCE

The length of the pregnant cervix is inversely proportional to the risk of preterm delivery. Cervical length (CL) measurements by transvaginal ultrasound (TVUS) have been shown to have the highest interobserver reproducibility and are more accurate at predicting preterm delivery than are digital examinations. Such imaging is an important tool for identifying those women at increased risk for preterm birth who may benefit from additional surveillance and/or intervention. The use of universal TVUS CL screening for patients without a history of preterm birth for prevention of preterm birth remains a topic of debate. Recently, it was demonstrated that transabdominal CL > 30 mm provides reassurance that the TVUS CL is > 20 mm, the length at which intervention is recommended in women without a history of spontaneous preterm birth.[3]

PROGESTERONE

Use of progesterone derivatives to prevent preterm birth has been recommended since a landmark study was published in 2003. Meis et al. reported that 17-alpha-hydroxyprogesterone caproate (17-OHPC), administered by weekly intramuscular injection, reduces the rate of recurrent preterm delivery by approximately 35%.[4] The mechanism for its pharmaceutical effects is not well understood. Progesterone is thought to work either by reducing inflammation or affecting collagen remodeling.

Not all categories of risk for preterm delivery have interventions that have been shown to improve outcomes.

Since 2003, many researchers have evaluated alternative indications for progesterone injections and alternative methods of delivery, such as progesterone vaginal suppositories. A major research focus is the effectiveness of progesterone in reducing the rate of preterm birth in populations besides those women with a history of a preterm delivery. A 2007 survey of ACOG members found that providers prescribe progesterone for multiple indications, including dilated or effaced cervix, short cervix on ultrasound, positive fetal fibronectin, preterm labor symptoms, multiple gestation and uterine anomalies.

Although vaginal progesterone has been shown to be effective for reducing the preterm birth rate among women with a shortened cervical length, expanded indications and alternative delivery methods (such as the use of intramuscular 17-OHPC for nulliparous patients with a shortened cervix)[5] have been shown to actually *increase* the rate of preterm births. For this reason, ACOG and SMFM have devised guidelines for use of progestational agents to reduce the risk of preterm birth and recommend against extrapolating to populations beyond which efficacy has been demonstrated.

CERVICAL CERCLAGE

Previously, cervical cerclage was offered to patients with a history consistent with cervical insufficiency, defined as recurrent painless 2nd-trimester cervical changes leading to early preterm births. In more recent studies, experts have recommend a move away from the traditional history-indicated or "prophylactic" cerclage to placement of cerclage guided by sonographic cervical length evaluation and shortening; i.e., the "ultrasound-indicated cerclage." By following this management scheme (offering cerclage only in the setting of cervical shortening for multiparous women with a prior preterm delivery < 34 weeks' gestation), 58% of cerclages that are placed based on history alone could be avoided, without an increase in the number of preterm births.[6]

NORTHWEST PERINATAL CENTER APPROACH

Patients with a singleton pregnancy and prior spontaneous preterm birth (preterm labor or PPROM). Patients with a prior spontaneous preterm birth between 20 0/7 – 36 6/7 weeks' gestation should be offered 17-OHPC 250 mg IM weekly, to be started between 16-20 weeks gestation and continued through 36 weeks' gestation. For those women whose prior preterm delivery occurred before 34 weeks' gestation, serial TVUS CL measurement between 16 – 23 6/7 weeks' gestation is also recommended. If the CL falls below 25 mm before 24 weeks' gestation in this subset of women, cervical cerclage would be offered at that time. 17-OHPC should be continued, with or without cerclage placement. New data suggests that a switch to the vaginal route of pregesterone administration might be appropriate; individualized counseling is recommended in this scenario. Using both formulations simultaneously is not recommended.

Patients with a singleton pregnancy without prior spontaneous preterm birth (preterm labor or PPROM). In this setting, which represents the majority of our patient population, a single transabdominal cervical length measurement at the time of the routine anatomic survey (recommended at 20 weeks' gestation) will be performed; however, if there is an indication for any earlier anatomic survey or if the patient is late to care, it is valid to assess cervical length between 18-24 weeks' gestation for the purpose of making management decisions. If the abdominal cervical length measurement is below 30 mm, the cervical length will be measured transvaginally.[3] In the setting of the asymptomatic patient, a cervical length greater than 25 mm requires no further follow up. In those patients with a TVUS CL less than 20 mm, daily vaginal progesterone is recommended and has been shown to decrease the rate of preterm birth, as well as perinatal morbidity and mortality.[1] Cervical cerclage has not been shown to decrease the rates of preterm birth or improve outcomes in this patient population. Currently endorsed regimens for vaginal progesterone include Prometrium 200 mg pV nightly or Crinone 8% gel, 90 mg, pV daily. Based on the cost of therapy, our recommended regimen is Prometrium 200 mg pV qhs.

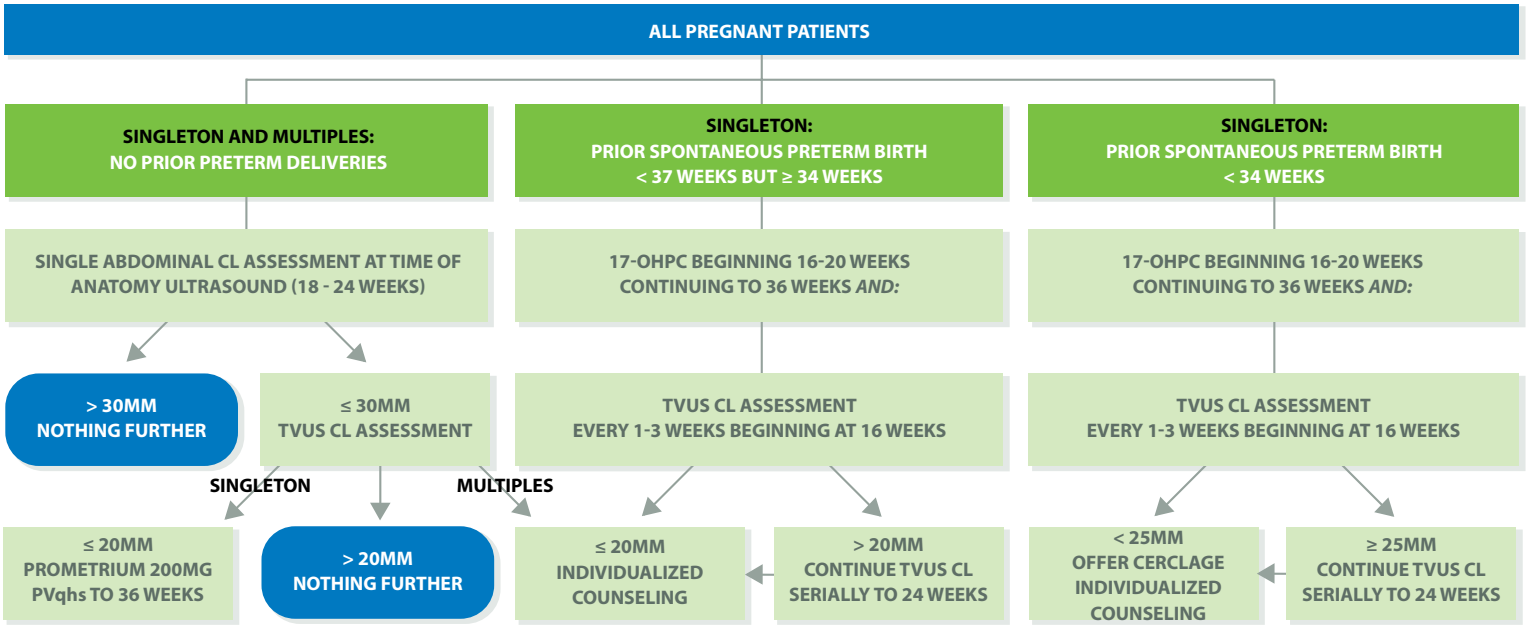
Multiple Gestations. Neither ACOG nor SMFM recommend serial CL surveillance in the setting of multiple gestations. We recommend a single transabdominal CL measurement at the time of the anatomic survey. If there is shortening, then a TVUS CL should be performed. If there is significant shortening, then individualized counseling should be offered. **This move away from routine TVUS CL assessment in asymptomatic women pregnant with multiples is a significant shift from our previous surveillance recommendations, and is based upon the absence of proven interventions to reduce the spontaneous preterm delivery rate in this patient population.** In a meta-analysis, cervical cerclage in the setting of a twin gestation was shown to increase the preterm delivery rate by 215%.[7] Neither vaginal nor injectable progesterone has been shown to be beneficial in this patient population. Weekly 17-OHPC injections administered to women pregnant with twins has not been shown to reduce the rate of spontaneous preterm deliveries.[8]

Symptomatic Patients. These guidelines are meant to be applied to asymptomatic women. However, when assessing the patient symptomatic with contractions or pelvic pressure, either in the outpatient setting or on labor and delivery, a CL measurement is more reliable and reproducible than digital examination. A TVUS CL greater than 30 mm is reassuring and is associated with a low risk for spontaneous preterm birth. Combining fetal fibronectin testing with CL assessment allows one to further stratify a patient's risk for preterm delivery.[9]

CONCLUSION

Universal transabdominal CL screening at the time of the anatomic survey is recommended for all low-risk patients with additional imaging, as indicated, for a short cervix. For those patients at risk for preterm birth, additional screening with TVUS CL measurements is recommended with the addition of progesterone, as indicated, based on history and exam. Consultation with Northwest Perinatal Center at any point in this process is welcome.

PROTOCOL FOR MANAGING ASYMPTOMATIC WOMEN AT RISK FOR PRETERM BIRTH



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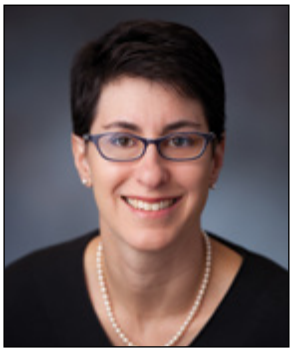

Dr. Fisher received her bachelor's degree from the University of California, San Diego. She completed her doctorate in biochemistry at the University of Wisconsin-Madison before attending the Medical College of Wisconsin. After completing her OB/GYN residency at the University of Utah Medical Center in Salt Lake City, she worked for the university as a general OB/GYN for several years before her maternal-fetal medicine fellowship at the University of Colorado School of Medicine. She is board certified in OB/GYN and board-eligible in maternal-fetal medicine.

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IN THIS ISSUE:

The clinicians of NORTHWEST PERINATAL CENTER specialize in complete medical services for the highest risk pregnancies. We are located in Portland, Oregon in the Peterkort medical offices near Providence St. Vincent Medical Center. We provide comprehensive high-risk obstetrical care that includes:

- Pre-pregnancy counseling
- Genetic counseling
- Prenatal screening for chromosomal abnormalities
- Ultrasound
- Prenatal diagnosis
- Amniocentesis
- Chorionic villus sampling
- Management of complicated pregnancies, such as:
  - recurrent miscarriages or stillbirths
  - multifetal pregnancies
  - hypertension/high blood pressure
  - diabetes
  - premature birth
  - Rh disease
  - fetal complications

When you refer a high-risk patient to Northwest Perinatal Center, you can be confident that your patient is cared for by an experienced and compassionate team of clinicians. Care options are designed to fit your preferences and your patient's individual needs, including one-time consultations, patient continuing co-management, or complete assumption of care by our clinicians. We also offer immediate in-hospital consultations and complete care for maternal transports. We use state-of-the-art technology in supporting the evaluation and care of your patient, and are committed to prompt follow-up in what are frequently stressful circumstances.

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