Volume 4, Number 1: April 2011

NORTHWEST PERINATAL CENTER

PERINATAL PROGRESS

A publication of Northwest Perinatal Center

MANAGING WOMEN AT RISK FOR PRETERM BIRTH

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Preterm birth (PTB) affects approximately 12% of deliveries in the United States. The rate of PTB had been gradually rising over the last three decades for a myriad of suspected reasons, such as changes in maternal population demographics, earlier deliveries of complicated pregnancies and an increase in multifetal gestations. In an effort to curtail the increasing rate of PTB, the clinical management of women at increased risk for preterm delivery has evolved significantly over the past decade. Contributing factors include new perspectives on the complex pathophysiology of preterm labor (PTL) and delivery, reevaluation of historic methods of prevention and acute intervention and the more prevalent use of sonographic cervical surveillance.

Encouragingly, recent data from the National Center for Health Statistics suggest the first consecutive two-year decrease in the rate of PTB in nearly 30 years from 2006 to 2008 (12.8% to 12.3%). The rate of late PTB between 34-36 weeks declined from 9.1% to 8.8%, and the rate of PTB prior to 34 weeks also decreased from 3.7% to 3.6%.[1] Whether this decline represents the start of a true downward trend or merely a short-term variation in population statistics is yet unclear.

This review describes the approach to the surveillance and treatment of women at risk for PTB commonly followed at Northwest Perinatal Center. Let us first examine some potential components of this proposed management algorithm.

CLINICAL RECOGNITION

Appropriately identifying patients at higher risk for PTB who may require increased surveillance and/or therapy early in the pregnancy is critical. Women who fall into this higher risk group may include patients with a prior PTB due to PTL or preterm premature rupture of membranes (PPROM), prior cervical surgery, sonographic cervical shortening, known Mullerian anomalies and multifetal gestations. Patients with a history of PTL in a previous pregnancy who later deliver at term may be less likely to receive benefit from increased scrutiny.

SMOKING CESSATION

Smoking cessation programs have been demonstrated to potentially reduce the rate of PTB by 14-31%.[2,3] At baseline, interventions to reduce or eliminate maternal smoking completely should always be discussed and reinforced throughout pregnancy, regardless of the risk for PTB. The potential reduction in the risk of PTB serves as one of its many benefits.

CERVICAL LENGTH SURVEILLANCE

The sonographic cervical length (CL) has been correlated with risk for preterm delivery.[4] The relative risk of spontaneous PTB increases as CL decreases. Ultrasound CL measurements have been shown to be more reliable and consistent between examiners when compared to digital cervical examination.[5] While CL surveillance has not been shown to independently reduce the rate of PTB, it has become a cornerstone for identifying patients at higher risk for PTB and for whom further interventions or therapies may be an option.

FETAL FIBRONECTIN

The presence of fetal fibronectin (fFN) in cervico-vaginal secretions in otherwise asymptomatic patients with a history of prior PTB has been noted to increase the relative risk of recurrent preterm delivery by greater than three-fold when compared to similar patients who are fFN negative.[6] Similar to CL surveillance, no studies to date have demonstrated a benefit from therapeutic interventions based upon fFN screening in asymptomatic patients, either alone or in combination with CL measurements. In contrast, the clinical value of fFN screening appears to lie in its negative predictive value among patients with frank symptoms of PTL. In symptomatic patients, a negative fFN test between 24-34 weeks suggests a risk for PTB within 14 days of less than 1%.[7]

PROGESTATIONAL THERAPY

As widely publicized, weekly administration of 17-alpha-hydroxyprogesterone caproate (17-OHP) has been shown to reduce the likelihood of recurrent singleton PTB by 33% in patients with a prior preterm delivery.[8] Subsequent studies performed in both twin and triplet pregnancies have not demonstrated any significant benefit from 17-OHP therapy.[9,10] More recently, a study examining the use of vaginal progesterone therapy in women with CL <15 mm before 26 weeks did dem-

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onstrate a significant benefit: a 46% reduction in PTBs <34 weeks.[11] Based upon these data, progestational therapy has become a significant part of the armamentarium used against PTB in singleton gestations. It is not, however, typically used in multifetal gestations unless other risk factors are present.

BED REST / ACTIVITY RESTRICTION

Bed rest and/or activity restriction have traditionally been a foundation for most approaches to patients with active PTL or who are at risk for PTB. However, the reduction of physical activity has never actually been demonstrated to improve outcomes. In fact, it carries with it numerous potential adverse consequences for patients, their families and the healthcare system as a whole. Unfortunately, data ojectively examining the utility of bed rest is very limited. A 2004 Cochrane review examined the available literature and could identify only one trial which indirectly addressed the question of bed rest efficacy and found no demonstrable difference in outcomes.[12] More contemporary limited studies have also been unable to demonstrate any differences in outcomes with activity restriction.[13] Given the absence of clinical data to either support or refute the use of activity restriction to reduce the risk of PTB, the recommendation for bed rest should be approached similarly to all therapeutic interventions – with deliberate attention to the potential risks and benefits of the therapy.

CERVICAL CERCLAGE

Historically, cervical cerclage has been a cornerstone of therapy to prevent PTB due to suspected cervical incompetence despite limited evidence to support its use.[14,15] Prior randomized studies have also suggested no benefit from cerclage placement in patients with incidentally noted cervical shortening or funneling.[16] However, a meta-analysis (2005) of trials specifically examining patients with a history of PTB who also have sonographic cervical shortening suggested a potential benefit to cerclage placement.[17] Thereafter, a multicenter, randomized trial examining pregnant women with a history of PTB and a short CL demonstrated a significant benefit from cerclage placement.[18] When the CL was below 25 mm, the study reported a 33% reduction in the rate of PTB under 35 weeks with cerclage placement. When the CL was below 15 mm, the study reported a 77% reduction in PTB under 35 weeks with cerclage placement. Based upon these studies, in the appropriate patient with a prior PTB and a shortened CL prior to 24 weeks, cerclage placement is a reasonable therapeutic option to consider.

NORTHWEST PERINATAL CENTER APPROACH

The initial approach to the patient specifically at risk for recurrent PTB includes 1) a detailed review of the obstetric history, including an account of the events leading up to the prior PTB; 2) a review of any related data, such as laboratory studies and placental pathology reports; and 3) consideration of ongoing maternal conditions that could further impact the risk of early delivery in the current pregnancy.

All patients are counseled regarding smoking cessation and those identified as having an increased risk for PTB are offered sonographic CL surveillance. This is typically started at 17 weeks with follow-up evaluations at intervals of one to three weeks based upon the CL up to 28 weeks' gestation.

Routine fFN surveillance is not utilized at NWP in the asymptomatic patient. The logistics of obtaining an fFN sample in conjunction with CL surveillance is cumbersome, since fFN testing must be performed prior to vaginal examination or the introduction of lubricating gel. As a result, **the use of fFN screening in the office setting is not routinely used in our practice on asymptomatic high-risk patients.**

Patients with a singleton pregnancy and a history of prior PTB are offered weekly 17-OHP. At NWP, the prophylactic regimen is typically started at 17 weeks and is continued until 34-36 weeks. Women with multifetal pregnancies are not offered 17-OHP in the absence of other risk factors.

If **cervical shortening below 30 mm** is observed during the course of surveillance, subsequent recommendations are based upon the length of the cervix (see Figure). Initial steps include 1) assessment of uterine activity and further in-hospital evaluation, if indicated, and 2) an increase in the frequency of CL evaluations. In patients with a prior PTB not on 17-OHP therapy, 17-OHP is readdressed with the patient.

With **cervical shortening below 25 mm**, activity restriction is discussed with the patient. At NWP, three varying levels of activity restriction may be recommended based upon the clinical situation. In patients with a prior PTB, cervical cerclage placement may be considered if cervical shortening is noted before 24 weeks' gestation. 17-OHP therapy is offered at this point to all patients <26 weeks' gestation, even without a history of PTB.

Managing preterm birth continued...

When the **CL falls below 15 mm**, both activity restriction and 17-OHP therapy (prior to 26 weeks) are recommended regardless of the pregnancy history. Cerclage placement is discussed and offered to patients with a prior PTB.And finally, if cervical shortening and membrane funneling are noted at or beyond the external cervical os before 24 weeks regardless of the pregnancy history, cerclage placement is discussed and offered in conjunction with the previously mentioned interventions, given the poorer prognosis in this clinical situation.

NWP PROTOCOL FOR MANAGING PRETERM BIRTH

	OBSERVATION	cervical length surveillance every 1-3 weeks	tocodynometer monitoring + hospitalization PRN	activity restriction	17-OHP therapy	cerclage placement
NO PRIOR PTB	CL >30 mm	-	-	-	-	-
	CL 25-30 mm	recommend	recommend	-	-	-
	CL 15-25 mm	recommend	recommend	offer	offer	-
	CL <15 mm	recommend	recommend	recommend	recommend	-
	Membranes at or beyond ext os w/ cervical dilation	recommend	recommend	recommend	recommend	offer

	OBSERVATION					
PRIOR PTB	CL >30 mm	recommend	-	-	recommend	-
	CL 25-30 mm	recommend	recommend	-	recommend	-
	CL 15-25 mm	recommend	recommend	offer	recommend	offer
	CL <15 mm	recommend	recommend	recommend	recommend	offer
	Membranes at or beyond ext os w/ cervical dilation	recommend	recommend	recommend	recommend	offer

CONCLUSION

The management of women at risk for PTB continues to be a significant challenge for OB care providers. Information from clinical trials over this past decade has significantly altered the obstetric care and surveillance methods for a substantial portion of this at-risk population. While it is unclear whether these changes in management have directly and positively impacted the most recent rates of PTB, we hope to see a continued downward trend.

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Dr. Lee attended Dartmouth College for his undergraduate studies, where he majored in biochemistry. He received his medical degree from the University of Pennsylvania School of Medicine in Philadelphia. After finishing his residency in Obstetrics & Gynecology at the Reading Hospital and Medical Center, he completed his subspecialty training in Maternal-Fetal Medicine at Women & Infants' Hospital of Rhode Island/Brown University. He is board certified in both Obstetrics & Gynecology and Maternal-Fetal Medicine.

Dr. Lee has been with Northwest Perinatal Center since 2002. While he thoroughly enjoys taking care of all high-risk pregancies, he has special interest in the fields of diabetes in pregnancy and preterm delivery. Dr. Lee currently leads the Health Information Management committee at Women's Healthcare Associates charged with EMR development and Meaningful Use compliance. He also serves as an Epic Clinicial Physician Champion in Obstetrics for the Providence Health System—helping to develop their hospital-based EMR.

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