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SEMINARS IN PERINATOLOGY

Recurrent Preterm Birth

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Recurrent preterm birth is frequently defined as two or more deliveries before 37 completed weeks of gestation. The recurrence rate varies as a function of the antecedent for preterm birth: spontaneous versus indicated. Spontaneous preterm birth is the result of either preterm labor with intact membranes or preterm prelabor rupture of the membranes. This article reviews the body of literature describing the risk of recurrence of spontaneous and indicated preterm birth. Also discussed are the factors which modify the risk for recurrent spontaneous preterm birth (a short sonographic cervical length and a positive cervicovaginal fetal fibronectin test). Patients with a history of an indicated preterm birth are at risk not only for recurrence of this subtype, but also for spontaneous preterm birth. Individuals of black origin have a higher rate of recurrent preterm birth.
Semin Perinatol 31:142-158. © 2007 Published by Elsevier Inc.

KEYWORDS recurrent preterm birth, indicated preterm birth, spontaneous preterm birth, rupture of membranes, parturition

Preterm birth is the leading cause of perinatal morbidity and mortality worldwide.[1] A preterm delivery is a risk factor for subsequent preterm birth.[2-22] Preterm birth can be the result of three obstetrical circumstances: 1) preterm labor with intact membranes; 2) preterm prelabor rupture of membranes (PROM); and 3) "indicated" preterm birth, which occurs when maternal or fetal indications require delivery before 37 weeks of gestation. The most common indications are preeclampsia and small for gestational age (SGA). Spontaneous preterm parturition is a syndrome caused by multiple etiologies (Fig. 1), which are expressed by synchronous or dyssynchronous activation of the common terminal pathway of parturition. The reader is referred to recent reviews for full consideration of this concept.[23,24]

Although many studies have focused on the rate of preterm birth,[25-57] an important consideration is whether these deliveries are the result of spontaneous labor (with intact or ruptured membranes) or "indicated" preterm deliveries. The need for this distinction is based on the premise that the risk factors for recurrent preterm PROM, preterm labor with intact membranes, preeclampsia, and/or SGA are different. However, recent observations suggest that there may be overlap among these conditions,[18,19] so that a patient with an "indicated" preterm birth may also be at risk for spontaneous preterm birth.[18,19] The converse may also be true (ie, that a patient with a spontaneous preterm birth is at risk for an "indicated" preterm birth in a subsequent pregnancy).

This review will present a summary of the literature and aims to clarify the risk of recurrent disease and the biological basis for recurrent preterm birth.

Definition of Preterm Birth

Preterm deliveries are those occurring between fetal viability and 37 completed weeks of gestation (menstrual age). However, the lower limit of gestational age used to define a preterm birth has ranged from 13 to 24 weeks of gestation among various reports.[21,58,59] Our view is that the delivery of a previable fetus should be considered a spontaneous abortion rather than a spontaneous preterm birth. Otherwise, perinatal and infant mortality estimates in a population or country will be biased by the frequency of late spontaneous abortions.

The precise definition of viability, however, is subject to debate given the increased frequency of survival at very low

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 0146-0005/07/$-see front matter © 2007 Published by Elsevier Inc.
doi:10.1053/j.semperi.2007.04.001

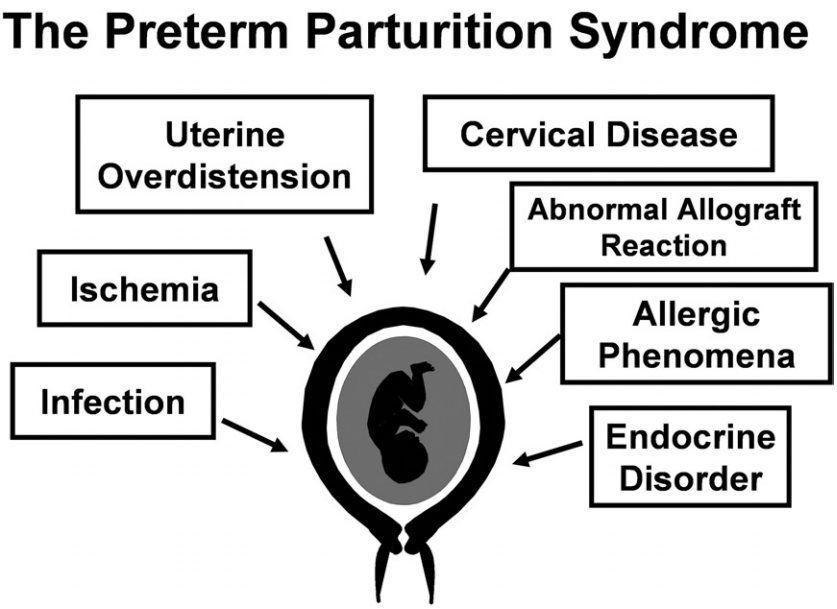

Figure 1 Pathological processes implicated in the preterm parturition syndrome. (Reproduced with permission from Romero and coworkers.[24])

gestational ages. Clearly, some infants can survive around 24 weeks of gestation, but none at 20 weeks. Therefore, we propose the range of 24 to 36 6/7 weeks of gestation for the definition of preterm birth. If and when technological advances allow substantial survival below 24 weeks of gestation, this definition should be revised.

A birth weight of 500 g has also been used to define the lower limit of viability.[11,60] The popularity of this definition derives from its simplicity. Birthweights can easily be obtained anywhere in the world at a very low cost. The limitations of this approach are that viable neonates born at viable gestational ages and affected by intrauterine growth restriction (IUGR) may have birthweights below 500 g, and that some previable infants may weigh more than 500 g. Ideally, gestational age at birth should be used to define viability. There are, however, practical obstacles derived from the uncertainty of gestational age estimation in many countries. This problem can be overcome in areas where ultrasound is performed routinely in early pregnancy, but not elsewhere, including underdeveloped countries. The criteria for the definition of viability have implications for the calculation of vital statistics and comparisons of these among different populations.

Recurrent Preterm Birth

Recurrent preterm birth is defined as two or more deliveries before 37 completed gestational weeks.[2,9,12,59,61,62] However, the definition among studies is not uniform. Criteria that have varied and may affect estimation of the rate of recurrent preterm birth include: 1) gestational age thresholds used for defining the upper (ie, 35 or 36 weeks)[9,12,63,64] and lower (ie, 13 to 28 weeks)[10,59] limits of preterm birth; 2) inclusion of multiple gestations[65-67]; 3) inclusion of spontaneous, as well as indicated preterm births[11,64]; 4) the number of preterm births required to fulfill the definition of recurrent preterm birth[8]; and 5) the requirement that the preterm births be consecutive.[8]

Recurrent Spontaneous Preterm Birth

The Frequency of Recurrent Spontaneous Preterm Birth

Recurrent spontaneous preterm birth is defined as more than one preterm birth related to spontaneous onset of labor with intact membranes or preterm PROM.

Several studies have consistently indicated that patients with a previous spontaneous preterm birth are at risk for a subsequent spontaneous preterm delivery.[2-22] Iams et al[9] reported the results of a secondary analysis of the data from the Preterm Prediction Study, conducted under the leadership of Goldenberg et al.[68] Among 378 patients with a prior spontaneous preterm birth or spontaneous abortion in the second trimester (gestational age range: 18-36 weeks), the rate of recurrent spontaneous preterm birth (<35 weeks) varied between 14% and 15%, in contrast to the 3% rate of spontaneous preterm birth among 904 parous women with a previous uncomplicated term delivery (Table 1).

The rate of recurrent preterm birth was modified according to the sonographic cervical length in the index pregnancy and the presence of a positive test for fetal fibronectin in cervicovaginal fluid at 22 to 24 weeks of gestation.[9] Among women with a previous spontaneous preterm birth, the rate of recurrence (<35 weeks) was the highest (64%) among women with a sonographically short cervix (<25 mm) and a positive fetal fibronectin test. The lowest rate of recurrence (7%) occurred in patients with a sonographic cervical length >35 mm and a negative fetal fibronectin test.[9]

Patients with a positive fibronectin test were at higher risk for spontaneous recurrent preterm birth regardless of cervi-