The clinical content of preconception care: reproductive history

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A history of previous birth of a low birthweight infant, previous cesarean sections, multiple previous spontaneous abortions, prior stillbirth, or uterine anomaly identifies women at increased risk for recurrent abortion, preterm birth, or stillbirth. We review the evidence for the potential benefit of reproductive history in identifying strategies for evaluation and treatment to prevent recurrent adverse pregnancy outcome. We offer evidence-based recommendations for management of women with these histories.

Key words: low birthweight, preconception, preterm birth, reproductive history

Preconception risk assessment includes a comprehensive evaluation of a woman's reproductive history to identify factors related to previous poor pregnancy outcomes that may be amenable to intervention before any future pregnancies occur.[1,2] Because an adverse outcome in an earlier pregnancy is associated with an increased risk for adverse outcomes in subsequent pregnancies, information such as previous spontaneous abortion, preterm birth, fetal growth restriction, stillbirth, surgical delivery, diabetes, and pregnancy-induced hypertension should be collected.[3] Preconception diagnosis and treatment of certain conditions, including maternal autoimmune disease and uterine malformations, may reduce the risk of recurrent pregnancy losses.

Prior low birthweight infant

Burden of suffering: A birthweight of less than 2500 g includes infants that were born preterm (< 37 weeks) and infants that suffer from fetal growth restriction (FGR), whether born before or after 37 weeks. About 30% of preterm infants are growth restricted as well.

Preterm birth

Preterm birth is now the leading cause of neonatal death in the United States and is the leading cause of infant mortality for nonwhite babies.[4] Women who have had a preterm birth have increased risk for subsequent preterm birth.[5-8] The earlier in gestation the first preterm birth, the greater the risk for another. Women with 1 preterm birth before 35 weeks have a 16% risk of a second preterm birth. Risk increases to 41% after 2 preterm births and to 67% after 3 preterm births.[9] Other than multiple gestations, previous preterm birth is often found as the single most important risk factor for another preterm birth among multiparous women. Multivariate analysis in a large Alabama study of a primarily low income population reported that women with previous preterm delivery had an odds ratio of 2.8 for preterm birth in subsequent pregnancy.

The only other risk factor of similar magnitude was prepregnancy maternal weight of less than 50 kg.[7] Early preterm delivery (23-27 weeks' gestation) was closely associated with subsequent early preterm delivery (< 28 weeks).[10] A population-based study from Texas concluded that prior preterm birth accounted for 10% of subsequent preterm births.[9] A number of conditions are associated with recurrent preterm birth: African American ethnicity, inflammatory changes in the placenta, low maternal prepregnant weight (< 50 kg) or body mass index less than 19.8 kg/m^2, a large interpregnancy weight loss (> 5 kg/m^2), cigarette smoking, short interpregnancy interval (< 12 months), history of cervical insufficiency, or short cervix on transvaginal ultrasound during subsequent pregnancy.[8] All but the first 2 could potentially be influenced before the next pregnancy. Maternal periodontal disease is associated with increased risk for preterm delivery. However, treatment during pregnancy has not been consistently beneficial. This prob-

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lem is considered in detail elsewhere in this supplement.[11]

Fetal growth restriction

Growth-restricted fetuses account for almost half of all stillbirths.[12] They are also at high risk for fetal asphyxia during labor, meconium aspiration, serious neonatal morbidity, and death. Risk continues into childhood and adulthood. A growing literature associates FGR birth with hypertension, coronary artery disease, diabetes, obesity, and other chronic health problems among adult survivors.[13]

The etiology of FGR is complex but can be described in 3 broad categories: maternal, fetal, and placental.[13,14] Maternal risk factors include low prepregnancy weight, malnutrition, poor weight gain during pregnancy, maternal age younger than 16 years or older than 35 years, a short interpregnancy interval, and smoking and substance abuse as well as number of chronic maternal illnesses that are detailed in other papers in this supplement.

Chronic maternal vascular disease, hypertension, renal insufficiency, diabetes mellitus, and the collagen vascular diseases (especially when complicated by preeclampsia) account for nearly one-third of FGR cases.[15] Fetal risk factors include chromosomal abnormalities, a number of genetic syndromes, fetal viral and protozoal infections, and multiple gestations. Placental factors include chronic placental abruption, placenta previa, placental infarctions, and chronic placental villitis. Placental mosaicism accounts for up to 25% of unexplained FGR. Malaria accounts for a high proportion of FGR births and stillbirths in areas in which transmission is high.[13,15] The recurrence risk of FGR is about 20%.

How detectable is the condition? In the United States, virtually all infants are weighed at birth, and women generally know the birthweight of their infants. Maternal illness can be identified by a careful history and obtaining the patients' medical records from the previous delivery. Transvaginal measurement of cervical length during a subsequent pregnancy identifies women with a short cervix ($<$ 25 mm at 20-24 weeks, $<$ 30 mm at 16-20 weeks) who have markedly increased risk for preterm birth.[8,16] However, there are no validated, standardized ways to confirm a diagnosis of cervical insufficiency prior to pregnancy.[17] Determining the presence of placental inflammation requires obtaining a pathology report from the previous low birthweight pregnancy. Pathological examination of the placenta is not routine, although this is increasingly performed in the case of an abnormal birth outcome.

FGR is diagnosed in utero by ultrasound measurement of fetal biparietal diameter, abdominal circumference, femur length, and calculated estimates of fetal weight in comparison with standardized curves of these parameters versus gestational age. FGR is diagnosed in the neonate by birthweight corrected for gestational age. The usual criterion for defining FGR is birthweight below the 10th percentile of births at that gestational age.

How effective are the current treatments? Low maternal prepregnancy weight and large interpregnancy weight losses are important risks for both preterm birth and low birthweight, and weight gain prior to pregnancy might reduce risk for these women, but this has not been tested. The complex associations of body mass index with pregnancy outcomes are described elsewhere in this supplement.[18]

Smoking cessation programs are effective in reducing pregnancy loss.[19] Interpregnancy interval can be extended by contraception; however, no interventional studies exist at present.

Incompetent cervix is identifiable in some cases by a history of painless dilatation in the previous labor. Cervical cerclage procedures prior to pregnancy have been used for many years for women with a history of multiple late midtrimester losses and appear effective when compared with the same patient's past history, but there are no randomized prospective trials.[17] A very large international trial compared cerclage during pregnancy plus bed rest with bed rest alone and found a small but statistically significant reduction in delivery prior to 33 weeks and very low birthweight deliveries.[20] With the recognition that a short cervix found by transvaginal ultrasound during pregnancy identifies women at risk for recurrent preterm delivery, there is great interest in how to treat this group. Most evidence to date is that cervical cerclage during pregnancy is not beneficial.[21] However, in 1 metaanalysis, risk of preterm birth was reduced by cerclage for the subgroup of women with a singleton pregnancy, prior preterm delivery, and a short cervix by ultrasound in the current pregnancy.[22]

Recent studies found highly significant reductions in subsequent preterm birth if women with a previous preterm infant are treated with injections of 17-hydroxyprogesterone caproate from 16 to 36 weeks of gestation.[23] Additional benefits include reductions in neonatal death, respiratory distress syndrome, bronchopulmonary dysplasia, intraventricular hemorrhage, and necrotizing enterocolitis in the progesterone-treated group. Similar benefits have been reported with daily use of vaginal suppositories of natural progesterone.[24] A 2005 metaanalysis of 10 trials confirmed these findings.[25] Use of progestational agents once labor has started is not effective. Recent evidence suggests that progesterone is of benefit to women with a shortened cervix.[26] 17-Hydroxyprogesterone caproate is presently available only through compounding pharmacies. It has been granted orphan drug status by the US Food and Drug Administration (FDA). An FDA panel has recommended approval for the indication of preventing preterm birth.[27] Progesterone suppositories are also available only through compounding pharmacists.

Dietary long-chain polyunsaturated fatty acid supplementation is discussed in the nutrition section of this supplement.[18] Supplementation has been found to slightly increase the mean gestational length but not with any reduction in low birthweight, preterm birth, or rate of preeclampsia.

Management of women with a history of an FGR infant includes obtaining the records of the previous pregnancy and