Ceruloplasmin and Preterm Premature Rupture of the Membranes

Premature rupture of the membranes (PROM), defined as rupture of the chorioamniotic membranes before the onset of labor, is a very common clinical problem in human pregnancy. In clinical obstetric terminology, PROM is defined as rupture of the membranes at term (within 3 weeks of the Estimated Date of Confinement, or due date). The reported incidence of PROM in term pregnancy is 8–10%. Approximately one-fourth of PROM cases occur remote from term (i.e., at less than 37 completed gestational weeks) and are termed preterm PROM (often called PPROM).

Term pregnancies complicated by PROM are at increased risk for several complications for mother and fetus. The likelihood of ascending maternal infection, or chorioamnionitis, is directly related to the duration of membrane rupture, increasing from an overall rate of 0.5% to 3–15% with progressive duration of PROM (1). The risk of neonatal sepsis (0.2% for all term newborns) also increases both with the presence of PROM (1%) and with the duration of PROM (3–5% with PROM >24 h). The dominant etiology for neonatal sepsis in contemporary American obstetric practice is the group B β-hemolytic streptococcus, and contemporary practice algorithms amply document the association of PROM, particularly PROM of >18 h duration, as a risk factor for neonatal sepsis requiring additional medical treatments for mother and newborn (2).

Women of reproductive age now represent the most rapidly expanding population of AIDS patients, and it is now clear that untreated HIV-positive pregnant women have a 25–35% risk of transmitting the HIV virus to their infant at the time of delivery (3). Vertical transmission can be minimized by appropriate antiretroviral prophylaxis, scheduled cesarean section at 38 weeks (4), and by avoidance of certain recognized obstetric risk factors. These include invasive procedures, prematurity, chorioamnionitis, and prolonged duration of ruptured membranes (particularly >4 h) (5). The ability to precisely predict term PROM could be of value in these women vis-à-vis timing of abdominal delivery.

The etiology of term PROM remains unclear and likely involves a final common pathway for several related intrinsic and/or extrinsic processes. However, studies comparing the tensile strength of membranes from patients with term PROM to membranes from control patients show no differences in tensile strengths except in the membranes near the cervix, suggesting an ascending etiology (6). Growing evidence also suggests that ascending, usually subclinical, infection and/or inflammation plays an integral part in this process (7).

Elsewhere in this issue, Ogino et al. (8) report an association of active ceruloplasmin in cervicovaginal secretions of third-trimester pregnant women who subsequently develop PROM. Ceruloplasmin is a known plasma antioxidant that increases in concentration during inflammation (9), and it is likely that the findings reported in this issue are further confirmation of the hypothesis that inflammation plays a role in PROM.

The association of active ceruloplasmin with term PROM is exciting and worthy of rapid confirmation by other investigators. However, the real potential value for these findings involves patients with preterm PROM. In the developed world, the dominant contributor to perinatal morbidity and mortality in structurally normal babies is premature birth. Despite aggressive tocolysis, the frequency of preterm birth has not diminished over the past 40 years (10). There is increasing evidence linking infection, both obvious and occult, with preterm birth (11). The biggest identifiable etiology of spontaneous premature birth is preterm premature rupture of the membranes, associated with 28–64% of all preterm births (12). There currently is no method available that will accurately predict subsequent preterm PROM.

High fetal morbidity and mortality rates occur with preterm PROM because of infection, premature labor, fetal compromise from umbilical cord compression, and/or fetal deformation (pulmonary hypoplasia and/or arthrogryposis) (13). Maternal complications are also more common with preterm PROM, with chorioamnionitis rates as high as 25–35%. We now know that antibiotic treatment of women who experience this complication will increase the interval to delivery and reduce maternal and neonatal infection rates (14).

Late 20th Century American obstetric practice is heavily invested in the notion of population screening. Readers of this journal are likely all familiar with algorithms for double, triple, and quadruple midtrimester serum screening, hepatitis B screening, glucose-tolerance screening, and Group B β-hemolytic streptococcal screening among others. There is interest in some circles to consider screening of the obstetric population with tests that may identify women at increased, or decreased, risk of spontaneous preterm labor. These screening tests currently include transvaginal ultrasound (15), fetal fibronectin measurements in cervicovaginal secretions (16), and salivary estriol (17). Unfortunately, all of these techniques suffer from variably low sensitivity and specificity in asymptomatic low-risk pregnant women and are not currently in widespread clinical use. The results reported by Ogino et al. (9), IF equally applicable to preterm PROM, could improve our ability to identify that small subset of the general obstetric population at risk for a devastating and costly complication of pregnancy. This would then open the possibility of prophylactic strategies and/or randomized prevention trials.

References

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