Amniotic Fluid Infection May Be Linked to Risk for Premature Birth
By Dr. William E. Wagner

Preterm deliveries are those that occur at less than 37 weeks gestational age. In the United States the preterm delivery rate is 12-13 percent. Preterm births account for 75 percent of perinatal mortality (PNM) and more than 50 percent of the long term morbidity. Neonatal intensive care units have improved the survival of preterm babies even at extremes of gestational age, but they are still at increased risk of neurodevelopmental impairment and respiratory and gastrointestinal complications.

The obstetric precursors leading to preterm birth are: (1) delivery for maternal or fetal indications (MFI); (2) spontaneous preterm labor (SPL) with intact membranes; and (3) preterm premature rupture of membranes (PPROM) which respectively are 30-35 percent, 40-45 percent, 20-25 percent. Spontaneous preterm birth is most commonly caused by preterm labor (PTL) in Caucasians, but PPROM is more common in African American women. They may also be stratified by gestational age (GA): < 28 weeks (5 percent); 28-31 weeks (15 percent); 32-33 weeks (20 percent); and 34-36 weeks (60-70 percent). The final common pathway leading to labor initiation implicates inflammatory decidual activation. At term, decidual activation seems to be mediated at least in part by the fetal - decidual paracrine system (localized changes in progesterone concentration), in many cases of preterm labor, decidual activation seems to arise in the context of intrauterine bleeding or occult intrauterine infection. This summary will focus on intrauterine infection.

Intrauterine infection is a frequent and important mechanism leading to preterm birth. The mechanisms by which intrauterine infections lead to PTL are related to activation of the innate immune system. Microorganisms are recognized by pattern-recognition receptors which in turn elicit the release of inflammatory mediators (chemokines and cytokines), e.g. interleukin 8 (IL 8), interleukin 1β, and tumor necrosis factor (TNF) α. Microbial endotoxins and proinflammatory cytokines stimulate the production of prostaglandins, other inflammatory mediators, and matrix-degrading enzymes. Prostaglandins stimulate uterine contractility, degradation of extracellular matrix in the fetal membranes increases the likelihood of PPROM.

Intrauterine infection accounts for 25-40 percent of preterm births, although it is likely underrepresented by culture techniques as the
rate of microbial colonization if the chorioamnion is twice that seen in the amniotic cavity. Intra-amniotic infection is a chronic process. The earlier the gestational age at which women present with PTL, the higher the frequency of intrauterine infection. At 21-24 weeks gestation, most spontaneous births are associated with histological Chorioamnionitis compared with ~ 10 percent at 35-36 weeks. Intrauterine infection can be confined to the decidua, extend to the space between the amnion and chorion, and reach the amniotic cavity and the fetus.

Microorganisms can gain access to the amniotic cavity by: (1) ascending from the vagina and cervix; (2) hematogenous dissemination through the placenta; (3) iatrogenic through invasive procedures; and (4) by retrograde flow through the fallopian tubes. The most common of these is ascending (vertical) transmission. The exact timing is unknown, but colonization of the decidual membranes becomes pathologically important when the membranes become tightly applied at about 20 weeks, which given the closed system, essentially forms an abscess, with the pathway of inflammatory response leading to preterm contractions, labor, and preterm delivery. Once the infection involves the fetus, subclinical infection leads to inflammatory response, again with the final common pathway leading to likely preterm delivery, and more importantly may lead to long term handicap including periventricular leukomalacia, CP, and chronic lung disease.

Bacterial vaginosis (BV)-a disorder characterized by a change in the microbial ecosystem of the vagina, is implicated as a risk factor for preterm delivery. African American women in both the United States and the UK are three times more likely to have BV than are Caucasian women, which has been postulated to explain 50 percent of the excess preterm births in black women. Trichomoniasis seems to be associated with preterm birth with a relative risk (RR)of about 1-3. Chlamydia is associated with preterm birth in the presence of an immune response, with a RR of ~ 2. Vaginal group B strep, Ureaplasma, and Mycoplasma, colonization is NOT associated with increased risk for preterm birth.

In summary, preterm labor and delivery is a complicated process with a multifactorial etiology. It is much more complex than the concept of “Term labor gone bad.” The potential infectious etiology leading to a common final pathway of decidual activation and inflammation continues to be a central focus of perinatal research. Despite new technology and markers which can predict risk of preterm delivery, we still have not seen a substantial reduction in the preterm birth rate in the United States.

References


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