Effects of Chorioamnionitis on the Fetal Lung

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KEYWORDS

• Respiratory distress syndrome • Bronchopulmonary dysplasia • Lung development • Lung maturation • Lung injury

KEY POINTS

- Very preterm infants are commonly exposed to a chronic, often asymptomatic, chorioamnionitis that is diagnosed by histologic evaluation of the placenta only after delivery.
- The reported effects of these exposures on fetal lungs are inconsistent because exposure to different organisms, durations of exposure, and fetal/maternal responses affect outcomes.
- In experimental models, chorioamnionitis can both injure and mature the fetal lung and cause immune nodulation.
- Postnatal care strategies also change how chorioamnionitis relates to clinical outcomes such as bronchopulmonary dysplasia.

CHORIOAMNIONITIS: A MULTIFACETED FETAL EXPOSURE

Overview

There is no consensus about the relationships between chorioamnionitis and 3 pulmonary outcomes of concern for preterm infants: respiratory distress syndrome (RDS), pneumonia/sepsis, and bronchopulmonary dysplasia (BPD). The difficulty in defining clear relationships results from the multiple variables contributing to the antenatal exposures, the postnatal exposures, and care strategies that contribute to the diagnoses of the short-term outcomes of RDS and pneumonia/sepsis, and the longer term outcome of BPD. Multivariate analyses of large data sets are imperfect tools to define relationships because of the inter-related nature of the variables, the poorly defined fetal exposures, and the imprecision of diagnosis of diseases such as RDS and BPD. This article discusses these problems based on the clinical data. In contrast, research with animal models provides solid information about how experimental chorioamnionitis can affect the fetal lung. The combination of an appreciation of the clinical complexity and the experimental effects of chorioamnionitis provides insight into

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how individual preterm infants present and respond to therapy. The focus of this article is the lungs of preterm infants born at less than 32 weeks' gestation, during the period of saccular expansion and before alveolarization.

Diagnosis

Chorioamnionitis can be diagnosed before the infant is born by findings such as maternal fever, increased white blood cell count, tender uterus, and by amniotic fluid analyses for bacteria, inflammatory mediators, or inflammatory cells. Histologic chorioamnionitis is a postdelivery diagnosis that is graded by the amount of inflammatory cells and the amount of necrosis in the chorioamnion.[1] The diagnosis of clinical chorioamnionitis does not reliably predict the presence or severity of histologic chorioamnionitis, which is more common following very preterm birth. Furthermore, the diagnosis of histologic chorioamnionitis is not reproducible between pathologists.[1]

The diagnosis of chorioamnionitis correlates with the clinical presentation of a pregnancy at risk for very preterm delivery. Preterm premature rupture of membranes is a surrogate for chorioamnionitis with a high concordance. Preterm labor of unknown cause or with a short cervix is frequently associated with chorioamnionitis.[2] In various populations, 50% to 70% of women delivering very preterm infants have chorioamnionitis, with the incidence increasing as gestation at delivery decreases.[2,3]

The Organisms

The organisms associated with early gestational delivery can be single species or polymicrobial aerobic and anabolic isolates that generally are vaginal flora (**Table 1**).[4] More than 50% of amniotic fluids collected by amniocentesis or at cesarean delivery from women with preterm premature rupture of membranes were positive for *Ureaplasma*.[5] These organisms are not usually considered to be pathogens. The generally accepted pathway to the subclinical histologic chorioamnionitis associated with very preterm birth is a diffuse ascending colonization of the endometrial-chorionic space with extension into the fetal membranes, the amniotic fluid, and ultimately the fetus.[6] Recent pathologic analyses suggest that another route may be more common. A localized epithelial colonization of the endometrium may breach the chorioamnion locally, contaminating the amniotic fluid with subsequent extension to the fetal membranes and fetus.[7] The identification of organisms associated with chorioamnionitis by culture does not capture the entire population of organisms; more nonculturable organisms can be identified by polymerase chain reaction (PCR).[8]

Table 1
Organisms cultured from chorion in association with preterm deliveries[a]

Organism Type			
Ureaplasma/Mycoplasma	**Aerobes**	**Anaerobes**	**% of Culture-Positive Placentas[a]**
+	–	–	9
–	+	–	30
–	–	+	21
+	+	–	3
+	–	+	4
–	+	+	28
+	+	+	6

[a] 51% of 1365 placentas were culture positive.

Data from Onderdonk AB, Delaney ML, DuBois AM, et al. Detection of bacteria in placental tissues obtained from extremely low gestational age neonates. Am J Obstet Gynecol 2008; 198:110.e1–7.