Postnatal Infections and Immunology Affecting Chronic Lung Disease of Prematurity

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KEYWORDS

• Prematurity • Neonatal immunology • Neonatal infection • Virus • Lymphocytes
• Bronchopulmonary dysplasia • Chronic lung disease of prematurity • Preterm

KEY POINTS

- In the first year of life, preterm infants are rehospitalized twofold to fivefold times more frequently than infants born at term, primarily for respiratory symptoms.
- Mediators of inflammation tend to enhance lung maturation but impair alveolar septation and developmental vascular remodeling.
- The developmental age of the immune system at birth, and at early-age infections, may significantly alter the acute response, and the sequelae, to inflammatory stimuli.
- Prenatal and postnatal infection and immune responses contribute to the severity of chronic lung disease of prematurity.

INTRODUCTION

Each year, approximately 1 in 9 infants in the United States, more than 440,000 infants yearly, are born prematurely (<37 weeks gestation).[1] These infants suffer from complications of exposure to a diverse environment at a time in development when the respiratory tract and immune system are intended to be protected and maintained in a relatively naïve intrauterine state. During infancy and early childhood, premature infants suffer significant inflammatory and infectious respiratory morbidities with extended negative consequences for health, quality of life, and health care costs.

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As compared with approximately 8% of full-term newborns, 17% of late-preterm (LPT, born at 34 0/7–36 6/7 weeks) and 30% to 40% of early preterm infants (EPT, born at <32 weeks) are rehospitalized within the first year of life, most commonly for viral respiratory infections.[2–4] Respiratory infections that are less severe, not requiring hospitalization, are even more common, recurrent and, in total, costly in the very young.[5] The incidence and severity of respiratory tract infections in infants younger than 1 year is attributed at least in part to immune immaturity, a problem magnified by preterm birth and influenced by genetic traits and environmental exposures. Differences in gastrointestinal tract colonization patterns and the development and balance of the intestinal microbiome have been shown to influence immunologic development in full-term infants, and have begun to be evaluated in the premature.[6–8] Viral infections, either subclinical or severe, may also alter immunologic development both directly and by altering the bacterial microflora. Preterm infants are exposed to maternal and hospital-based flora, frequently with additional pressures of antibiotics, indwelling catheters, and tubes, that alter the establishment of diverse, health-promoting microbiota on the skin and respiratory mucosa, as well as in the gastrointestinal tract, and increase the risk of invasive disease with predominant organisms.

Recurrence of respiratory symptoms in the first year of life correlates inversely with gestational age at birth, directly with in utero exposure to inflammation (chorioamnionitis), and with non-white race. The pathogenesis of chronic lung disease of prematurity, bronchopulmonary dysplasia (BPD), has been recently reviewed and is closely correlated with in utero inflammation, oxygen toxicity, ventilator-induced trauma, and prealveolar lung development at birth (Fig. 1).[9–11] Premature birth induces a slowing or arrest of lung development that underlies BPD and likely occurs in a spectrum of severity in all prematurely born infants. Perinatal therapeutic and environmental exposures, most notably oxygen exposure and environmental tobacco smoke, have been reproducibly related to chronic respiratory morbidity, independent of mechanical ventilation and

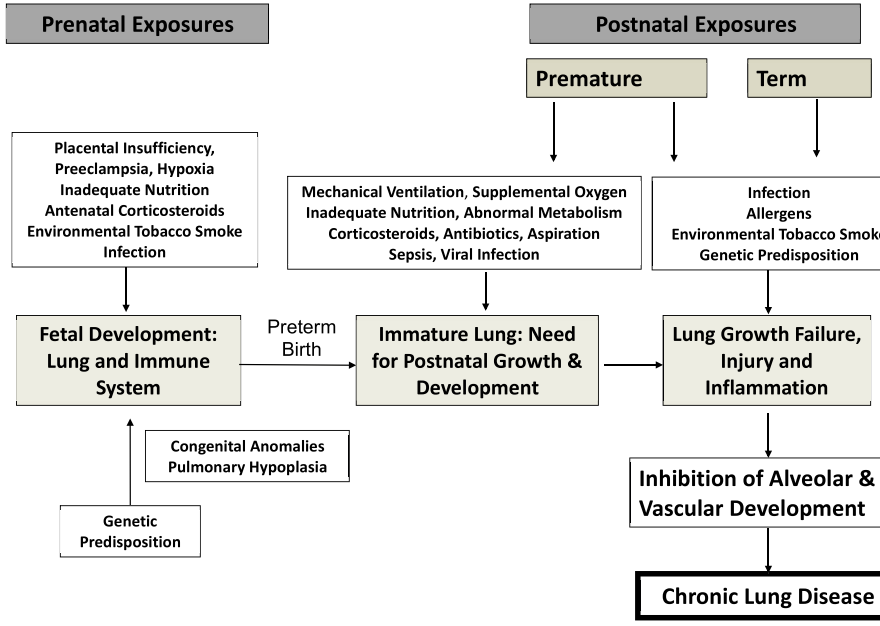

Fig. 1. Factors implicated in the pathogenesis of chronic lung disease of prematurity.