



Mini-Symposium: Chronic Neonatal Lung Disease CNLD/BPD

Normal Development of the Lung and Premature Birth

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SUMMARY

The following review focuses on the normal development of the lung from conception to birth. The defined periods of lung development—Embryonic, Pseudoglandular, Canalicular, Saccular and Alveolar—will be explored in detail in relation to gestational age. Cellular differentiation, formation of the conducting airways and respiratory zone and development of the alveoli will be reviewed. Pulmonary vascular development will also be examined within these periods to relate the formation of the blood-air barrier to the lungs for their essential function of gas exchange after birth. The development of the surfactant and cortisol systems will also be discussed as these need to be mature before the lungs are able to take on their role of respiration following birth. It is clear that premature birth interrupts normal lung development so the effect of preterm birth on lung development will be examined and the respiratory consequences of very preterm birth will be briefly explored.

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INTRODUCTION

Investigations into the structure and function of the lung began over a century ago. These investigations led to detailed descriptions of each period of lung development and the realisation that the lung is a complex structure in which steady development begins during the embryonic period at 0 to 7 weeks gestation and continues into early childhood. In fact, there is still great debate as to when lung development is complete.

It has become clear from these investigations that premature birth interrupts the normal development of the lung. Infants born prematurely have underdeveloped lungs and often require assistance to maintain adequate respiration. While many strategies that accelerate lung development and assist in providing adequate gas exchange have benefited a large number of infants, the smallest and most preterm infants are still at the greatest risk of developing Bronchopulmonary Dysplasia

The following review explores normal development of the lung and the effect premature birth has on this development.

PRENATAL LUNG DEVELOPMENT

The growth and development of the lung is divided into four characteristic periods (Figure 1). The nomenclature of the periods

of lung growth were confirmed by the International Congress of Anatomists meeting in Leningrad, 1970 (Nomina Embryologica).¹ While it is agreed there is some overlap of the beginning and end of each of these periods, it is generally accepted that weeks 0 to 6 of gestation comprise the embryonic period, weeks 6 to 16 the pseudoglandular period, weeks 16 to 24 the canalicular period and weeks 24 to term (40 weeks) the saccular period.²

Development of the pulmonary circulation occurs in parallel with lung development (Figure 1). During foetal life there is an increase in vessel length and diameter but no change in density.³ By the 20th week of gestation the full number of pre-acinar pulmonary vessels is present in each segment. During each period of gestation structural remodelling and changes in growth and maturation take place. Lung vascular growth involves two basic processes, vasculogenesis—formation of new blood vessels from endothelial cells⁴ and angiogenesis—formation of new vessels from capillaries via sprouting.⁵

Embryonic Period (weeks 0 to 6)

This is the period of organ development—organogenesis. At the end of the fourth week of gestation the lung appears as a ventral bud of the oesophagus.⁶ By the end of the sixth week lobar and segmental portions of the airway tree are preformed as tubes of “high columnar epithelium”.⁶ By seven weeks subsegmental branching is evident.⁷ Alescio and Cassini⁸ originally documented, in mouse lung, that the branching pattern is driven by signals from the mesenchyme to the budding airway. Their investigations showed that the pulmonary mesenchyme consists of a bronchial

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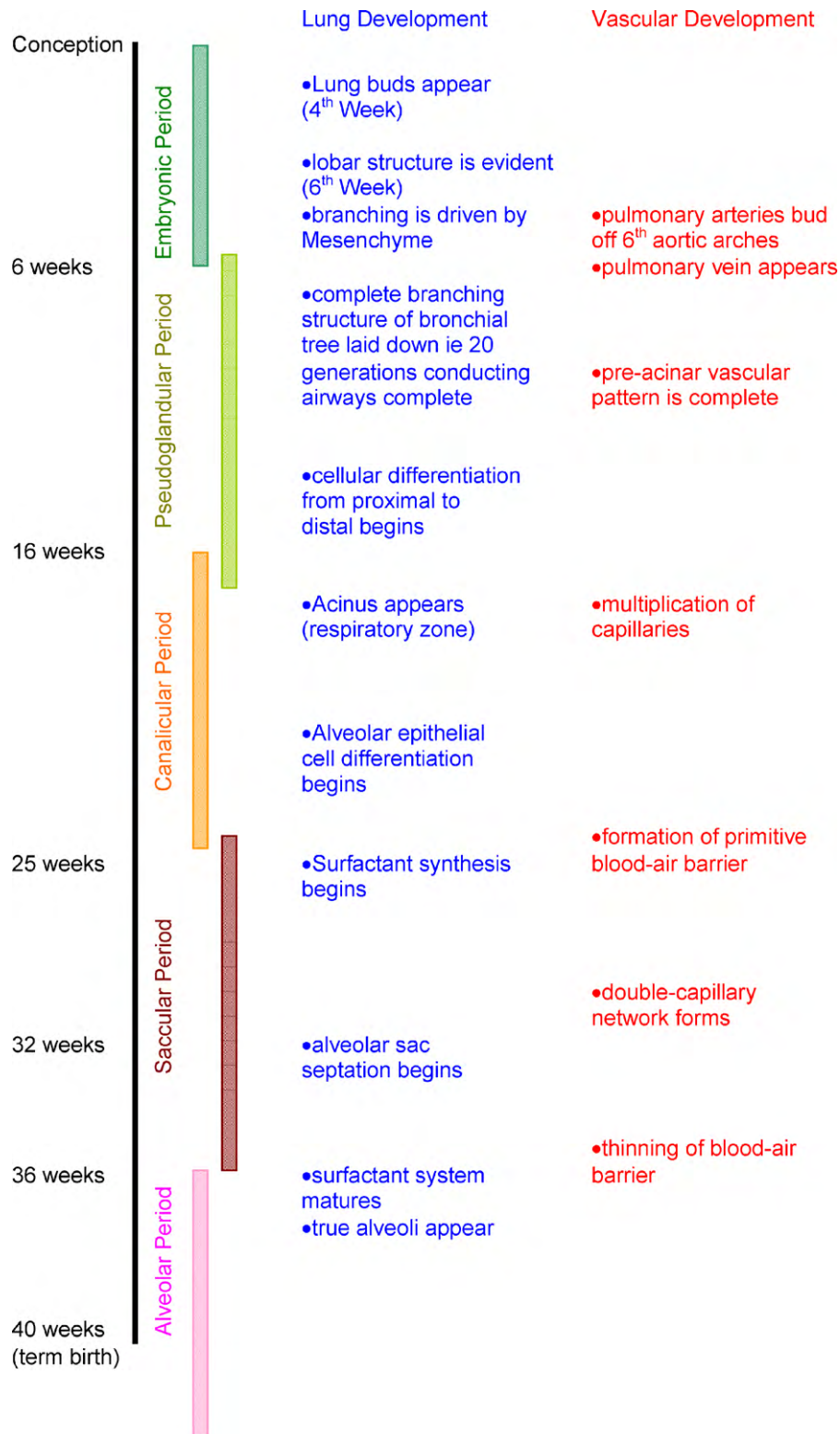


Figure 1. Overview of Gestation.

portion, which induces budding from the epithelium and a tracheal portion that does not. They also demonstrated that without the bronchial mesenchyme, branching of the epithelium does not occur.⁸

Vasculogenesis occurs within the immature mesenchyme. The pulmonary arteries bud off the 6th pair of aortic arches growing down to the mesenchyme and surround the lung tubules as a

vascular plexus.⁶ The pulmonary vein appears as a small tubule growing out from the left atrial portion of the heart.² By the sixth week of gestation, the adult pattern of central vascular and airway structures consisting of lobar and segmental branches is present.⁹

After the age of seven weeks the lung resembles a primitive small gland (giving the next stage its name) and has so entered the Pseudoglandular period of development.⁶

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