

the acinar epithelium, and development of the distal pulmonary circulation. Through the processes of angiogenesis and vasculogenesis, capillary networks derived from endothelial cell precursors are formed, extend from and around the distal air spaces, and connect with the developing pulmonary arteries and veins. By the end of this stage, the thickness of the alveolar capillary membrane is similar to that in the adult.

During the saccular or prenatal alveolar stage (between 24 and 38 weeks' gestation), vascularized crests emerging from the parenchyma divide the terminal airway structures called *sacculi*. Thinning of the interstitium continues, bringing capillaries from adjacent alveolar structures into close apposition and producing a double capillary network. Near birth, capillaries from opposing networks fuse to form a single network, and capillary volume increases with continuing lung growth and expansion.

During the alveolar postnatal stage (between 36 weeks' gestation and 2 years of age), alveolar development continues, and maturation occurs. The lung continues to grow through the first few years of childhood with the creation of more alveoli through septation of the air sacs. By age 2 years, the lung contains double arterial supplies and venous drainage systems, a complex airway system designed to generate progressive decreases in resistance to airflow as the air travels distally, and a vast alveolar network that efficiently transfers gases to and from the blood.

The processes that drive lung development are tightly controlled, but mishaps occur. Congenital lung disorders include cystic adenomatoid malformation of the lung, lung hypoplasia or agenesis, bullous changes in the lung parenchyma, and abnormalities in the vasculature, including aberrant connections between systemic vessels and lung compartments (e.g., lung sequestration) and congenital absence of one or both pulmonary arteries. In children without congenital abnormalities, lung disorders are uncommon, except for those caused by infection and accidents.

Congenital lung disorders are rare compared with the number of infants born annually with abnormal lung function as a result of prematurity. In premature infants, the type II pneumocytes of the lung are underdeveloped and produce insufficient quantities of surfactant, a surface-active substance produced by specific alveolar epithelial cells that helps to decrease surface tension and prevent alveolar collapse. This disorder is called *infant respiratory distress syndrome* (IRDS). The treatment of IRDS is administration of exogenous surfactant and corticosteroids to enhance lung maturation. To sustain life while allowing maturation, mechanical ventilation and oxygen supplementation are required but may promote the development of bronchopulmonary dysplasia.

TABLE 13-1 STAGES OF LUNG DEVELOPMENT

STAGE	PERIOD	COMMENTS
Embryonic	3-7 wk	Embryonic lung bud emerges from the foregut.
Pseudoglandular	5-17 wk	Airway tree is formed through a process of monochotomous and dichotomous branching accompanied by growth.
Canalicular	17-24 wk	Angiogenesis and vasculogenesis form the developing vascular network.
Saccular	24-38 wk	Alveoli begin to form through thinning of the mesenchyme, apposition of vascular structures with the air spaces, and maturation.
Alveolar (postnatal)	36 wk-2 yr	Further alveoli development and maturation occurs.

PULMONARY DISEASE

Epidemiology

Diseases of the adult respiratory system are some of the most common clinical entities confronted by physicians. According to the Centers for Disease Control and Prevention data for 2010, three of the top 10 causes of death due to medical illnesses in the United States are lung diseases: lung cancer, chronic lower respiratory diseases, and influenza or pneumonia.

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death and the second leading cause of disability in the United States. At a time when the age-adjusted death rate for other common disorders such as coronary artery disease and stroke is decreasing, the death rate for COPD continues to increase. More than 16 million Americans are estimated to have COPD, but the number is expected to rise because COPD takes years to develop and the incidence of cigarette smoking (the most common etiologic factor for COPD) is staggering. In 2010, more than 46.6 million Americans were daily smokers, and 40% of

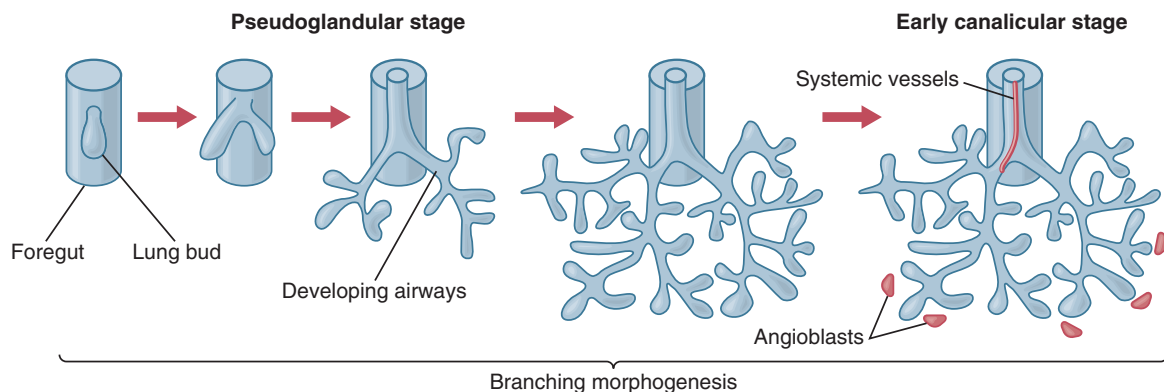


FIGURE 13-2 Lung branching morphogenesis occurs during the pseudoglandular stage of lung development. It is the process by which the embryonic lung develops the primitive airway system through monochotomous and dichotomous branching.