Development of the Human Lung

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Learning Objectives:

- Understand the growth and functional development of the respiratory system
- Identify the stages of lung development and the major events of each stage
- Understand the physical and biochemical requirements for alveolar development and function
- Identify the developmental causes of neonatal respiratory failure, tracheoesophageal fistula and diaphragmatic hernia

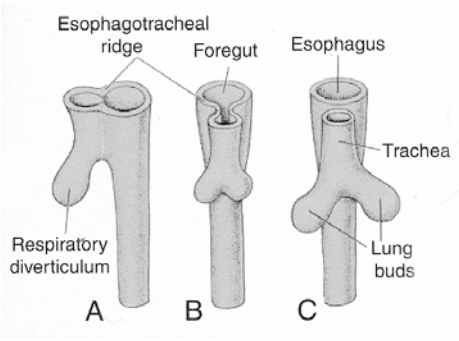
Phases of Lung Development

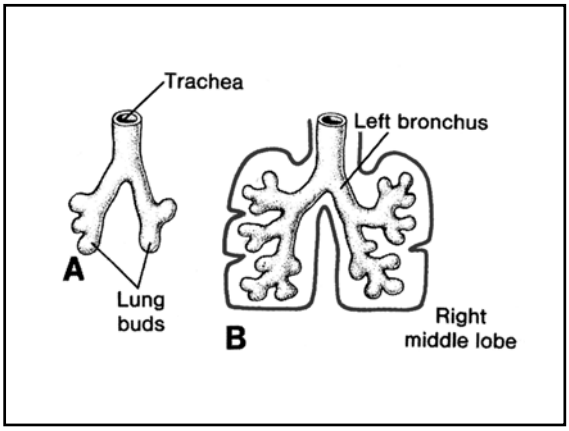
- Lung Growth
  - Structural development
  - Anatomic development
  - Affected by physical factors
- Lung Maturation
  - Functional development
  - Biochemical development
  - Affected by hormonal factors

The end result of the development of the lung is an organ with a tremendously large surface area that is approximately 50-100 m^2, capable of exchanging oxygen and carbon dioxide.

Maturation of the Lungs

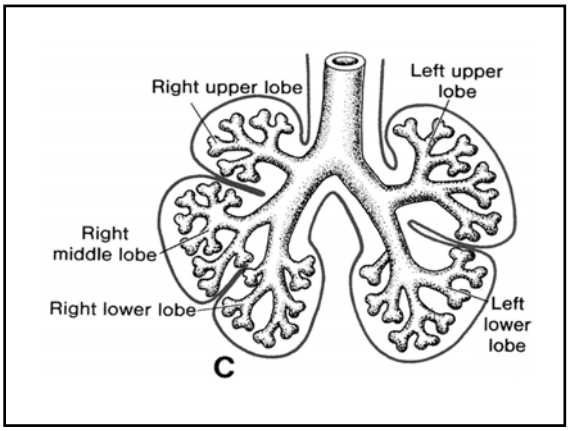
Pseudoglandular period	5–16 weeks	Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli are present.
Canalicular period	16–26 weeks	Each terminal bronchiole divides into 2 or more respiratory bronchioles, which in turn divide into 3–6 alveolar ducts.
Terminal sac period	26 weeks to birth	Terminal sacs (primitive alveoli) form, and capillaries establish close contact.
Alveolar period	8 months to childhood	Mature alveoli have well-developed epithelial endothelial (capillary) contacts.



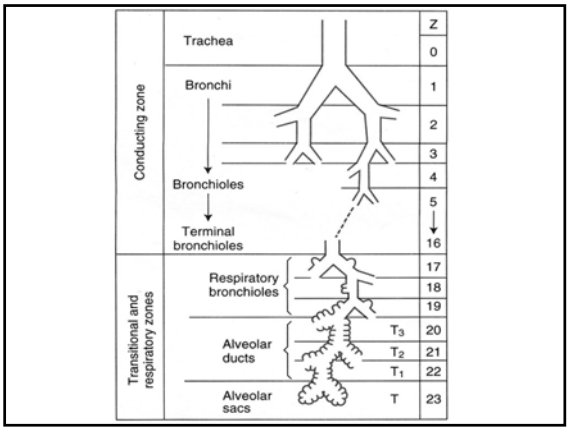


Derivation of lung elements

- Lung buds lined by **endodermally** derived epithelium—differentiates into respiratory epithelium, which lines airways and specialized epithelium that lines the alveoli
- **Ectoderm-**contributes to innervation
- **Mesoderm**- blood vessels, smooth muscle, cartilage and other connective tissue



- The **pseudoglandular stage** takes place between the 7th and 16th week of embryonic development

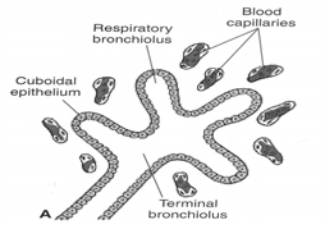


- For branching to occur, bronchial mesoderm is required.
- The rate and extent of branching is proportional to the amount of mesenchyme present.
- After 16 weeks, further growth occurs by branching and elongation.

- Cilia appear in the proximal airways by 13 weeks.
- There is a transition from bronchial epithelial cells (ciliated and columnar cells) to alveolar Type II cells.

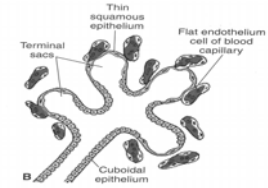
- Mesenchyme is necessary for epithelial differentiation to occur.
- Differentiation of mesenchyme requires the presence of lung epithelium.

Canalicular Period 16-26 wk



- By 20 weeks the alveolar Type 1 cell is present
- Lamellar bodies start to appear in Type 2 cells

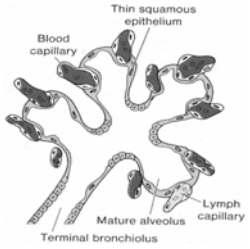
Terminal Sac Period 26 wk →



- Surfactant appears in lamellar bodies of Type 2 cells.
- Stability of the lung at birth correlates with the number of lamellar bodies present.

- By 20 weeks, the alveolar Type 1 cell is present.
- Lamellar bodies start to appear in Type 2 cells.

Primitive Saccule



- Approximately 20 x 10^6 saccules present at birth.

Postnatal stage

"Adult" configuration reached by 5 weeks.

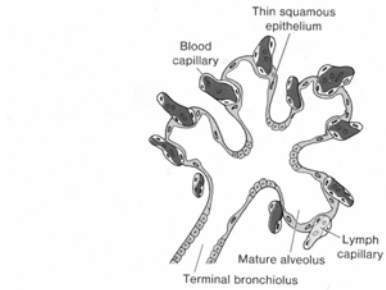
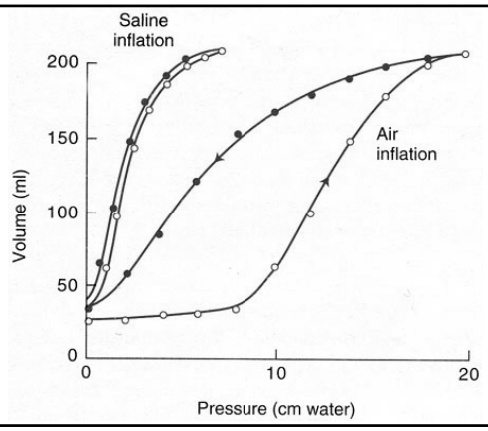
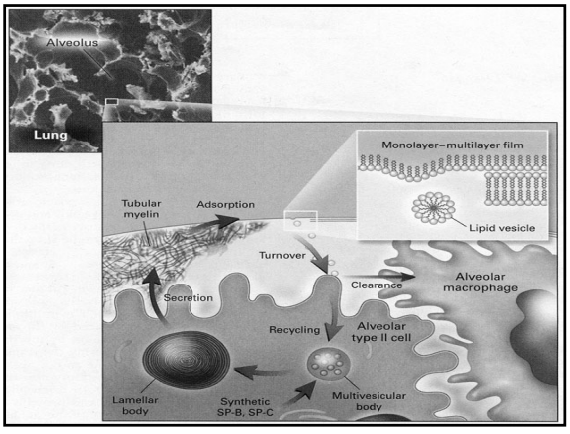


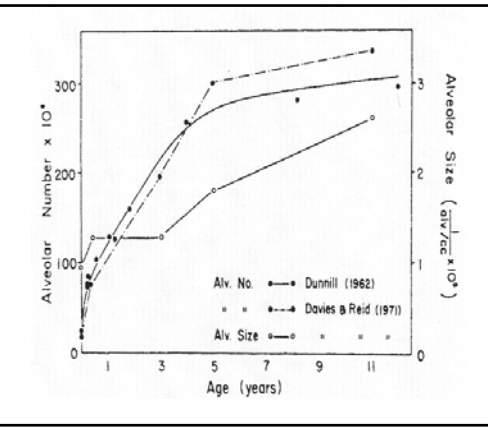
Figure 12.9. Lung tissue in a newborn. Note the thin squamous epithelial cells (also known as alveolar epithelial cells, type I) and surrounding capillaries protruding into mature alveoli.

Characteristics of Mature Alveolus

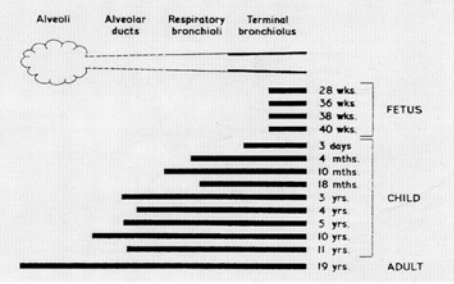
- Connected to alveolar duct
- Lined with Type 1 cells, which are in intimate contact with capillaries
- Each capillary is exposed to 2 alveoli
- Contains surfactant
- Has interconnections with adjacent alveoli through pores of Kohn.







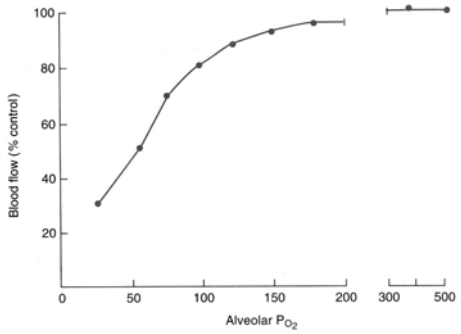
Development of Pulmonary Arterial Muscle



Control of Pulmonary Blood Flow

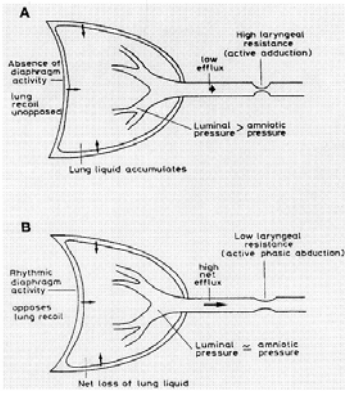
- Physical Location of Lung Unit
- Gravity
- Oxygen
- Nitric oxide

Hypoxic Pulmonary Vasoconstriction



Physical Influences on Lung Growth

- Lung Liquid

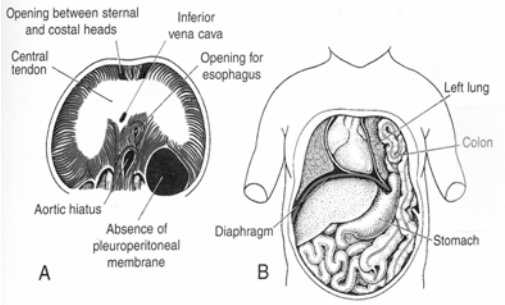


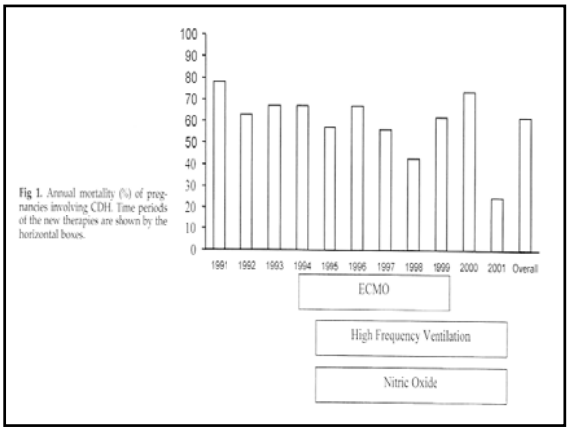
Physical Influences on Lung Growth

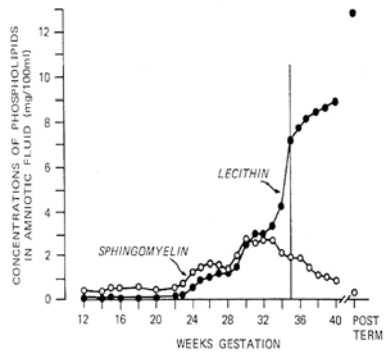
- Amniotic fluid
  - Oligohydramnios→Potters syndrome

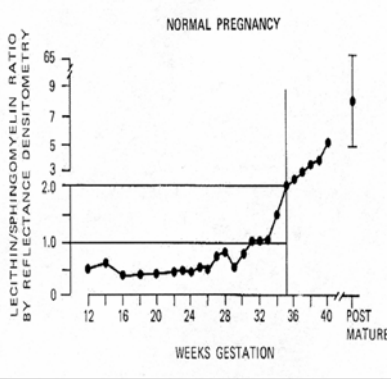
Physical Influences on Lung Growth

- Congenital diaphragmatic hernia
- Musculoskeletal abnormalities of the chest wall
- Space occupying lesions of the thorax, e.g. pleural effusions
- Oligohydramnios associated with renal or urinary tract abnormalities







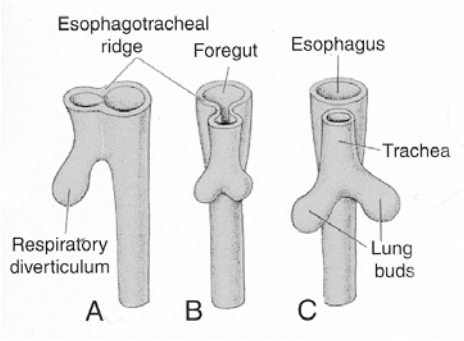


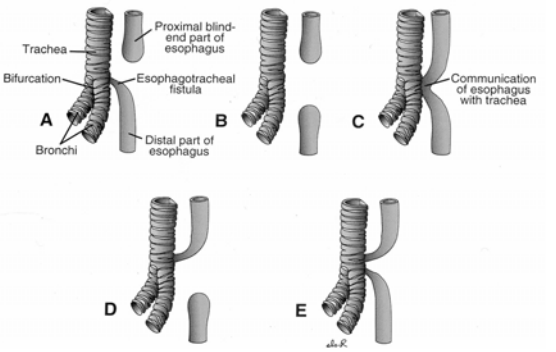
Hormonal Influence on the Lung

- Corticotropin stimulates cortisol
- Cortisol stimulates fetal lung fibroblast to produce fibroblast pneumocyte factor, which,
- Stimulates surfactant production in Type 2 cells
- Thyroid hormone is also necessary for surfactant production

Hormonal Influence on the Lung

- At birth, epinephrine and arginine vasopressin suppress fetal lung fluid production and play a role in its reabsorption





The Problem of Prematurity

- Birth before 36 weeks may be associated with respiratory compromise and failure.
- 80,000 cases/yr of neonatal respiratory failure
- 8,500 deaths
- CNS injury in survivors
- Cost = $4.4 billion/yr

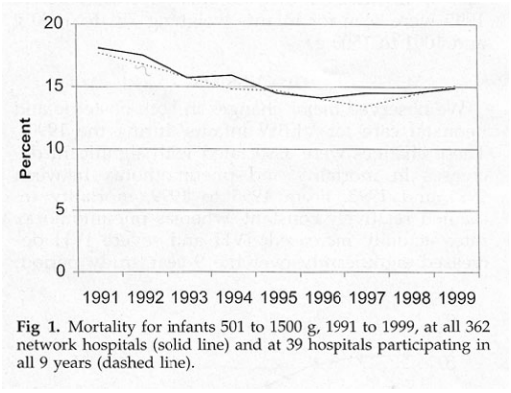


Fig 1. Mortality for infants 501 to 1500 g, 1991 to 1999, at all 362 network hospitals (solid line) and at 39 hospitals participating in all 9 years (dashed line).

Gregory GA, Kitterman JA, Phibbs RH, Tooley WH, Hamilton WK.

Treatment of the idiopathic respiratory distress syndrome with continuous positive airway pressure.

N. Eng. J. Med. 284:1333-40 , 1971

Neonatal Respiratory Failure

- Incidence
  - 20/1000 boys
  - 15.6/1000 girls
  - 29/1000 blacks

The lung is ignored only at your own peril!

DON'T HOLD YOUR BREATH!