

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

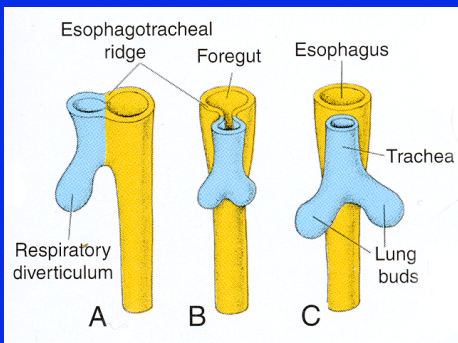
Phases of Lung Development

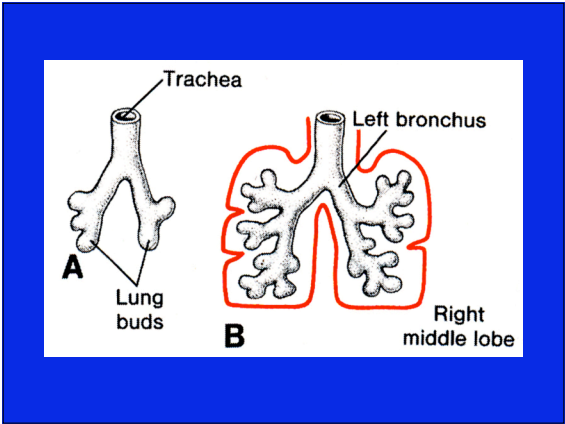
- Lung Growth
 - Structural development
 - Anatomic development
 - Affected by physical factors
- Lung Maturation
 - Functional development
 - Biochemical development
 - Affected by hormonal factors

The end result of the development of the lung is an organ with a tremendously large surface area that is approximately 50-100 m², 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.

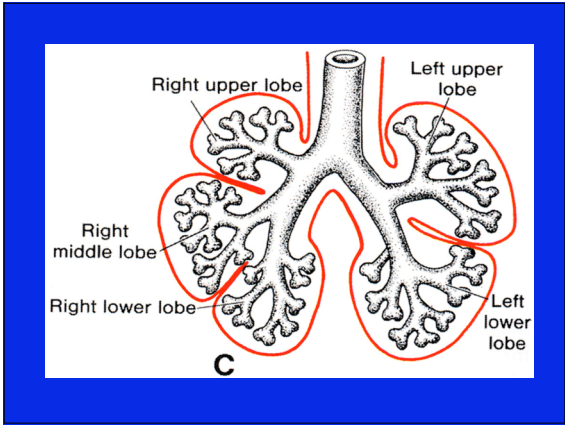


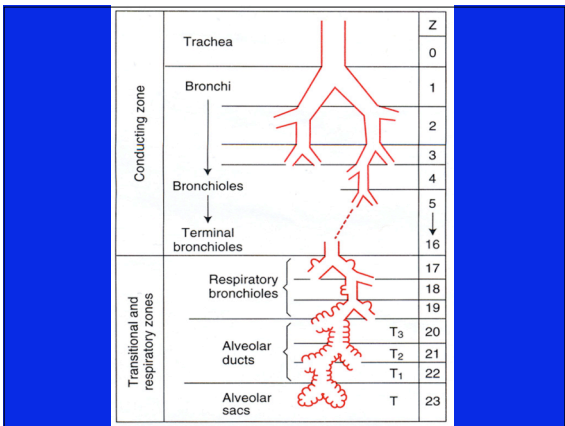


Derivation of lung elements

- 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



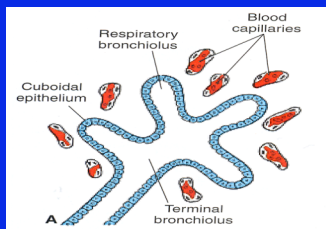


- For branching to occur, bronchial mesoderm is required.
- The rate and extent of branching is proportional to the amount of mesenchyme present.
- After 16 weeks, further growth occurs by widening and elongation.

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

- 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.

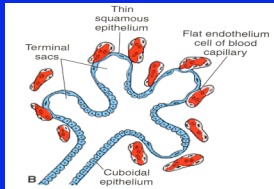
Canalicular Period 16-26 wk



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

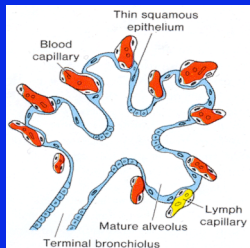
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- Lamellar bodies start to appear in Type 2 cells.

Terminal Sac Period 26 wk →

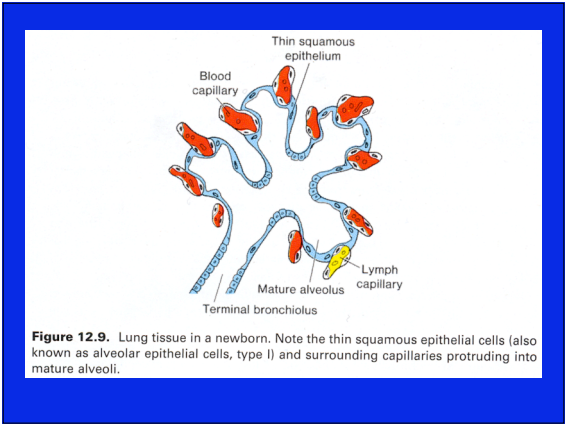


- Surfactant appears in lamellar bodies of Type 2 cells.
- Stability of the lung at birth correlates with the number of lamellar bodies present.

Primitive Saccule



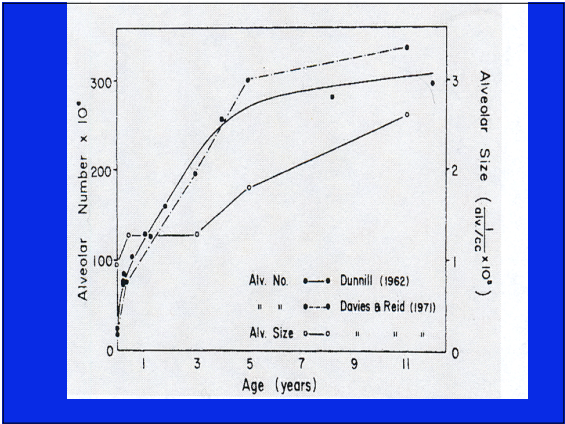
- Approximately 20×10^6 saccules present at birth.



Postnatal stage

“Adult” configuration reached by 5 weeks.

- 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.



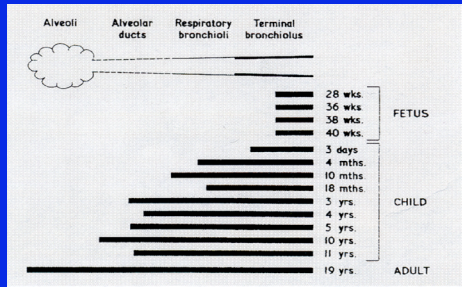
Hormonal Influence on the Lung

- 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

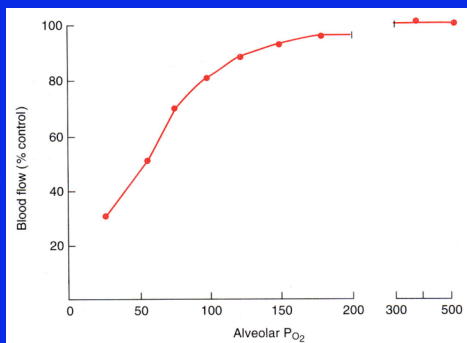
Development of Pulmonary Arterial Muscle

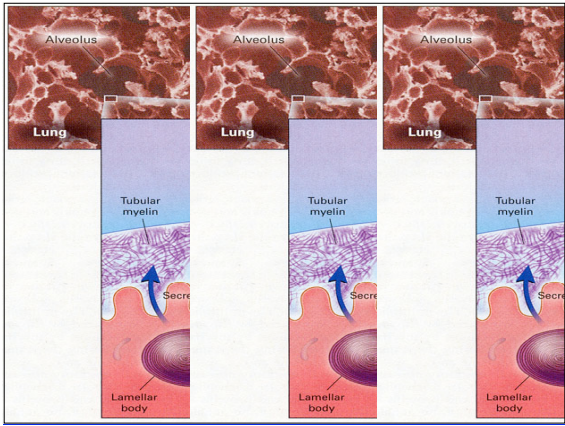


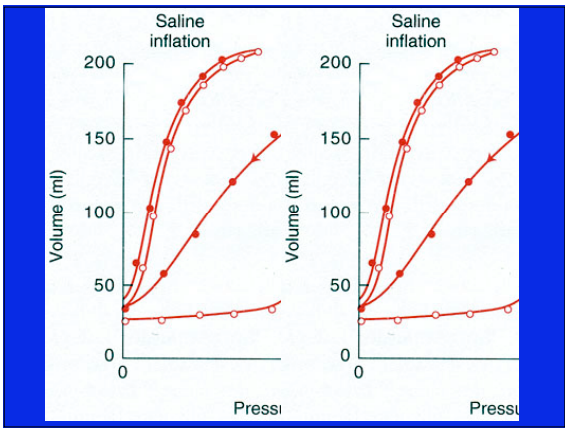
Control of Pulmonary Blood Flow

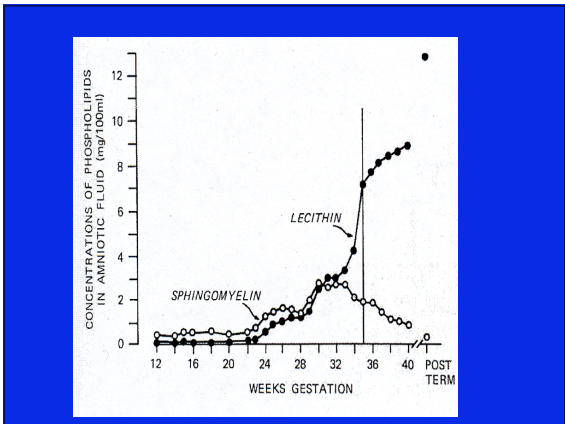
- Physical Location of Lung Unit
- Gravity
- Oxygen
- Nitric oxide

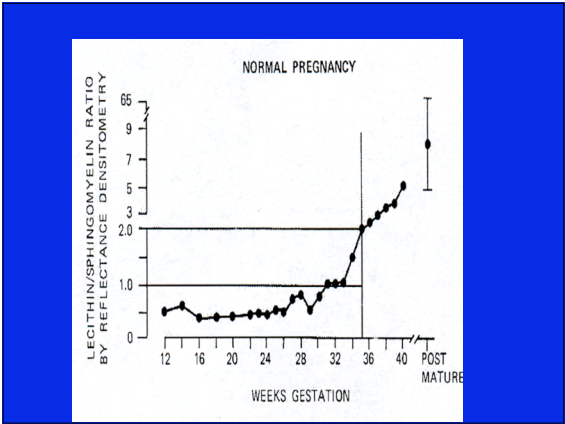
Hypoxic Pulmonary Vasoconstriction





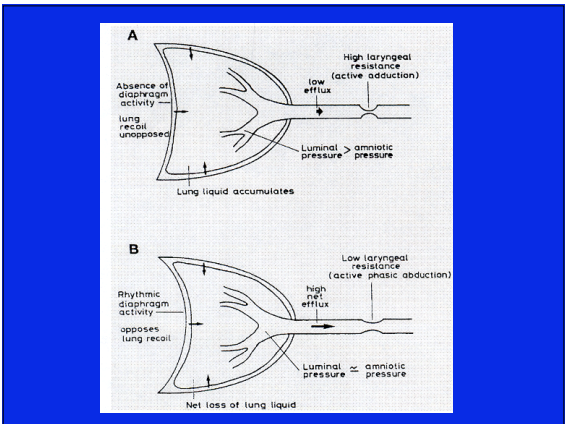






Physical Influences on Lung Growth

- Lung Liquid

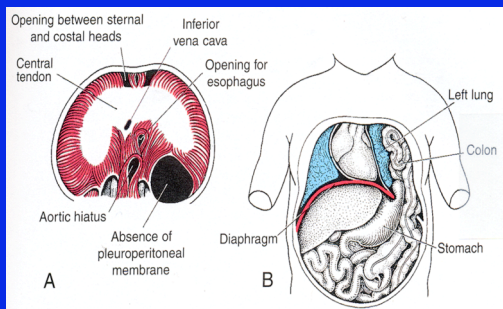


Physical Influences on Lung Growth

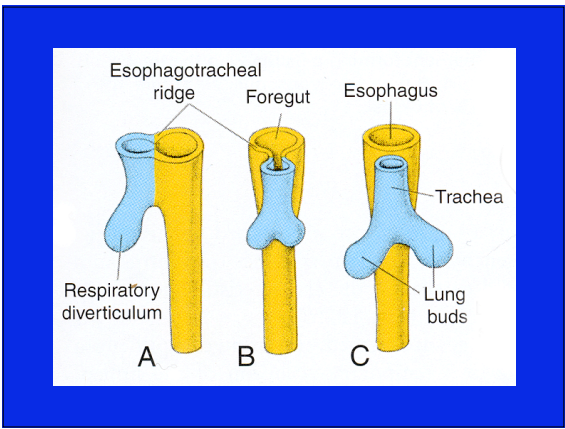
- Amniotic fluid
 - Oligohydramnios → Potters syndrome

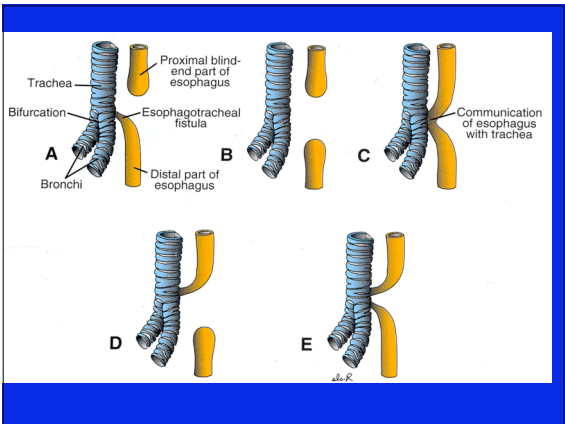
Physical Influences on Lung Growth

- 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









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



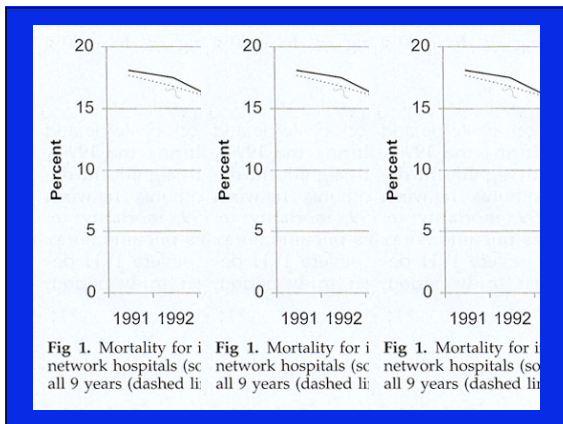


Fig 1. Mortality for i network hospitals (sc all 9 years (dashed li

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!
