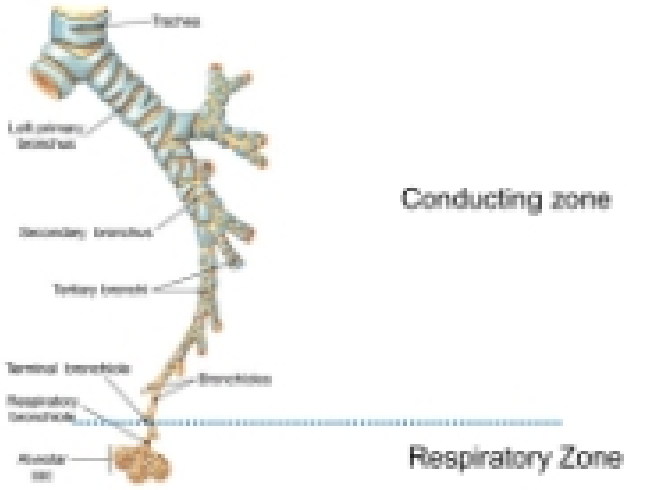
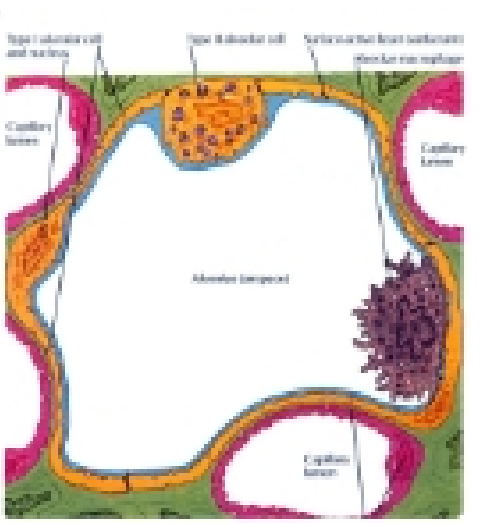
1) Review of Mature Anatomy

- Lungs
  - Right lung: 3 lobes- superior, middle, lower
  - Left lung: 2 lobes- upper and lower, L lung has to make room for heart, lingula (tongue) of the L upper lobe in the analogue of R middle lobe
  - Ventilation: movement of air thru conducting system
  - Respiration: exchange of gas across membrane
- Components of respiratory system
  - conducting zone: larynx, trachea, bronci, bronchioles, terminal bronchioles
  - respiratory zone: respiratory bronchioles, alveolar ducts and sacs, alveoil
    - bronchoiles don't have cartilage, smooth m. absent at levels of alveoli (becomes progressively thinner)
    - dense network of capillaries and alveoli
    - clinicians: alveolus= terminal respiratory unit of the scientist
      - alveolar ducts and 2,000 alveoli, approx. 5 mm in diameter



- Respiratory membrane (lining of alveoli)
  - Type I cells (pneumocytes): 90% of alveolar surface, fused basement membrane w/capillaries, thin walled
  - Type II cells (pneumocytes): secrete surfactant (a complex phospholipid) that decreases surface tension preventing the collapse of the alveolus, reduces effort of ventilation, less air needed to maintain voume

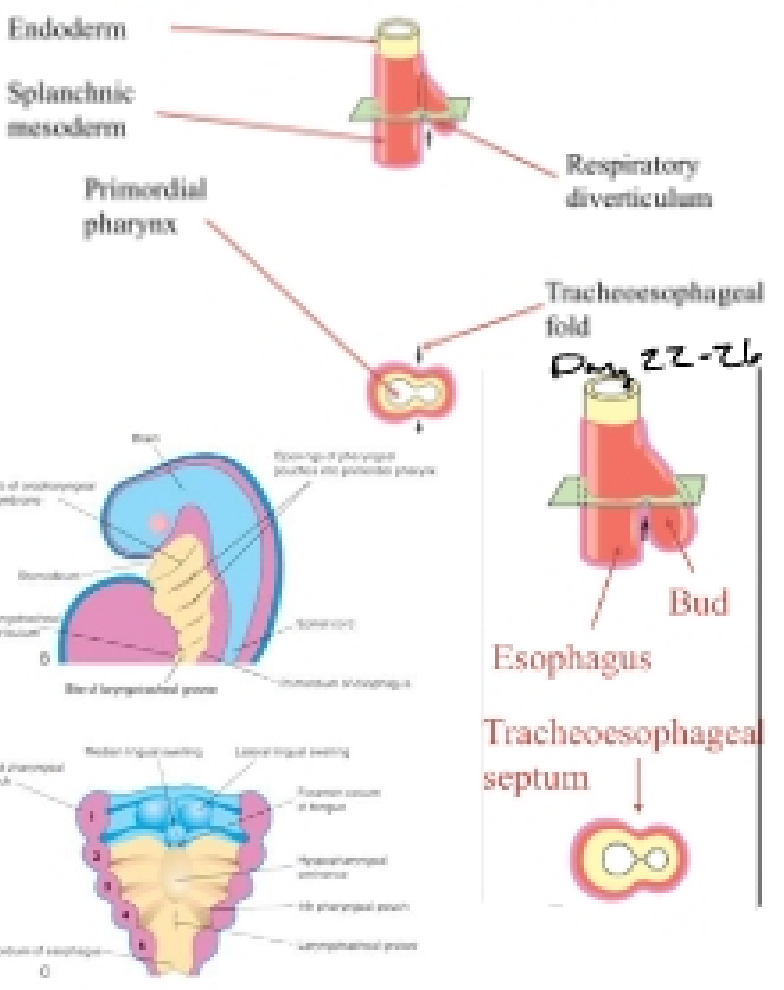


2) Development of the lung--Stages of lung development

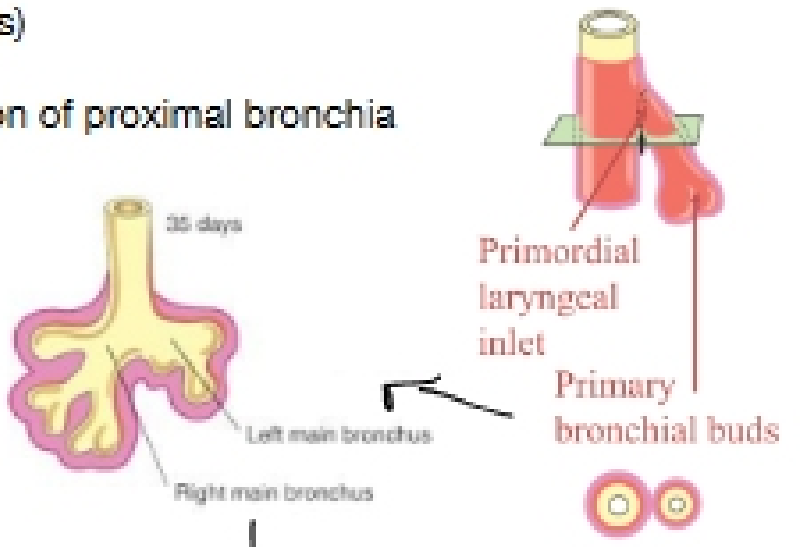
- dev. of the resp. systems begins on Day 22, ends in childhood (about age 8) , dev. lof trachea and lungs
- no clear dividing line between eacch stage
- story of branching and re-branching over 23 generations
- part of the organogenetic period in weeks 4-8: folding and growth of the embryo also occurs

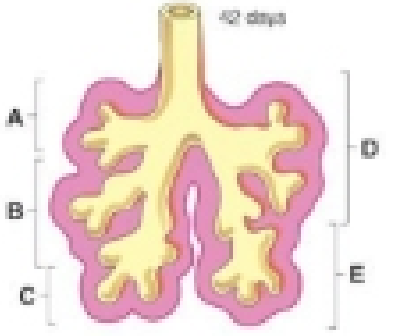
a. Embryonic stage: Day 26- Wk. 6

- Primordia of both lungs and lobes
- 3 branchings (first bifurcation Day 26)
- Day 22:
  - lung bud forms, arises from endoderm of foregut
  - respiratory diverticulum= lung bud
  - grows into surrounding mesochyme
- Tracheoesophageal fold begins partitioning (pinching in) of foregut into esophagus and laryngotracheal tube
- Day 22-26: Respiratory diverticulum grows ventrocaudally, surrounded by mesochyme
- Week 4:
  - pharyngeal appparatus and respiratory system
  - primordial pharynx and laryngotracheal groove
  - larynx develops below 4th pharyngeal arch: sulcus epithelium from endoderm, muscles from mesoderm of arches 4 and 6--> innervated by vagus nerve, laryngeal cartilages derived from mesoderm of 4 and 6
- Day 26:
  - First bifurcation

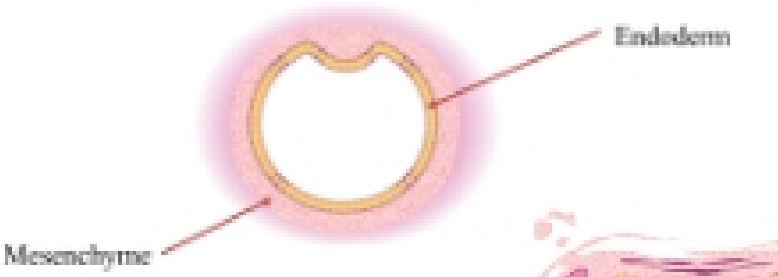


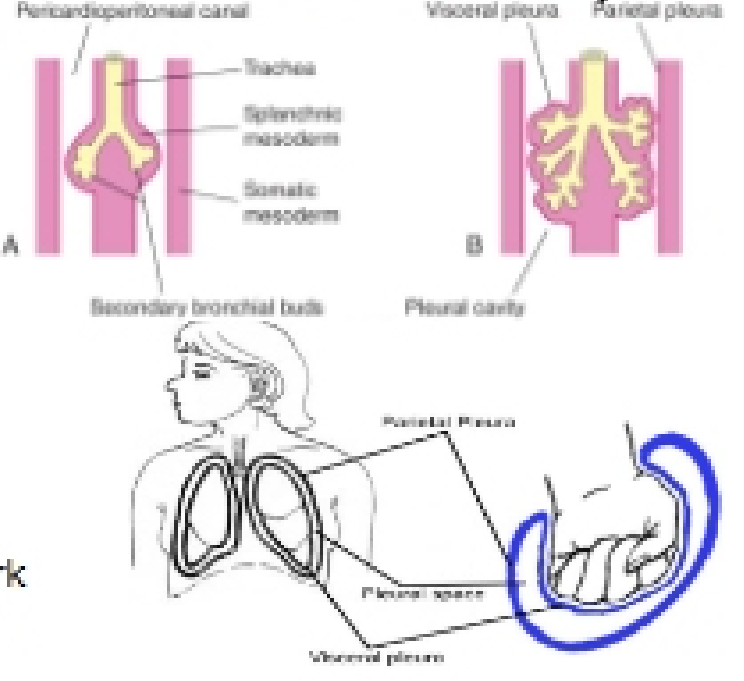
- Stem begins to separate from pharynx (esophagus)
    - proximal stem forms the trachea and larynx
    - formation of trachea may be indep. of formation of proximal bronchia buds
- Week 5:
    - primary bronchi branch early
    - right 3 secondary bronchial buds: upper, middle, and inferior
    - left 2 secondary bronchial buds: superior and inferior
- Week 6:
    - further branching:
        - 10 tertiary bronchi per side
        - bronchopulmonary segments --> will become segments of the mature lung





b. Pseudoglandular stage: Weeks 6-16
- Lung looks like a gland on histology
- 14 branchings to terminal bronchioles (dev. of lower conducting airways to terminal bronchioles)
- Lower conduction system
- Airways differentiate
- Mucous glands develop
- Smooth muscle
- Connective tissue
- Epithelial-mesenchymal induction occurs: complex, large # of factors involved incl. various growth factors, txn factors
    - cartilage begins to develop in mesenchyme (middle ring), outer ring is embryonic CT
- Week 12:
    - laryngotracheal tube: further differentiation--> epithelium and glands, CT, muscle, cartilage
- Lungs expand into splanchnic mesenchyme adjacent to walls of primordial pleural cavities
- Pleural/pericardioperitoneal channels: lungs grow here, the channels enlarge as the lungs enlarge





c. Canalicular stage (canals): Weeks 16-26
- 3 divisions
- Respiratory vasculature
- Respiratory bronchioles developing
- Beginning of relationship between capillaries and terminal respiratory units
- Last few generations of airways added
- Angiogenesis:
    - Proliferation of microvasculature -- pericanicular network
    - Cells sep. by only 1 basement membrane (formation of blood-air barrier, governing not understood)
- Heart developing during this time

    - Pulmonary arches branch off from 6th aortic arteries and descend to newly formed lung buds.
    - R 6th arch --> right pulmonary artery
    - L 6th arch --> pulmonary trunk
    - pulmonary veins develop as an evangination in sinoatrial part of heart
- Cell specialization
    - Ciliated
    - Secretory
    - Alveolar precursor cells
        - Type 1: alveolar wall
        - Type 2: Surfactant production

d. Saccular/Terminal sac stage: 26 weeks -> birth
- Last divisions
    - Alveolar ducts
- Terminal sacs (primitive alveoli)
    - some gas exchange possible
    - 20-70 million sacs ante-partum
    - process continues post-partum
    - at birth, you have 1/6th of your adult alveoli
- Lung gets aerated appearance
- But at birth, lungs are still filled w/fluid (a newborn's lungs will sink if placed in water)
- Distal airways expand
- Interstitial space decreases
- Dense capillary network forms
- Surfactant production
    - Type 2 cells begin making surfactant--prior to this infant won't be able to survive
    - increases chance of survival if born prematurely
- Elastin deposition
    - imp. for alveolar formation

e. Alveolar stage: Begins Week 28-32/8 months (in utero)--> childhood
- Continues after birth, not a clear transition from saccular to alveolar
- Epithelium thins
- Septation
- Capillary nets fuse
    - Doubling of the capillary net
- 300-400 M alveoli
- Distal airways expand

3) Development of the diaphragm
- Diaphragm is composed of 4 things:
    1) Septum transversum
    2) Plueroperitoneal membranes
    3) Body wall mesoderm
    4) Esophageal mesenchyme
- Folding produces intraembryonic coelom
    - dorsal mesentery and ventral mesentary
        - most of ventral mesentary disappears
    - dorsal mesocardium and ventral mesocardium
- **Septum transversum**