EMBRYO LECTURE 2

Lungs and Bronchial tree development

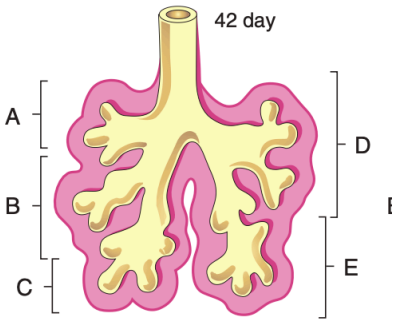
Trachea, Bronchi, and Lungs

- During its **separation from** the **foregut**, the **lung bud forms** the **trachea and two lateral outpocketings known as** , the **bronchial buds**,
  - the lining epithelium is endoderm, the cartilage and muscles come from splanchnic mesenchyme.
- At the **beginning** of the **fifth week**, **each** of these **buds enlarges** to **form right and left main bronchi**.
  - **Characteristics** of each one:

    Right: **shorter**, **wider**, **more vertical**.

    Left: **longer**, **narrower**, **more horizontal**.

- The **right** then **forms three secondary bronchi** (lobar bronchi) then **divide into tertiary bronchi**, **to:**
  - A- superior lobe: has 3 segment:
    - Apical
    - Anterior
    - Posterior
  - B-middle lobe: has 2 segment:
    - Middle
    - Lateral
  - C-posterior lobe: has 5 segment:
    - Apicobasal
    - Anterior
    - Posterior
    - Middle
    - Lateral

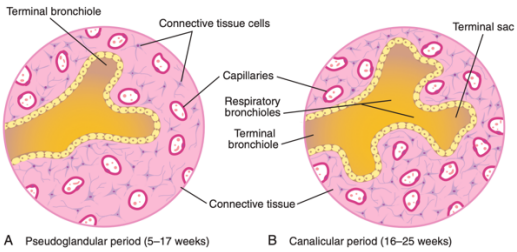


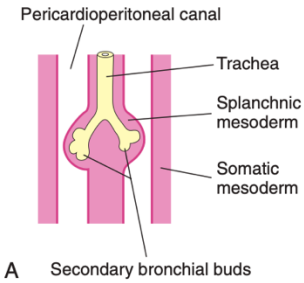
- and the left, two then divide into tertiary bronchi:
  - D- superior lobe which has apico-posterior segment then dived into:
    - Apical
    - Posterior,
  - E- posterior lobe we have antero-medical segment which also dived into:
    - Anterior
    - Middle

finally- with other segments that you know, getting ten in the left

- thus foreshadowing the **three lobes** on the **right** side and **two** on the **left**

- As we go **distally**, the **bronchopulmonary segments form** the **bronchioles**> **terminal bronchioles**> **respiratory portion** (respiratory bronchioles, alveolar duct> sac> alveoli).
- The **development** of **pleura**:
  - With **subsequent growth** in **caudal** and **lateral directions**, the **lung buds expand into** the **body cavity**.

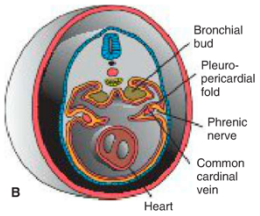




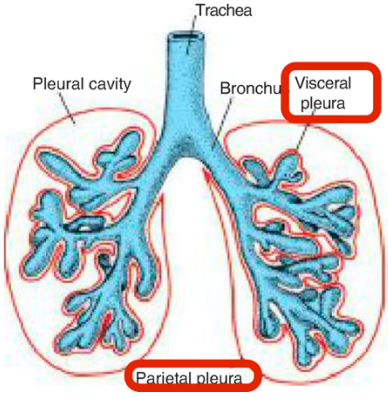
We have **two cavities**:

- **Pericardioperitoneal**
- **pleuropericardial**.

- The **spaces** for the **lungs**, the **pericardioperitoneal canals**-
- They **lie on each side** of the **foregut**
- **Ultimately** the **pleuroperitoneal and pleuropericardial folds separate the pericardioperitoneal canals from** the **peritoneal and pericardial cavities**.
  - Each one will separate and give:
    - **1- Pericardioperitoneal:**
      - **peritoneum cavity**-contains **abdominal viscera**.
      - **pericardium** – the **heart**.
    - 2-**pleuropercardial**:
      - **percardium cavity**.



- and the **remaining spaces form** the **primitive pleural cavities**
- The **mesoderm**, which **covers** the **outside** of the **lung**, **develops** into the **visceral pleura**.
- The **somatic mesoderm** layer, **covering** the **body wall from** the **inside**, **becomes** the **parietal pleura**.
- The **space between** the **parietal and visceral pleura** is the **pleural cavity**.



- During **further development**, **secondary bronchi divide repeatedly** in a **dichotomous fashion**, **forming 10 tertiary (segmental) bronchi** in the **right lung** and **8-post natal become 10**-in the **left**, creating the **bronchopulmonary segments of the adult lung.**
- By the **end** of the **sixth month**, **approximately 17 generations of subdivisions** have **formed**.

• Note: the start of these divisions from the bronchioles to alveolar ducts to the sac to the alveoli. This division must be repetitive to reach millions of alveoli (the one divide into two>four> eight and so on).
• How much longer do we still have divisions ? Up to 10 years- imagine-

.

- **Before** the **bronchial tree reaches** its **final shape**, however, an **additional 6 divisions form during postnatal life**.
- **Branching** is **regulated by epithelial-mesenchymal interactions between** the **endoderm** of the **lung buds** and **splanchnic mesoderm** that **surrounds** them.
- **Signals** for **branching**-the **driving force**- , which **emit from** the **mesoderm**, **involve members** of the **fibroblast growth factor (FGF) family.**
- **While** all of these new **subdivisions** are **occurring** and the **bronchial tree** is **developing**, the **lungs assume** a **more caudal position**, so that **by** the **time of birth** the **bifurcation of** the **trachea is opposite** the **fourth thoracic vertebra**.

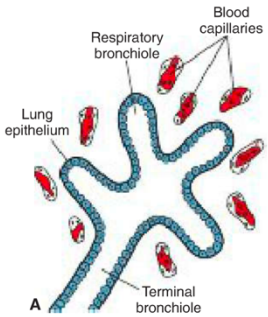
Maturation of the Lungs

- As a rule: if the baby reaches the seventh month it can survive,
- Primitive alveoli: alveoli can do gas exchange

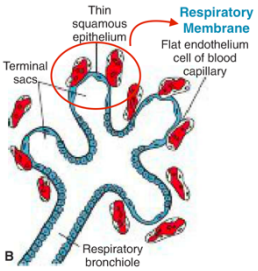
TABLE 12.1 Maturation of the Lungs

Pseudoglandular period	5–16 weeks Or 6	Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli are present. → But still inactive , or they are absent
Canalicular period	16–26 weeks	Each terminal bronchiole divides into 2 or more respiratory bronchioles, which in turn divide into 3–6 alveolar ducts. Still no respiration.
Terminal sac period	26 weeks to birth	Terminal sacs (primitive alveoli) form, and capillaries establish close contact. We have respiration,some respiratory membranes are formed
Alveolar period	8 months to childhood	Mature alveoli have well-developed epithelial endothelial (capillary) contacts. Well- developed respiratory membrane

- **Canalicular phase:**



  - **Up to** the **seventh prenatal month**, the **bronchioles divide continuously into more** and **smaller canals** (canalicular phase).
    - The **lining epithelium** is **cuboidal** and **may** be **found clara cells**. The **capillaries** are **far from each other** and **from** the **respiratory bronchioles** so no **formation** of **respiratory membrane**.
  - the **vascular supply increases steadily**.
  - **Respiration** becomes **possible when some** of the **cells** of the **cuboidal respiratory bronchioles change** into **thin**, **flat cells**(**simple squamous cells**) .

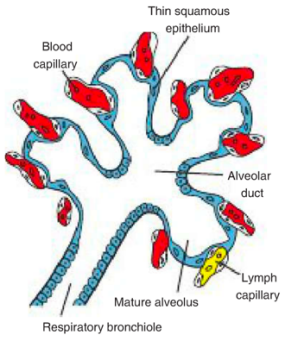


Terminal sac period(phase):

- **Cuboidal cells> simple squamous epithelium.**
- **Capillaries adhere** to **these flat cells forming respiratory membrane**.

  - These **cells** are **intimately associated** with **numerous blood and lymph capillaries**, and the **surrounding spaces** are **now known as terminal sacs or primitive alveoli**.
  - **During** the **seventh month**, **sufficient numbers** of **capillaries** are **present to guarantee adequate gas exchange**, and the **premature infant** is **able to survive**.

- **Alveolar Phase**



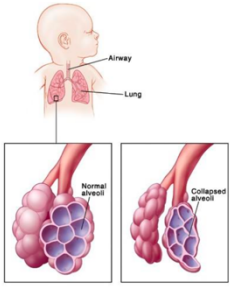
  - **During** the **last 2 months** of **prenatal life** and **for several years thereafter**, the **number** of **terminal sacs increases steadily**
    - **More capillaries adhere** to the **flat cells**.
  - In addition, **cells lining** the **sacs**, **known** as **type I alveolar epithelial cells**, **become thinner**, so that **surrounding capillaries protrude into** the **alveolar sacs**.
    - Type II ? Already formed by the end of sixth month.
    - **Lymph capillaries also** are **formed**.
  - This **intimate contact between epithelial and endothelial cells makes** up the **blood-air barrier**.
  - **Mature alveoli** are **not present before birth**.
    - **maturation happens after birth**, the **alveoli before birth called primitive alveoli- still developing-**

  - In addition to endothelial cells and flat alveolar epithelial cells, **another cell type develops at** the **end** of the **sixth month**. These **cells**, **type II alveolar epithelial cells**, **produce surfactant**
  - **Before birth** the **lungs** are **full of fluid** that **contains**:
    1- a **high chloride concentration**,
    2- **little protein**, **some mucus** from the **bronchial glands**,
    3- **surfactant from** the alveolar epithelial cells (**type II**).

* We put a tube to suction these fluids from the oral cavity and trachea after delivery to clean the airway passage

- The **amount** of **surfactant in** the **fluid increases**, **particularly during** the **last 2 weeks before birth**.
- **Fetal breathing movements begin before birth** and **cause aspiration of amniotic fluid** which is **important** for **maturation** of the **lungs**.
- These **movements** are **important** for **stimulating lung development** and **conditioning respiratory muscles**
- **When respiration** begins at **birth**, **most** of the **lung fluid** is **rapidly resorbed by** the **blood** and **lymph capillaries**, and a **small amount** is **probably expelled via** the **trachea and bronchi during delivery**.
- **When** the **fluid** is **resorbed from alveolar sacs**, **surfactant remains deposited** as a **thin phospholipid coat** on **alveolar cell membranes**.
- With **air entering alveoli during** the **first breath**, the **surfactant coat prevents development** of an **air**- **water** (**blood**) **interface** with **high surface tension**
- **Without** the **fatty surfactant layer**, the **alveoli** would **collapse**(or **may rupture**) **during expiration** (atelectasis).
- **Respiratory movements after birth bring air into** the **lungs**, which **expand** and **fill** the **pleural cavity**.
- **Although** the **alveoli increase somewhat** in **size**, **growth** of the **lungs after birth** is **due primarily** to an **increase** in the **number** of **respiratory bronchioles and alveoli**.
- It is **estimated** that **only one**-**sixth** of the **adult number** of **alveoli** are **present** at **birth**.
- The **remaining alveoli** are **formed during** the **first 10 years** of **postnatal life through** the **continuous formation** of new **primitive alveoli**.

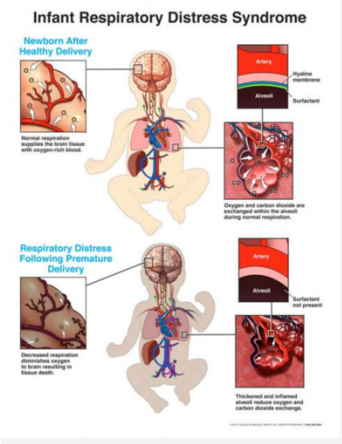
Anomalies of the lung



Clinical notes (RDS)

- What the doctor is interested about:
  - The **type** of **surfactant**- **producer cells**? **Type 2.**
  - The **function**? **decreases surface tension**, the **ability** to **expand**.
  - In **RDS**? **Not enough surfactant**, the **alveoli** may **rupture** and **shrinking during expiration**.
- **Surfactant** is **particularly important** for **survival** of the **premature infant**.
- When **surfactant** is **insufficient**, the **air**-**water** (**blood**) **surface membrane tension becomes high**, bringing **great risk** that **alveoli** will **collapse during expiration**.
- As a result, **respiratory distress syndrome** (**RDS**) **develops**.
- This is a **common cause** of **death** in the **premature infant** (**30% of all neonatal diseases**)

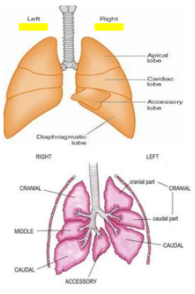
- In these cases, the **partially collapsed alveoli contain** a **fluid** with a **high protein content**, **many hyaline membranes**, and **lamellar bodies**, **probably derived from** the **surfactant layer**.
- **RDS**, is **therefore also known** as **hyaline membrane disease**, **accounts** for **approximately 20% of deaths among newborns.**
- **Intrauterine Asphyxia** may **produce irreversible changes** in **type II cells.**
- **Recent development** of **artificial surfactant** and **treatment of premature babies with glucocorticoids** (betamethasone)- **before delivery**- to **stimulate surfactant production** have **reduced** the **mortality associated** with **RDS**.
- **Thyroxine** is the **most important stimulator** for **surfactants production**.
- It Also **allowed survival** of **some babies** as **young as 5.5 months** of **gestation**, by **putting** the **cute baby** in an **incubator providing** the **intrauterine conditions** and **supplying with** the **oxygen until** the **baby can breathe**(the **seventh month**)



Clinical notes (Other Anomalies)

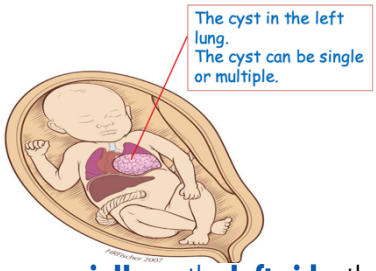
- Although many abnormalities of the lung and bronchial tree have been found:
  1- **blind-ending trachea** with **absence of lungs**
  2- **agenesis** of **one lung** – the **baby has one lung**;
     a. his **life depends** on the **function** of **this lung** to **afford** him with **enough oxygen**)
  3- **ectopic lung**- **finding** the **lung** in **abnormal location**.
- fortunately, **most** of these **gross abnormalities** are **rare**.
- **Abnormal divisions of** the **bronchial tree** are **more common**; **some result** in **supernumerary lobules**.
- These **variations** of the **bronchial tree have little functional significance**, but they **may cause unexpected difficulties during bronchoscopies**.
  4- **ectopic lung lobes arising** from the **trachea or esophagus**.
     * **accessory lobes** are **formed**.

Distinguish from ectopic lung.



- It is **believed** that **these lobes** are **formed from additional respiratory buds of** the **foregut** that **develop independently** of the **main respiratory system**.

- **Most important clinically** are **congenital cysts** of the **lungs** which are **formed** by **dilation** of the **terminal or larger bronchi**
- These **cysts may be small** and **multiple**, **giving** the **lung** a **honeycomb appearance** on **radiograph**
- **Or** they may be **restricted to one or more larger ones**
- **Cystic structures** of the **lungs usually drain poorly** and **frequently cause chronic infections**



Lung Hypoplasia

- In **infants with** congenital diaphragmatic hernia (**CDH**) – **especially** on the **left side**- the **lung** is **unable** to **develop normally**.**due** to the **diaphragm compression on** the **chest** which will **lead** the **hypoplasia** of the **lung**
- Because it is **compressed by** the **abnormally positioned abdominal viscera**.
- It is **characterized by reduced lung volume**.
- **Most infants** with **CDH die** of **pulmonary insufficiency** as their **lungs** are **too hypoplastic** to **support life**.

Oligohydramnios and lungs

- When **oligohydramnios**--**opposite to polyhydramnios--** (**reduced amniotic fluid**) is **severe lung development** is **retarded**.
- **Severe pulmonary hypoplasia results**.

Lungs of the newborn infants

- **Fresh** and **healthy lungs contain some air** , so **pulmonary** samples in **forensic medicine**- **float** in **water** **due** to the **minimal volume** of air.
- The **lungs** of the **stillborn infants** are **firm** and **sink** in **water** because they **contain fluids not air**